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▶ Movement Assessment Battery for Children: 2nd Edition (MABC-2)

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MacArthur-Bates Communicative Development Inventories (MCDIs)

▶ Communicative Development Inventories

MacArthur-Bates Communicative Development Inventories, Second Edition

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Synonyms

CDIs

Description

The CDIs (Fenson et al., 2007) are a set of parent-informant measures designed to evaluate the communicative skills of young typically developing children from their "early signs of comprehension, to their first nonverbal gestural signals, to the expansion of early vocabulary and the beginnings of grammar" (Fenson et al., p. 7). To accomplish this, two separate forms were developed. These are the *CDI: Words and Gestures* and the *CDI: Words and Sentences.*

The *CDI: Words and Gestures* is designed for typically developing children ages 8–18 months as a measure of emerging receptive and expressive vocabulary and the use of communicative or symbolic gestures. It has two major parts. Part I, Early Words, is divided into four sections. Section A, First Signs of Understanding, includes three yes-no items (e.g., "[Does your child] respond when name is called?") intended to determine whether the child has started to respond to language. Section B, Phrases, is a 28-item checklist designed to tap the understanding of everyday language in the context of interactional routines (e.g., "Don't touch"). Section C, Starting to Talk, consists of two items to assess the frequency (i.e., never, sometimes, often) with which a child imitates words and labels objects. Section D, the largest section, is called the Vocabulary Checklist. It is a 396-item checklist organized into 19 semantic categories. Ten of these reflect different noun classes, but a variety of other categories are also

MacArthur-Bates Communicative Development Inventories, Second Edition, Table 1 Communicative Development Inventory: Words and Gestures

	Description	Example
Part I: early words		
A. First signs of understanding	General items about early comprehension of familiar words and phrases (3 items)	Child responds to his/her name
B. Phrases	Comprehension of everyday phrases and routines (28 items)	Responding to "don't touch"?
C. Starting to Talk	Imitation and labeling (2 items)	i.e., imitating words and naming objects
D. Vocabulary checklist	A 396-item checklist organized into 19 semantic categories with separate columns for comprehension and production	Vroom, moo (sound effects and animal sounds), bear (animals names), ball (toys)
Part II: actions and gestures		
A. First communicative gestures	Nonverbal communicative and intentional behaviors (12 items)	Reaching, pointing, nodding
B. Games and routines	Engagement in games/interactional routines (6 items)	Playing peekaboo
C. Actions with objects	Acting upon objects in conventional ways (17 items)	Eating with a spoon or fork?
D. Pretending to be a parent	Pretending to care for stuff animal or doll in a parental manner (13 items)	Kissing or hugging a doll
E. Imitating other adults actions	Attempts to simulate adult activities with real or toy implements (15 items)	Washing dishes

represented (e.g., verbs, adjectives, pronouns, quantifiers). For each item, the respondent indicates whether the child "understands" and/or "understands and says."

Part II, Actions and Gestures, is divided into five sections. Section A, First Communicative Gestures, includes 12 items to assess the frequency (i.e., never, sometimes, often) of nonverbal communicative intentions (e.g., reaching, pointing, nodding). Section B, Games and Routines, is comprised of six yes-no items (e.g., "playing peekaboo"). Section C, Actions with Objects, uses 17 yes-no items (e.g., "eat with a spoon or fork"). Section D, Pretending to be a Parent, includes 13 yes-no items where respondents indicate the kinds of actions a child engages in during pretend play with a stuffed animal or doll (e.g., "Kiss or hug it"). Section E, Imitating Other Adult Actions, includes 15 yes-no items (e.g., "wash dishes") intended to assess the child's attempts to simulate the actions of adults using real or toy implements. A table summarizing the content of the *CDI: Words and Gestures* form is presented in Table 1.

Unlike the *CDI: Words and Gestures* form which is designed to evaluate receptive *and expressive language*, the *CDI: Words and Sentences* form is intended to assess *expressive language only*. It is designed for typically developing children ages 16–30 months as a measure of developing expressive vocabulary and a number of aspects of early grammar development. Part I, Words Children Use, is divided in two sections. Section A, Vocabulary Checklist, is a 690-item checklist organized into 22 semantic categories. The categories are similar to those used in the CDI: Words and Gestures form except some categories are further divided and two categories are added (i.e., helping verbs and connecting words). For each item, respondents simply indicate those items the child "says." Section B, How Children Use Words, includes five items to assess the frequency (i.e., never, sometimes, often) with which a child talks about things and people that are not in the here and now (e.g., talking about an absent toy, pet, or person). Part II, Sentences and Grammar, is divided into five sections. Section A, Word Endings/Part 1,

MacArthur-Bates Communicative Development Inventories, Second Edition, Table 2 Communicative Development Inventory: Words and Sentences

	Description	Example
Part I: words children use		
A. Vocabulary checklist	A 680-item checklist organized into 22 semantic categories with column for production only	Moo (sound effects), tiger (animals), coat (clothing), when (question words)
B. How children use words	Use of language to refer to the past, future, and absent people and objects (5 items)	Talking about an absent toy, pet, or person
Part II: sentences and grammar		
A. Word endings/part 1	Use of plural -s, possessive -s, present progressive (-ing), and regular past tense (-ed) (4 items)	Shoes, Daddy's, running, opened
B. Word forms	A list of irregular plural nouns (5 items) and irregular past tense verbs (20 items)	Children, men, fell, heard
C. Word endings/part 2	A list of overregularized nouns (14 items) and overregularized verbs (31 items)	Foots, ated
Combining	A question about whether the child has begun to combine words (1 item)	i.e., Has the child begun to combine words?
D. Examples	A request to write examples of the three longest sentences that the parent has heard the child say in the recent past (basis for the mean length of utterance)	n/a
E. Complexity	Sentence pairs that contrast in length and grammatical complexity (37 items pairs); asks the parent to indicate which one sounds most like the way the child currently talks	Go bye bye versus wanna go bye bye

uses four items to assess the frequency (i.e., not yet, sometimes, often) with which the child produces early emerging morphemes that appear at the end of words (i.e., plural -s, possessive -s, present progressive -ing, regular past tense -ed). Section B, Word Forms, is a checklist of 25 items intended to tap production of irregular nouns (e.g., children) and verbs (e.g., ate). Section C, Word Endings/Part 2, is a 31-item checklist of overregularized nouns (e.g., childs) and verbs (e.g., ated) which occur naturally in children's speech and indicate increasing linguistic sophistication. A single question (combining) then asks whether the child has begun to combine words (not yet, sometimes, often). Section D, Examples, is intended to provide a basis for estimating mean length of utterance (MLU). Here, the respondent is asked to write three examples of the longest sentences that the child has said recently. Section E, Complexity, is 37-item checklist designed to assess syntactic complexity. Each of the 37 items is comprised of a pair of sentences that contrast in complexity (e.g., "two shoe" versus "two shoes," "turn on the light" versus "turn on the light so I can see"). Using a forced-choice format, respondents are asked to judge which sentence in each pair sounds most like the way their child talks. A table summarizing the content of the *CDI: Words and Sentences* form is presented in Table 2.

Detailed administration and scoring procedures (with examples) are provided in the technical manual, and comprehensive descriptive data are presented for all CDI sections. Separate percentile rank data for boys and girls using 1-month intervals are provided for all sections except two sections of the CDI: Words and Gestures form (i.e., First Signs of Understanding, Starting to Talk) and two sections of the CDI: Words and Sentences (i.e., How Children Use Words, Word Endings/Part 1). When percentiles are not provided, the percentage of affirmative answers is calculated for comparison with the percentages given in the manual. When percentiles are provided, they can be unstable. Specifically, restriction in the range of scores sometimes occurred for ages at which the skills in question were just emerging. When this happens, small differences

in raw scores can have dramatically different effects on percentile ranks. As Fenson et al. (2007) explain:

> Because relatively few items can have such a large effect on the child's percentile scores in these instances, users should be very cautious in drawing strong conclusions based on these reported values. (pp. 33–34)

The original and expanded versions of a Basic Information Form are included in the CDI. The forms are designed to gather demographic information useful in interpretation of test scores. The expanded version also contains several questions regarding child health history. Each CDI form takes between 20 and 40 min to complete. It should be noted that CDI short forms are available (Fenson et al., 2000). Although these may be useful to researchers and professionals who seek a quick assessment of early language, the short forms likely lack the precision of the full CDIs and must be administered and interpreted with caution (Fenson et al., 2007). Members of the CDI advisory board have developed Mexican Spanish versions (including short forms) of the CDIs (Jackson-Maldonado et al., 2003). The measures have also been developed in a number of languages other than English by other researchers. A comprehensive list of these versions is available on the CDI web site (http://www.sci.sdsu.edu/cdi/adaptations.htm).

Historical Background

As Fenson and colleagues (2007) explain, the first systematic attempts to use questionnaires to tap parents' knowledge of their children's language skills were conducted by Elizabeth Bates (a codeveloper of the CDIs) and colleagues in the 1970s and 1980s (e.g., Bates, Camaioni, & Volterra, 1975). These inventories were later refined to tap parents' knowledge of their children's vocabulary and grammar and, along with the work of another prominent researcher in the area (Leslie Rescorla), laid the foundation for the development of the CDIs (Fenson et al., 2007). The CDI is an example of a measure that relies exclusively on parent report. It has endured the test of rigorous scientific scrutiny, and there is now tremendous evidence in support of its reliability and validity. As a parent-informant measure, the CDI is especially important as parent-reports can provide a more representative sample of language than may be obtained in clinical settings where spontaneous speech or test results may be influenced by characteristics of the child (e.g., shyness) or testing situation (e.g., familiarity with the examiner) (Fenson et al.). For all of these reasons, the CDI has become a well-respected measure, which continues to lend support to the notion that parents are valuable, reliable, and accurate sources of information. It has been particularly welcomed from a family-centered perspective (e.g., Westby, 1998) where parents and other caregivers are recognized as valuable partners in the assessment process.

Psychometric Data

The *CDI: Words and Gestures* is normed on a sample of 1,089, and the *CDI: Words and Sentences* is normed on a sample of 1,461 with a relatively even distribution of girls and boys across the age ranges sampled. Although these 2007 expanded norms more closely approximate national demographic statistics than the original 2,000 norms, the developers note that the sample still underrepresents children and families with low educational and/or socioeconomic backgrounds. In addition, Caucasians are slightly overrepresented, whereas Hispanics are underestimated (a likely result of exclusion criteria requiring children to be from a home where English was the primary language). Normative data for birth order and exposure to a second language are comparable to the US census statistics.

Two types of reliability of the CDIs are well documented. Internal consistency, or the degree to which items on a test measure the same content domain, indicates a very high degree of consistency. The test-retest reliability over an approximate 1–2-month interval is also high indicating excellent stability over time.

The validity of the CDIs is similarly well established. First, the CDIs demonstrate good

content validity, which is the degree to which the test covers the intended content domain. Indeed, the content of the CDIs was developed in line with the language development literature, is supported by over 30 years of child language research, and has been credited as adequately sampling early vocabulary and grammar development (e.g., Westby, 1998). Concurrent validity, based on the relationship between CDI scores and various child performance measures, is particularly impressive. Moderate to high correlations have been reported across numerous studies on typically developing children as well as children with language impairment and developmental delays. For example, sections of the CDI are significantly correlated with standardized tests like the *Bayley Expressive Language Scales*, the *Peabody Picture Vocabulary Test*, and the *Expressive One-Word Vocabulary Test* as well as language sample measures like the *Index of Productive Syntax* (Scarborough, 1990) and Number of Different Words (NDW).

Clinical Uses

The CDIs were normed on a sample of young typically developing children, and they are not intended to screen for, or identify children with, autism spectrum disorder (ASD). On the other hand, the evaluation of language is important in the assessment of young children with ASD who often demonstrate qualitative impairments in language as well as language delay. In this light, the CDIs have gained utility as a clinical tool in ASD when supplemented by direct measures of child performance, and evidence of the accuracy of the CDIs for screening (Filipek et al., 1999) and diagnosing ASD (e.g., Luyster, Qui, Lopez, & Lord, 2007) is accumulating.

The inventories are well suited as one component of a broader screening procedure (Klee et al., 1998) for language delay, which typically includes the criterion that a child of 24 months uses fewer than 50 words. Experience suggests that this criterion is commonly applied to young children at risk for ASD through use of the CDIs. In a related vein, research shows that deficits in

both receptive and expressive language are more predictive of language impairment than expressive language deficits alone (e.g., Thal, Tobias, & Morrison, 1991). Because the inventories tap both receptive and expressive vocabulary, they can facilitate this analysis with the understanding that no single measure should ever be used as a basis for identification or assessment (Fenson et al., 2007). The use of the CDIs as an evaluation and assessment tool is reinforced by the finding that it has been found to discriminate children with language impairment from those who are developing typical language (Skarakis-Doyle, Campell, & Dempsey, 2009).

Charman, Drew, Baird, and Baird (2003) systematically examined the language profiles of preschoolers diagnosed with ASD using the CDIs. Despite considerable variability, children with ASD demonstrated the expected receptive and expressive language deficits described above. Compared to the typical pattern, however, the word production of children with ASD was relatively in advance of word comprehension. With regard to gestures, later developing gestures (pretending to be a parent) were relatively in advance of early developing gestures (e.g., reaching, pointing), which involve joint reference and direct social interaction. Studies such as these are important because they demonstrate how the CDI can be useful in clinical work with young children with ASD (Charman et al., 2003).

Fenson et al. (2007) report that the CDIs are useful for documenting the language abilities of older children representing special populations, including ASD, and they have become increasingly popular for that purpose. Of course, successful implementation of the inventories to assess the language development in children with ASD requires that the scores obtained never exceed the developmental level tapped by the CDI (i.e., 30 months). The developers of the CDI are clear that when scores of older children from special populations exceed this level, serious misjudgments of communicative skills can occur due to ceiling effects.

The CDIs have also been used in the development of intervention strategies. Fenson et al. (2007) suggested that the measure be used to

identify overall receptive vocabulary deficits but not to identify specific words that are or are not understood for remediation. They further note that the case may be different for productive vocabulary where specific words are unambiguously present or absent. "Clinicians may wish to use the CDIs to identify classes of words that appear to require remediation and supplement these findings with more targeted behavioral assessments of individual words" (p. 44).

In summary, the CDIs have proven to be clinically useful for assessment of language deficits, which represents a major characteristic of ASD. When combined with direct measures of child performance, it can be used to screen and evaluate the presence of a language deficit. It can also be used to document the language abilities of children with ASD and guide intervention efforts. As noted above, the CDIs may be particularly attractive because, unlike formal child performance tests, they are not influenced by child situational or motivational factors. Instead, they rely on parent knowledge that has accumulated over time during which the parent has had the opportunity to observe and form impressions about the child's skills.

Of course, each clinical application raises questions to consider when determining the appropriateness of the measure and interpretation of scores. In particular, use of the CDI norms with children whose developmental age exceeds the upper limit of the inventories is not recommended. It is also prudent to recall that percentile data for some sections of the CDI are unstable, and so interpretation of all percentile data requires care.

See Also

- ▶ Age Appropriate
- ▶ Age Equivalents
- ▶ Communication and Symbolic Behavior Scale
- ▶ Communication Assessment
- ▶ Developmental Delay
- ▶ Early Language Milestone Scale
- ▶ Expressive Language
- ▶ Infant/Toddler Checklist
- ▶ Language Tests
- ▶ Mullen Scales of Early Learning
- ▶ Peabody Picture Vocabulary Test
- ▶ Prelinguistic Communication Assessment
- ▶ Preverbal Communication
- ▶ Receptive Vocabulary
- ▶ Rossetti Infant-Toddler Language Scale
- ▶ Screening Measures
- ▶ Validity
- ▶ Vocabulary

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Macrographia

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Definition

Macrographia is abnormally large handwriting. It might be seen in patients with cerebellar disease (Haymaker, 1956) as well as in patients with basal ganglia dysfunctions such as Huntington disease (Phillips, Bradshaw, Chiu, & Bradshaw, 1994). It has also been observed in a sample of patients with aphasia (Fradis & Leischner, 1985). One study documented macrographia in a sample of subjects with autism spectrum disorder (Beversdorf et al. 2001). This finding might reflect abnormalities at the cerebellar level in this population. More empirical research is needed to specifically investigate possible handwriting abnormalities in autism.

See Also

▶ Micrographia

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Magnetic Resonance Imaging

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Definition

Magnetic resonance imaging (MRI) is a noninvasive technique by which detailed images of internal anatomy are constructed by measuring the response of atomic nuclei to strong magnetic fields and innocuous radio waves. The hydrogen proton (1H) is the atomic nuclei of choice due to its abundance in water molecules which makes up most of the human body's mass. During the procedure, protons emit unique signals which depend on their distinct chemical environment. These signals are then used to construct a series of two-dimensional images, which taken together, can provide valuable information of soft tissue (i.e., organ, muscle, etc.) anatomy in three dimensions. MRI uses no ionizing radiation and is well known for being a painless and harmless procedure. This is evidenced by its widespread use in the clinical and research arenas in populations spanning the entire age range from infants to the elderly. In clinical practice, MRI is best known as a diagnostic tool used to differentiate diseased from normal tissue. However, due to its tremendous versatility and ability to provide accurate, detailed information, MRI has widespread applications in contemporary clinical and research practice.

Historical Background

Nuclear magnetic resonance (NMR) describes the physical phenomenon on which MRI technology is based. The phenomenon of NMR was actually discovered in the 1940s and set the stage for the development of MRI for medical diagnostic use in the 1970s. NMR signals are created by certain atomic nuclei when excited by radio frequency energy in the presence of a strong magnetic field. In 1946, Edward Purcell and Felix Bloch independently developed methods for determining precise nuclear magnetic measurements. This was a monumental achievement, and both were recognized with awards for the Nobel Prize in physics (1952). Spurred by the development of computed tomography in the early 1970s and coupled with advances in the development of new image reconstruction algorithms, chemist Paul Lauterbur and physicist Sir Peter Mansfield created different methods to translate information regarding magnetic spin into cross-sectional images. This seminal work began a rapid progression of continuously improving imaging techniques, and both were jointly awarded the Nobel Prize in physiology or medicine (2003). Many further refinements at various stages have resulted in the acquisition of higher resolution depictions through the improved extraction of signal from tissue over background noise and improvements in the generation of tissue contrast.

Current Knowledge

In this section, a brief review is provided on the physics of MRI as there are now numerous texts covering this topic in detail (please see References). MRI exploits the magnetic properties of the atomic constituents of biological matter to construct a visual representation of tissue. Specifically in medical MRI, the signal from the nuclei of hydrogen atoms (1H) is used for image generation since hydrogen constitutes two-thirds of all atoms in the human body. The proton of the hydrogen atom is positively charged and possesses spin, an intrinsic property of all elementary particles. In essence, the proton rotates about its axis and is analogous to a spinning top. The proton, which is found in the nucleus of the hydrogen atom, has considerable mass relative to the electron which orbits around the nucleus. As a rotating mass, the proton possesses angular momentum that strives to retain the spatial orientation of its rotational axis. Since the proton is both charged and in constant motion, it additionally has a magnetic moment and can be imagined to behave as a small magnet. What is basically observed in MRI is the motion of the proton's magnetic axis, which is capable of generating a signal in the MRI scanner's receiver coil.

When an external force acts on the hydrogen proton and tries to alter the orientation of its rotation axis, the proton begins to wobble or precess around its axis of rotation. At the same time, friction caused by the interaction between the external force and the proton withdraws energy from the proton and slows down its rotation. As a result, the proton's axis of rotation becomes progressively more inclined and if imagined as a spinning top, finally falls over. More specifically, when hydrogen nuclei are exposed to an external magnetic field, the magnetic moments (or spins) align with the direction of the field and simultaneously undergo precession. The precession of the nuclei occurs at a characteristic speed that is proportional to the strength of the applied magnetic field and is called the Larmor frequency. The Larmor frequency is the rate at which spins wobble when placed in a magnetic field. The spin system eventually relaxes and settles into a stable state, but the longitudinal magnetization (Mz) builds up in the z-direction because the magnetic vectors representing the individual magnetic moments accumulate. The spins tend to align parallel and antiparallel to the magnetic field, with parallel alignment being slightly more preferred because it is energetically more favorable. Hence, a slightly larger fraction of spins aligns parallel to the main magnetic field. This small difference produces the measurable net magnetization Mz and is represented by the net magnetization vector. This energy difference between the two spin orientations depends on the strength of the

external magnetic field with Mz increasing as field strength increases.

Furthermore, energy can be introduced into this spin system by applying an electromagnetic wave of the same frequency as the Larmor frequency, a condition known as the resonance state. This wave is generated in a radio transmitter and applied to the object to be imaged using an antenna coil. The result is that the longitudinal magnetization becomes more and more tipped away from the z-axis toward the transverse xy-plane, which is perpendicular to the direction of the main magnetic field. All of the longitudinal magnetization is rotated into the transverse plane by a radio frequency pulse that is both strong enough and applied long enough to tip the magnetization by exactly 90°. This results in Mxy magnetization, which as its name suggests, lies in the xy-plane. Transverse magnetization rotates about the z-axis, which has the effect of an electrical generator and induces an alternating voltage of the same frequency as the Larmor frequency in the MRI scanner's receiver coil. This is called of the magnetic resonance signal which is collected and processed with sensitive receivers and computers to generate the magnetic resonance image.

The magnetic resonance signal rapidly fades due to two independent processes that reduce transverse magnetization and thus return the spin system to the stable state present prior to excitation. These two processes are spin-lattice interaction which causes T1 relaxation and spin-spin interaction which causes T2 relaxation. T1 is defined as the time required for 63% of the original longitudinal magnetization to be recovered. T2 is defined as the time required for transverse magnetization to decrease to 37% of the original value. T1 typically ranges from 200 to 2,000 ms and T2 commonly ranges from 30 to 500 ms. T2 denotes the process of energy transfer between spins, while T1 refers to the effects of additional field inhomogenities contributing to spins loosing coherence. A key strategy for how differences in T1 and T2 are exploited to generate tissue contrast involves strategic variation of timing and orientation of repetitive radio frequency pulse delivery.

MRI's ability to localize signals in the three-dimensional space of the brain is accomplished by using magnetic gradients which are magnetic fields which change gradually along an axis. Encoding of a three-dimensional volume begins by first dividing the tissue mass into slices. Then two distinct magnetic gradients orthogonal to each other are applied, effectively dividing each slice into rows and columns of pixels. By doing this, each pixel possesses unique precessional frequency and direction. A special mathematical operation, called Fourier transform, converts pixel data back into three-dimensional voxels, which are then assembled to form an image volume reconstruction of the original three-dimensional tissue mass. Optimal spatial resolution currently approximates 1 mm^3 or less.

Proton densities and differential T1 and T2 relaxation effects are properties intrinsic to brain tissues, and subsequently, their measurement forms the basis for the provision of differential tissue image contrast in MRI. Different tissue parameters can be differentially weighted, thus, yielding a variety of image types, each providing a unique range of diagnostic information. Different image modalities are usually identified by numeric values of key pulse sequence parameters set during acquisition. Use of shorter repletion time between pulse sequences during image acquisition interrogates tissues at a moment when their intrinsic T1 differences can be exploited to yield different signal intensity production and hence tissue contrast generation. The resulting image, whose contrast is based on tissue differences in T1, is termed T1-weighted. A repetition time less than 500 ms is considered short; a repetition time greater than 1,500 ms is considered long. Use of repetitive 90° pulses to detect T1-based tissue contrast is called a saturation recovery sequence. Alternatively, inversion recovery involves a sequence that begins with a 180° pulse followed by a 90° pulse. The 180° pulse reverses longitudinal magnetization, and all protons responsible for the net magnetic moment are inverted 180° in the applied longitudinal magnetic field. The signal that is received depends on the time between the 180- and 90° interrogation pulses, which

constitutes the repetition time for this particular pulse sequence. On the other hand, a primary strategy for generating T2-weighted images involves use of a pulse sequence termed spin echo. In spin echo, an initial 90° pulse generates transverse magnetization vector component. When 90° pulse is terminated, dephasing follows under the influence of T2. When 180° pulse is administered, the direction of dephasing protons is reversed. More slowly, precessing protons are now ahead of faster ones. Eventually, protons with faster precession frequencies catch up, culminating in proton precession rephrasing and thus detectable signal generation. This process is repeated, and protons again dephase, are again refocused by another 180° pulse, and so on. Therefore, it is possible to obtain more than one signal by repeating the spin-echo sequence.

In clinical practice, substances with short T1 producing high signals on T1-weighted imaging include fat, methemoglobin in subacute hemorrhage, and paramagnetic contrast agents. Substances with long T1 producing low signals on T1-weighted imaging include cerebral spinal fluid and tissues in which any process that increases local water has occurred (i.e., inflammation). T1 images are best for visualizing normal anatomy. Tissues with longer T2 generate higher signals on T2-weighted images. Because of the greater fluid content of a tissue, the longer the tissue's T2, the brighter that tissue's appearance on a T2-weighted image. Thus, T2-weighted images highlight fluid-containing regions, such as sulci and ventricular system. Also in a healthy brain, T2 constitutes the entirety of high intensity signal. Substances with short T2 produce low signals on T2-weighted images. Examples include iron-containing substances. Also, most brain lesions involve associated change in water content, such as cellular injury (infarction) and extracellular inflammatory lesions (mass lesions) which produce vasogenic edema. Because a final common pathway of many brain lesions involves increases in water content of brain, T2-weighted images, which highlight tissue with higher water content, demonstrate brain pathology as higher signal intensities. T2-weighted images are useful for evaluating sulcal widening in cortical atrophic syndromes and for evaluating hydrocephalus.

Future Directions

In the decades to come, advances in MRI technology include a widespread transition to higher magnetic field imaging, enhanced MRI coil sophistication incorporating even more channels, ultrashort echo-time imaging, tighter integration of multiple imaging modalities, and advances in molecular MRI agents. Currently, the typically used clinical imaging scanners operate at 1.5 T. While systems operating at even higher field strengths have become more prevalent, they are found mainly at major medical centers. Current clinical interest focuses on transitioning to 3 T scanners; however, it is already evident that much higher field strengths will eventually be used to examine patients (up to 7 T, which so far have only been used in research studies). Available data suggests that magnetic field strengths above 2 T involve no increased risk for patients, but the strongest argument for increasing field strength is the expectation that this will significantly boost signal-to-noise ratio. Improved signal-to-noise ratio leads to increased spatial resolution and/or reduced imaging time. An improved spatial resolution permits better anatomical evaluation. Shorter scan time leads to better tolerability and more cost-effective operation (more patients can be examined per unit time). Finally, imaging at 3 T or higher field strengths has the potential to improve more sophisticated applications of MRI such as functional imaging and carbon-13 or hydrogen-1 spectroscopy. For example, it is known that the chemical shift increases in proportion to magnetic field strength and the larger chemical shift is advantageous in spectroscopy because the spectral lines spread farther apart. Thus, this improves spectral resolution and discrimination of the peaks of fat and water, which in turn enables better calibration of the radio frequency pulse for fat suppression, which can significantly diminish the peaks of interest. Also, increasingly

higher numbers of radio frequency channels will become standard, having a significant impact in neurological examinations. Commercial products for simultaneous acquisitions of both positron emission tomography and MRI will become commonplace in many centers where their use will be justified by improved throughput, improved patient compliance, and improved image and diagnostic accuracy. Of key importance in combined modalities, however, is the validation of image quality acquired by one modality in the presence of the other. For example, the verification that positron emission tomography image quality is not impaired by placing the detector system into the magnetic field and that MRI quality is not degraded by the presence of the positron emission tomography detectors. In addition to multimodal imaging, the future will also bring a wider application of current methods into other body areas (such as the use of diffusion tensor imaging in nonneurological examinations). Finally, the development of targeted contrast media is a rapidly expanding area in MRI research and is already being frequently used in animal systems. These contrast agents show areas of abnormality in terms of passive accumulation of agent within the tissue, for example, a normal brain will exclude contrast from the parenchyma, but damaged tissue allows passive diffusion of contrast agent through the compromised blood-brain barrier, leading to image enhancement. The future will also bring very highly sensitivity agents that either are targeted to specific disease processes or provide specific information on regional metabolism.

See Also

▶ Diffusion Tensor Magnetic Resonance Imaging
▶ Functional MRI
▶ Magnetic Resonance Spectroscopy

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Magnetic Resonance Spectroscopy

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Definition

Magnetic resonance spectroscopy (MRS) is a technique similar to magnetic resonance imaging (MRI) that can extract chemical information about biological tissues. MRS is also known as nuclear magnetic resonance (NMR) spectroscopy, though this term tends to be avoided in in vivo work. MRS can be accomplished in most clinical MRI scanners and is similarly safe. However, rather than providing an image of the tissue as MRI would, MRS provides a "spectrum," or chemical signature, of the area under examination. From this, metabolic and biochemical disturbances can be identified in a region-specific fashion. MRS has applications across the body; however, one of the most prominent applications of MRS is to examine biochemical disturbances in the brain.

Historical Background

For a brief history of NMR, please see ▶ Magnetic Resonance Imaging.

Early work in the 1970s showed that MRS could be used to obtain chemical information from living animal tissue, such as blood cells or muscle tissue (de Graaf, 2008). However, it was not until the early 1980s that the brain was examined under 1H MRS in living mammals and humans (Ross & Bluml, 2001). These studies paved the way for neurospectroscopic applications, ranging from the evaluation of traumatic brain injuries to predictive markers of Alzheimer's disease risk to studies of neuropsychiatric disorders such as schizophrenia and autism.

Current Knowledge

Utility and Applicability of MRS
As MRS can typically be conducted with the same equipment as standard MRI, MRS can be considered a very accessible and well-tolerated radiological imaging modality (for comparisons with other modalities, see Siegel & Albers, 2006). As with MRI, MRS uses nonionizing radiofrequency pulses for excitation of nuclei and magnetic field gradients for spatial localization. MRS does require, however, specifically built pulse sequences for acquiring data and specialized algorithms and frameworks for analysis. These modifications and additions are widely available on most clinical MR machines.

However, it is also important to note that MRS encompasses a wide range of both clinical and research endeavors. Many types of specialized sequences exist (e.g., see MRS of GABA in Autism, below) as do specialized protocols (some of which look at other nuclei besides 1H that are MR-detectable, e.g., 31P, 13C). The bulk of this article will discuss applications that are most relevant to studies of autism, primarily in vivo 1H MRS of the human brain.

Differences Between MRI and MRS
In standard MRI, pulse sequences are chosen to emphasize specifics regarding the spatial distribution of protons, resulting in an image. Thus, the strongest contributors to an MRI profile are water and fats. By contrast, MRS seeks to optimize the provision of spectral information,

specifically isolating metabolites and other biochemicals in an organism. Because different nuclei on a molecule may exist in distinct chemical environments, and because each of these chemical environments can result in different levels of "shielding" from the external magnetic field of the MRI machine, this results in certain molecules having "chemical signatures" that are different from other molecules (see 1H Spectra of the Human Brain). However, the concentrations of these chemicals are often very low, and thus the signal from metabolites, e.g., in the brain, is approximately 10,000 times smaller than that of water. For this reason, additional steps are typically taken both at the time of spectral acquisition and data processing for eliminating dominating signals from water or fats so that other metabolites will be visible (de Graaf, 2008; Shic, Lin, Brown, Bluml, & Ross, 2010).

1H MR Spectra in the Human Brain
The most common form of MRS in use today for studying in vivo brain biochemistry is 1H MRS. This form of MRS uses the same type of head coils as MRI and can typically be conducted as part of a standard clinical imaging examination. A typical MR spectrum is shown below.
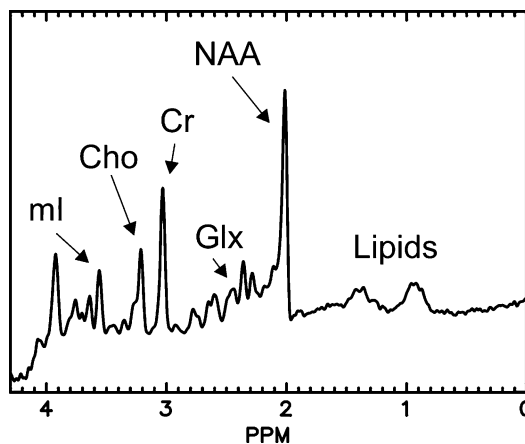
MR spectra are typically displayed with frequency (chemical shift) on the x-axis, expressed in parts-per-million (PPM). PPM is the frequency difference between a reference chemical

(typically tetramethylsilane) and a particular frequency, all divided by the frequency of the MRI machine and multiplied by a million. Since the frequency of the MRI machine scales linearly with its field strength, PPM provides a field-independent axis of chemical shifts for metabolites. The y-axis of MR spectra is the signal intensity, a value that scales with the concentration of a metabolite.

A detailed discussion of the clinical utility and biochemical processes underlying MRS-detectable metabolites is beyond the scope of this article (for more details, please see Ross and Bluml (2001) and Lin, Ross, Harris, & Wong (2005)), as are the optimizations necessary for obtaining high-quality spectra (for practical advice and theoretical considerations, see Blüml, 2011). Briefly, however, primary metabolites seen in in vivo 1H MRS of the brain include: (1) lipids, typically seen in voxels containing subcutaneous fats from the skull or in necrotic tissue; (2) lactate, which appears as a doublet at 1.33 PPM, a by-product of anaerobic glycolysis which is naturally occurring at low concentration levels in the cerebrospinal fluid but which can also be seen in hypoxia and stroke; (3) N-acetyl aspartate (NAA), a marker for healthy neurons, axons, and dendrites, which is decreased in events such as hypoxic or traumatic brain injury; (4) the glutamine and glutamate complex (Glx), which includes both glutamine and glutamate due to overlapping chemical profiles, is involved in inhibitory and excitatory neurotransmission in the human brain and is disturbed in some neuropsychiatric conditions such as schizophrenia; (5) creatine + phosphocreatine (Cr), energy markers of brain metabolism, which can be disturbed in brain trauma and hyperosmolar conditions such as hyponatremia; (6) choline (Cho), a myelin and membrane marker, elevated in certain tumors and in stroke; and (7) myoinositol, a brain osmolyte and a marker for astrocytes found to be elevated in Alzheimer's disease and diminished in hepatic encephalopathy.

Typically, the levels of metabolites are expressed as either a ratio (e.g., the peak height of NAA divided by the peak height of Cr, i.e., NAA/Cr) or as an absolute concentration level (typically enclosed in brackets, e.g., [NAA]). Creatine is often used as a reference signal for studies reporting ratios, given its relative homeostatic stability. However, it is important to note that creatine concentrations can be affected by some pathologies (see Ross & Bluml, 2001 for details). Several methods exist for quantifying absolute concentration levels of metabolites, but the analysis is more complex and often involves assumptions regarding the spectral shape of metabolites, the creation of model solutions for use as a basis set, and the use of brain water as a reference (Christiansen, Henriksen, Stubgaard, Gideon, & Larsson, 1993; Kreis, Ernst, & Ross, 1993; Poullet, Sima, & Van Huffel, 2008).

Single-Voxel and Multivoxel Spectroscopy

As in MRI, there exist many different protocols for acquiring MRS from the brain. Typical 1H clinical examinations can be broken down into single-voxel techniques and multivoxel techniques. In single-voxel spectroscopy, a small area in the brain is chosen a priori, based on scout images or prior MRI in the same session as the MRS session, and 1H MR spectra acquired from those locations. In multivoxel spectroscopy (also called spectroscopic imaging or chemical shift imaging), spectra are obtained from a wide area under additional phase encoding, thus providing chemical profiles from multiple locations within a larger spatial volume. The advantages of multivoxel techniques include increased ability to detect atypical neurochemical profiles over a larger space and greater time efficiency of detection over the volume compared to comparable serial single-voxel MRS. The disadvantages of multivoxel techniques are increased complexities in data analysis, increased difficulties in controlling for magnetic field inhomogeneities (due to the larger size of the whole volume), and "voxel bleeding" (i.e., contamination of chemical profiles within one voxel with spatially adjacent voxels) (see de Graaf, 2008 for details).

Short- and Long-Echo Spectroscopy

The appearance of 1H MR spectra is highly dependent on parameters of the pulse sequence employed. The width of peaks in MRS is partially

determined by T2* time, a property of a molecule that includes both T2, the transverse relaxation time of a metabolite, as well as magnetic field inhomogeneity effects. Less mobile molecules, such as lipids, tend to have lower T2 times (and hence lower T2* times), effectively translating into peaks that are broader and shorter. The echo time of an MRS pulse sequence (the TE time) will refocus (i.e., help to eliminate) inhomogeneity effects, but not T2 effects, with the resultant effect that longer TEs result in decreased visibility of short T2 time metabolites. This has advantages as well as disadvantages. The disadvantages include the decreased visibility of important metabolites with shorter TEs which become harder to identify at longer TEs and the generally decreased signal-to-noise (SNR) ratio associated with waiting for metabolite signals to decay. The advantages include less complex baselines, i.e., less contamination by "nuisance" molecules which alter the shape underlying the peaks of metabolites of interest. Some contributors to complex baselines include macromolecules, which have very short TEs (Behar, Rothman, Spencer, & Petroff, 1994). Typical short-echo times are TE = 30–35 ms, whereas long-echo times range from 135 to 144 ms (lactate, which is a j-coupled resonance, inverts in this range of echo times, making it somewhat easier to detect). Other researchers recommend a midrange TE, e.g., 40–50 ms, as a compromise for relatively flat macromolecular contributions and good SNR (Hetherington et al., 2005).

1H MRS Studies of Autism

Currently, MRS studies have painted a broad picture regarding neurochemical differences between ASD groups and controls, and some researchers have argued, based on low levels of specific neural markers, that autism may be characterized by disruption of neuronal integrity in a region-specific or global pattern (Dager, Friedman, Petropoulos, & Shaw, 2008). The earliest examinations with MRS are of children diagnosed with autism at 3–4 years of age (Friedman et al., 2003).

Region-specific abnormalities in autism reported by 1H MRS studies include decreased NAA in the hippocampus-amygdala (Gabis et al., 2008; Mori et al., 2001; Otsuka, Harada, Mori, Hisaoka, & Nishitani, 1999), transverse temporal gyrus (Hisaoka, Harada, Nishitani, & Mori, 2001), and medial temporal lobe (Endo et al., 2007). Several groups have also noted functional relationships between NAA concentrations and measures of social functioning (Endo et al., 2007; Hardan et al., 2008; Kleinhans, 2009; Oner et al., 2009). It is important to note, however, that several groups have found negative results in similar areas or with different subject populations (Kleinhans et al., 2009; Oner et al., 2009; Perich-Alsina, Aduna, Valls, & Muñoz-Yunta, 2002; Zeegers, Van Der Grond, van Daalen, Buitelaar, & van Engeland, 2007). Nonetheless, abnormal concentrations of metabolites in the temporal lobe, or relationships between temporal lobe and social functioning, are among the most reported results in 1H MRS as applied to the study of ASD. 1H MRS work by some researchers has also identified abnormalities in levels of brain metabolites other than NAA, such as Cho, mI, Cr, and Glx, in a region-specific fashion (e.g., DeVito et al., 2007; Gabis et al., 2008; Hashimoto et al., 1997; Kahne et al., 2002; Levitt et al., 2003; Mori et al., 2001; Murphy et al., 2002; Sokol, Dunn, Edwards-Brown, & Feinberg, 2002; Vasconcelos et al., 2008), though the results are somewhat varied, possibly due to differences in subject populations, acquisition parameters, and experimental protocols.

Some groups have also reported what appears to be globally depressed concentrations of all metabolites in autism, primarily as associated with brain gray matter (DeVito et al., 2007; Friedman et al., 2003, 2006; Kleinhans, Schweinsburg, Cohen, Müller, & Courchesne, 2007). Friedman et al. (2006), in a particularly relevant study, include as participants the youngest reported group of children with ASD: 45 children 3–4 years of age. Several of these studies, including Friedman et al., also report longer T2 times in autism. T2, also known as spin-spin relaxation time, reflects compartment differences (i.e., where the chemicals are being measured, e.g., intracellularly or extracellularly) and can be interpreted as an indicator of the mobility of the associated metabolite (Dager, Friedman, et al., 2008). As noted by

Dager, Oskin, T. L. Richards, and Posse (2008), the increased T2 times observed in children with ASD are not compatible with brain overgrowth models of autism which suggest that incomplete neuronal pruning leads to dense neuronal cell packing, as in this case T2 times would be decreased, expressing decreased cellular mobility.

MRS of GABA in Autism

Though standard 1H MRS protocols can paint a rich picture of neurochemical abnormalities in individuals with ASD, some particularly noteworthy metabolites are difficult to detect using these standard approaches. One such metabolite is GABA, the primary inhibitory neurotransmitter of the central nervous system. GABA exists in low concentrations in the brain, relative to the other metabolites outlined in the section above. Furthermore, the spectrum of GABA is overlapped by other metabolites, obscuring it from view. Recently, Harada and colleagues (2010) employed a specialized GABA-editing sequence in order to measure GABA levels in the frontal lobe and lenticular nuclei of adults with autism and matched controls. The authors of that study found that adults with autism showed decreased levels of GABA and GABA levels relative to glutamate in the frontal lobe but not the lenticular nuclei, suggesting a frontal lobe–specific disturbance in excitatory-inhibitory neurotransmission.

Mitochondrial Dysfunction in Autism

One application of MRS has been the study of brain mitochondria dysfunction in ASD. Using optimized proton echo-planar spectroscopic imaging, Corrigan and colleagues (2011) showed no presence of lactate in a longitudinal sample of children with ASD. Since the presence of elevated lactate levels has been suggested to be associated with mitochondrial dysfunction, the finding of no lactate in the study provided evidence against the belief of widespread mitochondrial dysfunction in ASD and, consequently, the practice of hyperbaric oxygen for the treatment of ASD. This study was followed by a healthy exchange of perspectives by researchers on the Corrigan et al. study and

proponents of hyperbaric oxygen treatment (Dager, Corrigan, Estes, & Shaw, 2011; Rossignol & Frye, 2011).

Future Directions

Despite some inconsistencies in the literature to date, modern research using 1H MRS is beginning to reveal rich interactions between brain neurochemistry and cognitive, behavioral, and social performance in autism. Technological advances, such as more stable spectrometers, increasing field strength, and more reliable and powerful gradients, all contribute to the increased reliability of MRS investigations. Future work will likely replicate and extend prior findings with increasingly specific predictions about the relationships between region-specific neurochemical levels, behavior, and outcome.

The continued application of more advanced MRS techniques, such as GABA and glutamate editing, will deepen our understanding of biochemical abnormalities in autism. As in the example of investigations of mitochondrial dysfunction in ASD, these techniques will augment the tool sets available to researchers for providing evidence against or for new and rising hypotheses about the underlying biological mechanisms of autism. However, given the currently high levels of sophistication necessary to enact some of these protocols and process the results, concerted efforts will be required to delineate the limits of these protocols and to make the techniques more easily available and accessible for translational applications.

A particularly promising application area for MRS research in autism is the use of MRS in tracking the progression and response of individuals with ASD to pharmacological treatment plans. Such strategies have already proven to be useful in other neuropsychiatric disorders (Mason & Krystal, 2006). Another area which has been little explored to date is the use of multinuclear MRS for examining nuclei other than proton (1H), e.g., carbon-13 and phosphorous-31. Multinuclear MRS, especially infusion studies of 13C glucose or acetate (e.g., see Bluml, Moreno-Torres, Shic,

Nguy, & Ross, 2002), has the potential to provide accurate descriptions of atypical brain metabolism and energetics in autism, potentially identifying points of biochemical vulnerability in a pathway- and individual-specific manner. When combined with genetic studies which may highlight the corresponding bases for these disorders, and the potential of MRS for monitoring and tracking treatment and disease progression, the role of MRS in the study of autism should only increase in the coming years.

See Also

▶ Magnetic Resonance Imaging

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Magnetoencephalography

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Definition

Magnetoencephalography (MEG) is a noninvasive neuroimaging technique that detects extracranial

**Magnetoencephalography, Fig. 1** A child sits in a whole-head biomagnetometer (MEG machine). Typically, somatosensory, visual, or auditory stimuli may be presented, and button-box responses collected synchronously with multichannel (in this case 275) recording of the magnetoencephalogram

magnetic fields produced by electrical activity in the brain, which occurs spontaneously or in response to external stimuli. The extracranial magnetic fields are sampled by an array of sensors, generally arranged in a helmet, within which the head is contained (see Fig. 1). These extracranial magnetic fields, which comprise MEG signals, reflect the synchronous postsynaptic activity of large populations of pyramidal neurons. Electrical activity associated with synaptic transmission produces magnetic fields orthogonal to the direction of the electric currents. The direction of the magnetic fields is governed by the "right-hand rule": When the right hand is made into a fist with the thumb pointing upward, the remaining fingers point in the direction of the flow of magnetic fields.

Recording magnetic fields associated with brain activity relies on specialized technology because the magnetic fields in the brain are extremely weak (on the order of 10fT–1pT, approximately 10 million times smaller than the earth's magnetic field). As such, the coils that detect the brain's magnetic fields and the superconducting quantum interference devices (SQUIDs) to which the coils are coupled are maintained at extremely low temperatures. This is accomplished by surrounding the sensors with liquid helium and encapsulating them within a dewar. In addition, containing the MEG system within a magnetically shielded room reduces competing environmental magnetism.

MEG recording takes place while patients or participants are either seated or lying supine, with the head positioned inside of the helmet that contains the MEG sensors. The size of the helmet is optimal for a typical adult head in the vast majority of MEG systems; however, MEG systems designed for infants and small children are currently being developed. Unlike MRI, MEG recording is silent. Patients or participants may be scanned during rest or during a variety of paradigms, from passive sensory processing to active task performance, and the signals recorded can be characterized as spontaneous, evoked, or induced. Spontaneous activity is that which is not related to the presentation of a stimulus and thus constitutes background activity. Evoked activity is strictly time-locked to a stimulus, whereas induced activity arises in response to a stimulus but not in a strict time-locked manner.
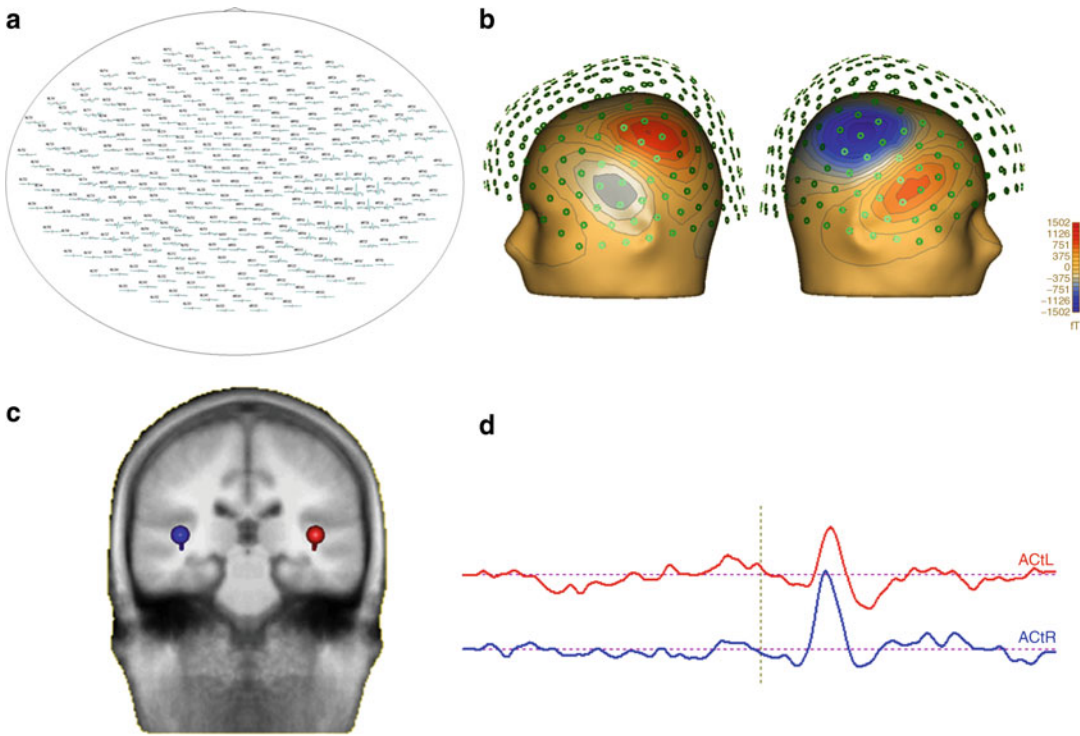
Magnetoencephalography, Fig. 2 (**a**) Spatial and temporal information in MEG represented by the spatial array of sensors each recording the time-varying magnetic field; (**b**) at any instant, the magnetic field topography can be described; (**c**) source modeling is used to transition for "sensor space" to "brain, or source, space," in this case, two equivalent current dipole sources in bilateral superior temporal gyri accounting for auditory evoked neuromagnetic fields; (**d**) time courses of neuronal electrical activity form the two brain sources illustrated in (**c**) during auditory stimulation

In order to localize the brain activity recorded at the MEG sensors, the source/s of the activity must be modeled. In so doing, researchers and clinicians are often faced with an inverse problem, that is, the data (in this case, MEG signals recorded outside of the head at the sensors) are used to estimate the model parameters (in this case, the source/s of the MEG signals within the brain). These inverse situations are conceptualized as "problems" because there is no unique solution, and it can be challenging to identify the best possible solution.

MEG source modeling is typically accomplished by combining the MEG signals with MRI images. During MEG data collection, several coils are affixed to the individual's head (usually the nasion and left and right periauricular areas) to establish a three-dimensional coordinate system so that his or her MEG data may be coregistered with his or her structural MRI. The most widely utilized method for MEG source localization is the single equivalent current dipole (ECD) method. This method involves modeling the pattern of MEG activity at relevant sensors with the assumption that the source of the activity is a focal location in the brain (see Fig. 2). An alternative approach to the ECD method is beamforming, which uses rastered spatial filtering to identify the neuromagnetic time course of any given point in the brain. Repeating this process for many points in the brain allows researchers and clinicians to construct images in which the MEG activity of interest is overlaid on the structural MRI.

MEG is related to EEG as the two techniques capitalize on the same neurophysiological processes. However, there are several key distinguishing features of MEG. First, whereas EEG signals are susceptible to distortion due to

the skull and scalp, MEG signals are impervious to these structures, thus yielding better spatial resolution in MEG than EEG. Second, whereas EEG detects both tangential and radial currents associated with neural activity, MEG detects only tangential currents. This means that MEG is primarily sensitive to activity in sulci. Third, whereas EEG relies on a reference electrode/s, which can be problematic if the reference is active, MEG is reference-free.

Historical Background

To date, magnetoencephalography has been utilized predominantly for clinical purposes. The most common applications are identifying abnormal patterns of neural activity, locating seizure focus in epilepsy, and preoperative assessment of eloquent cortex in patients with intractable epilepsy or brain tumors. In the latter, MEG findings have been demonstrated to be superior to EEG findings and consistent with (and perhaps eventually supplanting) invasive methods such as electrocorticography (ECoG).

Current Knowledge

Although MEG is widely considered the "gold standard" for noninvasive characterization of neuropathology in patients with epilepsy and brain tumors and the technique has demonstrated usefulness in the study of disorders such as Parkinson's disease and schizophrenia, MEG has not been widely applied to the study of autism spectrum disorders (ASD). The earliest MEG studies of ASD were published in the late 1990s, and the relatively small ASD MEG literature can be divided into the following broadly defined categories: (a) epileptiform abnormalities, (b) mirror neuron system integrity, (c) face processing, (d) the somatosensory system, and (e) auditory/language processing.

Epileptiform Abnormalities
One of the earliest MEG studies of ASD (Lewine et al., 1999) investigated the potential presence of abnormal patterns of neuromagnetic activity during sleep in children with regressive ASD, motivated by the substantial clinical overlap between autism and epilepsy. Results indicated a high prevalence of multifocal epileptiform activity in these children, even in the absence of a diagnosable seizure disorder. Similar epileptiform abnormalities have been subsequently reported in children with nonregressive forms of ASD (Muñoz-Yunta et al., 2008). Importantly, this line of research has demonstrated that epileptiform activity in ASD is detectable with MEG even in cases where it goes undetected by simultaneously recorded EEG.

Mirror Neuron System Integrity
Another small subset of the ASD MEG literature consists of studies examining the integrity of the mirror neuron system. Discovered serendipitously by Rizzolatti and colleagues (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996), who observed that neurons in a frontal area in monkeys fired not only when the monkey performed an action itself but also when it observed the experimenter performing a similar action, mirror neurons are purportedly involved in imitation and social cognition. Impairments in the mirror neuron system have been implicated in ASD, mostly with the use of EEG and fMRI. Although an early MEG study investigating electrophysiological signatures of biological motion perception in individuals with ASD (Avikainen, Kulomaki, & Hari, 1999) failed to identify abnormalities in ~20 Hz oscillatory activity in primary motor cortex, more recent work has identified spatio- and spectro-temporal abnormalities. Specifically, one finding indicated that although the peak activation latencies between adults with ASD and controls did not differ early in the processing stream (occipital cortex, followed by superior temporal sulcus, followed by inferior parietal lobule), the ASD group showed a significantly delayed response downstream in the inferior frontal lobe (Broca's area), coupled with reductions in the amount of activity in the inferior frontal lobe as well as primary motor cortex (Nishitani, Avikainen, & Hari, 2004). Results from another study revealed that the typical increase in beta (15–25 Hz) activity that occurs after an

individual observes an action (the "postmovement beta rebound") was reduced in adults with ASD in multiple regions in the mirror neuron system, including sensorimotor cortex, premotor cortex, and the superior temporal gyrus, as well as in the medial prefrontal cortex (Honaga et al., 2010).

Face Processing

Despite an extensive literature reporting face-processing abnormalities in ASD using fMRI, only two studies to date have examined face processing in ASD using MEG. One compared the processing of faces to that of mugs and geometrical patterns in adults with ASD (Bailey, Braeutigam, Jousmäki, & Swithenby, 2005). Results indicated that the neuromagnetic response to faces at short latencies (30–60 ms) is abnormal in ASD, and equivalent current dipole estimation revealed abnormal face-processing loci in ASD. The second study examined face processing in children with ASD, specifically with respect to processing of faces with direct versus averted gaze (Kylliainen, Braeutigam, Hietanen, Swithenby, & Bailey, 2006). Findings demonstrated that at early latencies (up to 100 ms), neuromagnetic activity was similar in the ASD and control groups, save a lack of repetition priming in ASD. However, at longer latencies, group differences were more pronounced, with greater responses in ASD to direct versus averted gaze at 240 ms poststimulus (a pattern inconsistent with that of the control group) and weaker responses at 300 ms poststimulus in ASD compared to controls.

Somatosensory System

Only two studies to date have examined the somatosensory system in ASD. Examining young adults with ASD, one study (Coskun et al., 2009a) investigated the variability of evoked responses to tactile stimulation and failed to find abnormalities in the ASD group. The other study examined the organization of somatosensory cortex via somatic maps and found abnormal cortical organization in young adults with ASD. Specifically, the cortical representations of the thumb and lip were further apart in the ASD group compared to the control group (Coskun et al., 2009b).

Auditory/Language Processing

The majority of the ASD MEG literature to date capitalizes on the ability of MEG to detect lateralized superior temporal gyrus (STG) activity in order to characterize auditory functioning in ASD, with the goal of elucidating biomarkers associated with language impairment in ASD. A number of studies have investigated auditory evoked responses to simple tones, with the hypothesis that impairments in the processing of simple auditory stimuli early in life would likely have cascading detrimental effects on language development. The evoked response most often examined is the M100, a ∼100-ms response elicited in passive listening paradigms that is modulated by stimulus parameters such as frequency. Several studies have shown abnormalities in the M100 response in children with ASD. Among these abnormalities are prolonged M100 latencies (Gage, Siegel, & Roberts, 2003; Gandal et al., 2010; Roberts et al., 2010), abnormal hemispheric asymmetry of the M100 (Schmidt, Rey, Oram Cardy, & Roberts, 2009), and abnormal modulation of the M100 by tones of different frequencies (Gage, Siegel, Callen, & Roberts, 2003).

Another feature of auditory processing in ASD that MEG studies have revealed to be abnormal is the mismatch field (MMF). The MMF occurs approximately 200 ms after an auditory stimulus and is a measure of acoustic change detection obtained by subtracting the evoked response to a frequently presented standard stimulus from the evoked response to an infrequently presented deviant stimulus. The presence of an MMF indicates passive, preattentive discrimination of the standard and deviant stimuli. MEG studies have demonstrated latency delays in the MMF in children (Oram Cardy, Flagg, Roberts, & Roberts, 2005; Roberts et al., 2011) and adults (Kasai et al., 2005) with ASD as well as reduced amplitude, or even absence, of the MMF in children with ASD (Tecchio et al., 2003).

The M100 and MMF abnormalities may provide insight into the language impairments characteristic of ASD in that atypical early acoustic processing may have cascading downstream effects on the processing of language, which is

inherently more complex and involves processing acoustic units presented in rapid temporal succession. Results from an MEG study of auditory processing of pairs of tones support this hypothesis; in children and adolescents with ASD, the majority of those with language impairment failed to show evoked responses to the second of two tones when the two tones were presented in rapid succession (Oram Cardy, Flagg, Roberts, Brian, & Roberts, 2005).

Future Directions

A number of novel approaches to the study of neural abnormalities in ASD are emerging in the MEG research community. One such approach is the study of resting-state neuromagnetic activity, which has the potential to shed light on abnormal patterns of neural activity in ASD in the absence of specific sensory processing. In addition, analyses of functional connectivity, or interactions between brain regions, both in the resting state and in sensory and cognitive processing are being implemented with increasing frequency. Functional connectivity analyses have the potential to provide insight into neural abnormalities in ASD at the network level. A clear benefit of MEG in this area of research is the ability to examine network interactions at multiple frequencies and with fine-grained temporal resolution.

Other exciting new applications of MEG in ASD research involve multimodal integration of MEG and complementary neuroimaging techniques, including diffusion tensor imaging (DTI) and magnetic resonance spectroscopy (MRS). Multimodal MEG and DTI studies afford the opportunity to investigate associations between electrophysiological measures (e.g., delayed auditory evoked 100-ms responses) and the structural integrity of white matter tracts. Multimodal MEG and MRS studies allow for investigation into associations between electrophysiological measures and neurotransmitter levels. Two particularly promising targets in ASD research are GABA and glutamate. With the growing number of applications of MEG to ASD research emerges the

potential to develop multidimensional classifiers that will help to further elucidate the neuropathology of ASD.

See Also

▶ Electroencephalogram (EEG)
▶ fMRI

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Maintenance of Treatment Effects

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Synonyms

Durability of treatment effects; Sustained treatment benefits; Treatment gain retention

Definition

The continued improvement in functioning and/or use of skills gained through an intervention over time. Maintenance of behavior change may be strengthened through procedures such as the occasional use of the intervention methods originally used to promote behavior change, provision of reinforcement for displaying the newly learned behavior, and overlearning (teaching until the learner is fluent at displaying the new behavior). Maintenance of treatment effects is often addressed alongside generalization of skills to maximize the retention of treatment gains.

See Also

▶ Generalization and Maintenance

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Major Depression

▶ Mood Disorders

Major Depressive Disorder

▶ Depressive Disorder

Maladaptive Behavior

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Synonyms

Problem behaviors

Definition

Maladaptive behavior is defined as behavior that interferes with an individual's activities of daily living or ability to adjust to and participate in particular settings.

Maladaptive behaviors lie along a spectrum from more minor, less impairing behaviors (i.e., nail biting, difficulty separating) to more severely impairing behaviors (i.e., self-injurious or over-sexualized behaviors) that seriously interfere with individuals' ability to maintain relationships with others, learn, and/or engage in adaptive, age-appropriate activities and settings. Because of their impairing nature, maladaptive behaviors are often the target of interventions. Problem behaviors are often a concern for children with developmental disabilities; maladaptive behaviors commonly associated with autism spectrum disorders include self-injurious behaviors (e.g., headbanging), stereotypies, aggression, and temper tantrums.

Although maladaptive behavior is related to adaptive behavior, or the personal and social skills necessary for day-to-day functioning, these two domains are distinct both conceptually and functionally. Thus, maladaptive behavior is not simply defined as the *absence* of adaptive behavior; reciprocally, adaptive behavior is not the absence of maladaptive behavior.

Maladaptive behavior is a term that is used most often in the discussion of adaptive behavior. In other contexts, maladaptive behaviors are usually considered under a broader umbrella of social-emotional and behavior problems that are measured with checklists.

See Also

▶ Adaptive Behavior Scales
▶ Maladaptive Behavior
▶ Vineland Adaptive Behavior Scales

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Male Turner

▶ Noonan and Ras/Mapk Pathway Syndromes

Mand Fluency Training

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Definition

Mand fluency training, or mand training, is an intervention approach designed to teach individuals with limited communication skills to express their needs and wants. A mand commonly takes the form of a request and is defined as a verbal act that is reinforced by a specified consequence (Skinner, 1957).

Historical Background

Mand training is based on B. F. Skinner's (1957) operant conditioning framework for analyzing the functions of verbal behavior. This behavioral approach to language training has been used extensively with individuals with developmental delays and autism, in particular, as part of early behavioral intervention programs. For example, intervention programs developed by Lovaas (2003) and Sundberg and colleagues (Sundberg & Partington, 1998) incorporate mand training as a key component for teaching early communication skills.

Rationale or Underlying Theory

Within an operant conditioning framework, mands are controlled by a motivative variable, often referred to as an establishing operation (Sundberg & Michael, 2001). For example, hunger and the desire for a cookie may lead an individual to say "I want a cookie." This behavior is then reinforced by the offering of a small piece of a cookie. A mand training approach can be contrasted with a traditional language perspective that emphasizes teaching the individual the meaning of different words (e.g., learning to say "cookie" when shown a cookie or "ball" when shown a ball; Sundberg & Michael). It has been suggested, however, that some children with autism do not spontaneously request items even if they have demonstrated understanding of the appropriate word for an item and, thus, need to be explicitly taught this skill (Sundberg & Michael). Because of the unique reinforcement provided through the establishing operation, mand training can facilitate children's willingness to participate in language training, in general (Sundberg & Michael).

Goals and Objectives

The ultimate goal of mand training is to increase an individual's spontaneous requesting behavior so that the individual can make his or her needs and wants known to others. Short-term objectives may include imitating mands and requesting basic items, such as food within sight. Longer term objectives may include requesting items or activities that are not present in the immediate environment.

Treatment Participants

Participants in mand training are individuals, typically young children, with developmental disabilities who have limited expressive language skills and who do not spontaneously make verbal requests to express their needs and wants.

Treatment Procedures

Mand training can be used as part of a larger early intervention program focused on developing language, cognitive, self-help, and play skills. For example, the *I Want* Program (Lovaas, 2003), which is one component of a large package of intervention techniques for individuals with developmental delays, is designed to teach participants to verbalize their choices when presented with desired and undesired items and to develop spontaneous verbal requesting behavior. The developer of the program recommends starting with teaching the

participant to request his or her favorite foods, objects, or activities to reinforce the behavior and possibly reduce problem behavior resulting from frustration with not being able to communicate desires (Lovaas). If necessary, the individual would first need to be taught how to imitate several "I want (item)" statements (e.g., *I want ball*, *I want cookie*, *I want juice*). The participant is then presented with the stimulus "What do you want?" and prompted to say "I want juice," for example. The participant's response is then reinforced by having access to a small amount of the item (e.g., a sip of juice, 5 s of playtime with the ball). As the participant reaches specified accuracy benchmarks, the prompts are faded and new items are introduced. Eventually the participant is prompted to request items that are not in sight and then progresses to being reinforced systemically for spontaneous requests that are not prompted. For individuals who are unable to echo sounds or imitate actions, mand training can be done using signs or pictures.

Important issues to include when selecting initial words for mand training include (a) choosing words that will be reinforcing to the participant and that the instructor can easily control, have access to, and that can be delivered multiple times; (b) selecting words the participant can imitate or for which the individual has demonstrated understanding; (c) choosing words that are relatively easy for the participant to say; (d) when using sign language, selecting signs that look like the objects they represent and that the individual can already imitate; (e) choosing words for items that are relevant to the participant's daily life; (f) selecting words for a variety of motivators (e.g., not all foods); (g) avoiding words that sound alike or rhyme; and (h) avoiding words that may represent something negative for the individual (Sundberg & Partington, 1998).

Efficacy Information

Mand training is often implemented as part of a broader behavioral intervention program, and its efficacy has not been examined extensively in isolation. However, smaller studies have provided some evidence for the efficacy of mand training in children with autism (e.g., Drash, High, & Tudor, 1999). There is also some evidence that it may be more efficient than discrete trial instruction for facilitating the acquisition of requesting behavior (Jennett, Harris, & Delmolino, 2008). Adding opportunities for rapid imitation of modeled motor behaviors during mand training has been shown to increase the efficacy of mand training, with evidence of increased spontaneous manding 3 months later (Ross & Greer, 2003). In general, however, there is limited information from published studies on the long-term generalization of skills taught during mand training.

Outcome Measurement

Efficacy research on mand training has utilized various metrics for progress monitoring and outcomes measurement, such as specified trial accuracy criteria (e.g., 9 out of 10 correct responses), percentage of correct responses, percentage of incorrect responses, or the number of spontaneous mands in a given period. Clinical intervention programs that include mand training typically use specific accuracy criteria for determining when an individual is ready to progress to the next stage (e.g., from imitating mands to being expected to produce them when prompted).

Qualifications of Treatment Providers

Mand training providers are typically professionals or supervised paraprofessionals with formal training in behavioral theory and applied behavioral analysis techniques. In some verbal behavior programs, parents and caregivers are also taught basic mand training techniques to facilitate generalization of the individual's skills beyond the therapy context.

See Also

▶ Applied Behavior Analysis
▶ Communication Interventions
▶ Early Intensive Behavioral Intervention (EIBI)

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Mands

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Synonyms

Command; Demand; Request

Definition

Mands are verbal acts that are reinforced by a specified consequence (Skinner, 1957). This term was introduced by B. F. Skinner and refers to a specific type of verbal action within an operant conditioning framework designed to analyze the functions of verbal behavior. Mands are considered to be the first type of verbal behavior that individuals typically acquire (Sundberg & Michael, 2001). As part of a verbal behavior training intervention, mands commonly take the form of requests for items, information, or removal of aversive stimuli (Sundberg & Michael). For example, if an individual who wants a cookie says "Cookie, please" and is then given a cookie, the individual's statement (i.e., "Cookie, please") would be considered a mand.

See Also

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Mania

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Synonyms

Elated, euphoric and grandiose; Elevated, expansive, or irritable mood; Overly talkative; Racing thoughts, distractibility, and psychomotor agitation

Short Description or Definition

The American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) defines a manic episode as "a distinct period during which there is an abnormally and persistently elevated, expansive, or irritable mood" (American Psychiatric Association [APA], 2000, p. 357). Symptoms of mania include a high activity level which may be directed toward a specific goal or may consist of psychomotor agitation, inflated self-esteem, a decreased need for sleep, racing thoughts, talkativeness, distractibility, and engaging in pleasure-seeking activities without regard for consequences. Individuals experiencing mania are often noted to have a change in personality, in which they become reckless, boisterous, and engage in high-risk activities. If the individual's mood is elevated, three of the prior symptoms are required; four if the mood is irritable. To qualify as a manic episode in DSM-IV-TR, the episode must last at least one week, or any duration if symptoms are severe enough to require hospitalization, and must result in impairment in the ability to function in daily life. Psychotic features, including delusions (false beliefs) or hallucinations, may be present. The manic episode cannot be caused by the effects of drugs of abuse, medications, exposure to a toxic substance, or a general medical condition (APA, 2000).

Categorization

A manic episode is one of the essential components of bipolar I disorder, which historically has been referred to as manic-depressive disorder. Although bipolar I disorder usually also includes episodes of depression, it is the occurrence of the manic episode that is the defining feature. A hypomanic episode is a less severe form of mania, which is not severe enough to cause substantial impairment in functioning in daily life, does not necessitate hospitalization, and there are no psychotic symptoms. Bipolar II disorder is characterized as a mood disorder in which hypomania, as opposed to mania, is present (APA, 2000).

Epidemiology

The lifetime prevalence of bipolar I disorder in the community is estimated at 3.9% (Perlis et al., 2004). There is less diagnostic clarity when the mood symptoms have their initial symptoms presenting in childhood, as many other disorders have overlapping symptoms. Twenty is the mean age of onset for a first manic episode, but retrospective studies suggest that about 60% of adults with bipolar disorder demonstrated some mood symptoms in childhood or adolescence. There has been a trend over time for the age of the first onset of symptoms to occur earlier in life. For adolescents who have suffered from recurrent major depression, about 10–15% will experience a manic episode and thus develop bipolar I disorder (Boris, Axelson, & Pavuluri, 2007). The lifetime prevalence of bipolar I disorder in the community is estimated at 3.9% (Perlis et al., 2004). There is less diagnostic clarity when the mood symptoms have their initial symptoms presenting in childhood, as many other disorders have overlapping symptoms. Twenty is the mean age of onset for a first manic episode, but retrospective studies suggest that about 60% of adults with bipolar disorder demonstrated some mood symptoms in childhood or adolescence. There has been a trend over time for the age of the first onset of symptoms to occur earlier in life. For adolescents who have suffered from recurrent major depression, about 10–15% will experience a manic episode and thus develop bipolar I disorder (Boris et al., 2007).

Men and women suffer from bipolar I disorder in about equal numbers. However, women more commonly have a major depressive episode first and suffer from more depressive episodes than manic episodes, whereas men most often experience their first episode as mania and have more equal numbers of manic and depressive episodes. Manic episodes frequently occur after a stressful life event. In about 2/3 of cases, a manic episode immediately follows or precedes an episode of major depression. Most individuals have periods of more normal mood states between episodes of either mania or depression. However, about one-quarter of individuals with bipolar I disorder

more persistently display a labile (fluctuating) or irritable mood (APA, 2000). In individuals over the age of 13 who are diagnosed with autism, approximately 3% suffer from manic episodes (Howlin, 2005).

Natural History, Prognostic Factors, and Outcomes

Mania, associated with bipolar disorder is a recurrent illness. In general, the earlier the age of onset of the disorder (either depressive or manic symptoms), the more recurrent and chronic the course of illness. Recovery from the first manic episode is very high (over 70%), but a similar number (up to 80%) will experience recurrence of the disorder within 2–5 years.

Early-onset bipolar disorder also has a high rate of persistent lower level mood symptoms. Child and adolescent onset of the disorder is often characterized by more rapid fluctuations in mood than when the disorder is not evidenced until adulthood.

Poor prognostic factors for manic episodes are early age of onset, long duration of symptoms, exposure to trauma and negative life events, low socioeconomic status, mixed or rapid cycling episodes, psychotic symptoms, and co-occurring psychiatric disorders. Suicidal ideation and attempts occur most often when an individual is depressed or using substances. For individuals with bipolar I disorder, the completed suicide rate is estimated at 10–15% (Geller, Tillman, Craney, & Bolhofner, 2004).

Clinical Expression and Pathophysiology

Elevated mood is the cardinal symptoms of mania. Individuals who experience mania often feel so elated and omnipotent that they do not recognize that they are ill in any way. It is those around them that notice the change in behavior. The manic individual often demonstrates poor judgment, may change personal appearance to a flamboyant style that is out of character, and

may exhibit high-risk behaviors, such as sexual promiscuity, substance use, or spending large sums of money. For youth presenting with mania, increased energy, distractibility, and pressured speech are the most common symptoms, while hypersexuality has been found to be the least frequent (Boris et al., 2007).

Very severe mania often includes psychotic symptoms. More than half of manic individuals experience delusions, usually of grandeur (the false belief that one is famous, has unusual powers, or is special in some other way). Religious delusions are also common. Hallucinations, usually auditory, occur in about one-fourth of individuals. Some individuals may experience symptoms of mania and major depression that alternate rapidly, with both experienced almost every day. This is referred to as a "mixed episode." Agitation, insomnia, rapid changes in appetite, psychotic features, and suicidal thoughts are frequent symptoms for individuals with mixed episode mood disorders (APA, 2000).

Although there are no specific laboratory tests that are diagnostic of a manic episode, some abnormal test results are frequently found in individuals with mania. These include abnormal polysomnograms (electroencephalograms or EEGs that occur during sleep) and increased cortisol secretion. Studies of neurotransmitter metabolites, neuroendocrine function, and pharmacological challenges suggest that there may be abnormalities of many of the central nervous system neurotransmitters: norepinephrine, serotonin, acetylcholine, dopamine, and gamma-aminobutyric acid (GABA).

Bipolar disorder has been demonstrated to run in families, according to multiple twin and adoption studies. Having a first-degree relative who has been diagnosed with bipolar disorder confers an increased risk (eight- to tenfold over community samples) of also being diagnosed with the disorder. Symptoms typically occur at an earlier age in children with a close family history of bipolar disorder. The heritability for bipolar disorder has been estimated at over 80% (Boris et al., 2007).

Mania, Table 1 Components of a diagnostic evaluation for mania

Chief complaint	From patient, family, significant others, referral source
Context	In what context does mania occur?
Multiple informants and collateral history	History of symptoms from family, significant others, referral source, primary care physician, etc. (with patient consent or from legal guardian if patient is a minor)
Timeline of mood symptoms	Frequency, intensity, number, and duration (FIND) of mood episodes
Developmental, social, and family history	Developmental milestones, educational history, level of functioning, social relationships, medical history, and family history of psychiatric disorders
Patient interview/mental status examination	Developmentally appropriate interview. Inquire about substance use, high-risk behaviors, suicidality and homicidality, legal problems, trauma history, sleep, and energy level. Assess for psychotic symptoms
Medical evaluation	Routine physical examination; further medical evaluation as indicated: illicit substances (toxicology screen); toxic (lead or toxin levels); autoimmune diseases (screen for lupus, and others); neurological (EEG for epilepsy; brain imaging for multiple sclerosis, etc.); metabolic/infections (thyroid levels, liver function tests, complete blood count, etc.); other diseases (e.g., Cushing's disease by cortisol level)
Rating scales	SADS, K-SADS, Young Mania Rating Scale, Child Behavior Checklist (CBCL), Parent Mood Disorder Questionnaire (MDQ)

Evaluation and Differential Diagnosis

The evaluation for mania includes a patient interview, collateral information from significant others, a medical workup, gathering family history of mood disorder, and the use of assessment scales (see Table 1). Structured and semi-structured interviews (SADS or for children the K-SADS) or a general checklist, such as the Child Behavior Checklist (CBCL), may be helpful diagnostically and for research purposes. For youth, the Young Mania Rating Scale (Young, Biggs, Ziegler, & Meyer, 1978) is the most widely used. Also for youth, parental report is more effective in identifying mania than youth or teacher reports. The Parent Mood Disorder Questionnaire (MDQ) is a widely used rating scale. Mood timelines or diaries may help track mood symptoms, and may also identify events that trigger these symptoms and document response to treatment (Nandagopal & DelBello, 2011).

Many other disorders have overlapping symptoms with early-onset bipolar disorder. Attention-deficit/hyperactivity disorder, disruptive behavior disorders and conduct problems, substance abuse disorders, schizophrenia, and pervasive developmental disorder with irritability are most common. Medical disorders that may present with manic symptoms include hyperthyroidism, head trauma, brain tumors, or Cushing's syndrome. Medications, such as corticosteroids, antidepressants, and stimulants, may be accompanied by mood fluctuations or precipitate manic symptoms.

In individuals diagnosed with autism spectrum disorders, the most common other psychiatric diagnoses are attention-deficit/hyperactivity disorder, depression, and anxiety disorders, with mania occurring with no more frequency than the rest of the population (Howlin, 2005; Matson & Nebel-Schwalm, 2007).

Treatment

Current treatments for mania aim to control the agitation, impulsivity, aggression, and psychotic symptoms and to help patients regain their pre-illness level of functioning. After the first episode of mania, many individuals demonstrate ongoing milder levels of dysfunction, which may or may not resolve fully. Mania, and thus, bipolar I disorder, is a recurrent disorder, and effective treatment must include acute, continuation, and maintenance phases. Effective treatment includes the use of appropriate medications in the mood stabilizing,

Mania, Table 2 Treatment of mania

Treatment: pharmacotherapy	
Lithium	Most evidence base for effectiveness in adults and adolescents. Used as monotherapy or in combination with an antipsychotic or anticonvulsant medication
Anticonvulsant medications: valproate, carbamazepine, lamotrigine, oxcarbazepine, topiramate	The most evidence for effectiveness in adults and adolescents are with valproate, carbamazepine, and lamotrigine. Used as monotherapy or in combination with lithium or an antipsychotic
Atypical antipsychotic medications: olanzapine, risperidone, quetiapine, aripiprazole, clozapine, ziprasidone	May be used as monotherapy but are often used to target symptoms of psychosis or for more rapid treatment response in conjunction with lithium or an anticonvulsant medication
Treatment: psychosocial	
Environmental	Safe and less stimulating environment, sleep hygiene, and routine. For severe mania, this may include psychiatric hospitalization
Psychoeducation and support	Active listening; restoration of hope; case management (collaborate with school, job, community resources, family regarding needed services); education about causes, symptoms, treatment, and prognosis
Therapeutic interventions	Day treatment or partial hospitalization program; individual therapy: cognitive-behavioral therapy, dialectic behavioral therapy, interpersonal therapy, supportive therapy; family therapy; skill-building groups

antiepileptic, and antipsychotic classes. These medications may be used in monotherapy or combined for enhanced effectiveness. Psychosocial interventions, including education about the disease, case management and coordination of services, family therapy, group therapy, and individual supportive and evidence-based treatments are also essential to optimize prognosis. Table 2 highlights the components of effective treatment.

See Also

▶ Comorbidity

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Manual Sign

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Synonyms

American Sign Language (ASL); Conceptually Accurate Signed English (CASE); Linguistics of Verbal English (LOVE); Manually Coded English (MCE); Seeing Essential English (SEE I); Sign language; Signed English; Signing Exact English (SEE II)

Definition

Manual sign is a system of communicating visually and spatially through signs created with the hands. The term "manual sign" does not specify a particular sign system such as American Sign Language (ASL) or manual codes of English such as Seeing Essential English (SEE I), Signing Exact English (SEE II), Linguistics of Verbal English (LOVE), and Conceptually Accurate Signed English (CASE). ASL is the natural language of the deaf community in the United States and much of Canada (Neidel, Kegl, MacLaughlin, Bahan & Lee, 2000). ASL is a distinct language from spoken English (see entry on ▶ American Sign Language (ASL)) while manual codes of English are based on spoken English and are an attempt to represent English on the hands. Manual codes of English were created in the 1960s primarily to aid in increasing the literacy skills of deaf and hard-of-hearing children (Schow & Nerbonne, 2007). Manual codes of English can be classified as "sign systems" and not "sign languages" because they borrow the semantics and syntax from spoken English. These sign systems follow English word order and use grammatical markers for morphological endings of words. For example, the word "smiling" is signed with two signs SMILE + ing. Additionally, unlike ASL, manual codes of English use signs for function words such as "the" and "an." Typically, when signing is employed in the language intervention for children with autism, the type of signing systems that are used is manual codes of English rather than ASL. The main reason for this may be the hope that using manual sign will lead to verbal communication, an outcome which has been supported by research (Schlosser & Wendt, 2008).

See Also

▶ American Sign Language (ASL)
▶ Sign Language

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Manually Coded English (MCE)

▶ Manual Sign
▶ Sign Language

MAP

▶ Miller Assessment for Preschoolers (MAP)

Marker

▶ Milestone

Marker X Syndrome

▶ Fragile X Syndrome (FXS)

Marketed as Geodon

▶ Geodon (Ziprasidone)

Martin-Bell Syndrome

▶ Fragile X Syndrome (FXS)

MAS

▶ Motivation Assessment Scale

Massed Practice

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Definition

The repeated presentation of a task over a short period of time, with no intertrial interval between presentations. The term was first introduced by Hermann Ebbinghaus, and a detailed study was published in the 1885 book *Memory: A Contribution to Experimental Psychology*. Since then, researchers have found that distributed practice, or spaced practice, in which short periods of learning are interspersed with periods of rest or alternative activities, produces better performance than massed practice in a variety of tasks (Hunter, 1929).

Studies investigating the influence of task variation on learning suggest that distributed practice produces superior levels of on-task responding and higher levels of child affect in children with autism (Dunlap, 1984). Researchers suggest that interspersing alternative activities with varying difficulty levels serves to increase the child with autism's motivation to respond to the tasks (Koegel & Egel, 1979).

Massed practice can also refer to a self-directed behavior change technique in which a person performs an undesired behavior repeatedly, which sometimes decreases the future frequency of the behavior (Cooper, Heron, & Heward, 2007).

See Also

▶ Distributed Practice
▶ Learning Styles

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Massive Infantile Spasms

Massively Parallel Sequencing

Maternal and Child Health Bureau

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Major Areas or Mission Statement

The Maternal Child Health Bureau (MCHB), a United States Federal commitment to addressing maternal and child health, was first established in 1912. In 1935, the MCHB was transferred to Title V of the Social Security Act and then converted to a federal block grant administered by the Health Resources and Services Administration (HRSA) in 1981. The mission of the MCHB is to provide leadership, in partnership with key stakeholders, to improve the physical and mental health, safety, and well-being of the nation's women, infants, children, adolescents, and their families, including fathers and children with special health-care needs.

Landmark Contributions

HRSA administers a wide range of programs to pregnant women, mothers, infants, children, and their families. MCHB programs serve more than 34 million women, infants, and children each year in the United States. The MCHB supports programs to reduce infant mortality by providing comprehensive prenatal and postnatal care for women, promotes an advocacy community-based group for Healthy Start programs, and is a proponent of preventative care (including rehabilitative services and immunizations) for children, research and training, genetic services, and newborn screening and treatments.

The HRSA awards grants to improve health care and other services for children and adolescents with autism spectrum disorders and other developmental disabilities. Funds are utilized to enhance awareness and reduce barriers to screening and diagnosis. Funds also support research of evidence-based interventions, evidence-based guidelines for interventions, training professionals to use valid screening tools for diagnosis and intervention, and improving technical assistance to facilities which provide services for children with autism spectrum disorders.

Major Activities

HRSA's implementation of the Combating Autism Act of 2006 ($48 million) addresses the most urgent issues affecting people with autism and their families. The goal of this act is to enable all infants, children, and adolescents who are at risk for developing or who have autism spectrum disorders and other developmental disabilities to reach their full potential by:

- Establishing a system of services, including early screening of children for autism spectrum disorders
- Conducting early, multidisciplinary evaluations to diagnose or rule out autism spectrum disorders
- Providing evidence-based early interventions when a diagnosis is confirmed

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Maternal Hypothyroidism and Autism

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Synonyms

Iodothyronine deiodinase (D2T3); Thyrotropin, Thyroid-stimulating hormone (TSH); Thyroxine (T)

Structure

The thyroid gland is part of the endocrine system. It regulates the rate of metabolism and impacts growth by its regulation of other tissues through secretion of hormones triiodothyronine (T3) and thyroxine (T4). The substrates these hormones are synthesized from are iodine and tyrosine. The rate that these hormones are produced is regulated by thyroid-stimulating hormone (TSH) from the anterior pituitary gland. TSH is itself regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus. The fetus begins to make T3 at 18–20 weeks' gestation and T4 by 30 weeks. This may be partially protective from maternal hypothyroidism.

Function

Thyroid hormones are critical to normal brain development.

The thyroid regulates metabolism and growth and impacts both calcium metabolism and catecholamine effects.

Typical symptoms of hypothyroidism (low hormone production) postnatally are decreased energy, constipation, weight gain, fatigue, cold intolerance, hair loss, and slowed heart rate. Typical symptoms of hyperthyroidism (increased hormone production) postnatally are mood swings, overactivity, decreased appetite, and increased heart rate.

Pathophysiology

Among the prenatal conditions that have been associated with autism spectrum disorders is prenatal exposure to maternal hypothyroidism. Although not clearly demonstrated as a cause of autism, this hypothesis has growing support from neuroembryonic research, and some have suggested links between environmental toxins, maternal hypothyroidism, and the autism "epidemic."

Twenty years ago, Gillberg, Gillberg, and Kopp (1992) noted that congenital hypothyroidism was associated with autism spectrum disorders, along with intellectual disability and other physical concerns. In 1999, Haddow et al. confirmed that children exposed in utero to maternal hypothyroidism manifesting as high gestational thyrotropin (thyroid-stimulating hormone, or TSH) levels, arising in response to relative low levels of thyroid hormone, resulted in significant neuropsychologic impacts at school age. Developmental abnormalities were present even in children of women whose hypothyroidism was subclinical or partially treated (Bernal, 2007).

Thyroid hormone receptors are present in the fetal cortex by 8–9 weeks of gestation and increase tenfold by 18 weeks (Bernal, 2007), and brain T3 and iodothyronine deiodinase (D2) activities increase during the second trimester (Kester et al., 2004). D2 is felt to play an important role in brain compensation for variations in ambient thyroid hormone levels. It is well established that thyroid hormone plays a role in brain development during the fetal period, that different parts of the brain are differentially sensitive to thyroid hormone at any one time during development, and that sensitivity to thyroid hormone is controlled, in part, by local control of hormone production. These observations imply that the consequences of thyroid hormone insufficiency during fetal development differ from those of thyroid hormone insufficiency during

postnatal development (Zoeller, 2005). However, it has also been shown that small fluctuations in maternal thyroid hormone levels can have measurable neurocognitive impacts on the developing fetus. One impact of hypothyroidism shown in animal models is reduced expression of reelin, which regulates neuronal migration (Alvarez-Dolado et al., 1999). Abnormality of reelin expression has been associated with ASDs (Fatemi et al., 2005), and although not universally accepted, abnormalities of reelin genes have been associated with ASDs (Serajee, Zhong, & Mahbubul Huq, 2006).

It has been noted that thyroid hormone deficiency before the onset of hearing has negative effects on peripheral and central auditory systems (Knipper et al., 2000). In animal models, maternal hypothyroidism has been shown to result in abnormal cochlear development, in abnormal neurotransmission in the developing auditory brainstem and hippocampus (Friauf et al., 2008), and in cerebrocortical and hippocampal synaptic activity (Taylor, Swant, Wagner, Fisher, & Ferguson, 2008). Based on these and other animal studies, it has been proposed that the rat exposed to mild, transient neonatal hypothyroidism may serve as a model for autism (Sadamatsu, Kanai, Xu, Liu, & Kato, 2006).

High TSH levels have also been noted to be associated with increased risk of breech presentation in term infants, based on samples of Dutch women followed for TSH elevation or evaluated for breech presentation (Kooistra et al., 2010). Inasmuch as breech presentation is one risk factor for ASDs (Bilder, Pinborough-immerman, Miller, & McMahon, 2009), this supports the relationship. The authors note that infants who present in the breech position often have low tone or reasons for less active body movements such as kicking, and that suboptimal maternal thyroid function might have a direct motor effect on the fetus. Alternatively, they quote literature (Van der Meulen, Davies, & Kisilevsky, 2008) that suggests that the sensory responses of fetuses in breech position are different from those in cephalic presentation.

Sweeten, Bowyer, Posey, Halberstadt, and McDougle (2003) replicated findings of Comi, Zimmerman, Frye, Law, and Peeden (1999), noting increased frequency of autoimmune disorders, with hypothyroidism being the most common, among parents of children with autism spectrum disorders. They acknowledge that this could be an effect of endocrine abnormality or, alternatively, the result of another immunologic abnormality having a direct effect on brain development.

An extensive review of the hypothyroidism/ASD association by Roman (2007) draws an association between maternal hypothyroidism and neuropathologic features found in individuals with ASDs, including abnormalities in cortex and hippocampus, "consistent with abnormal neuronal migration and alterations in the number, survival, and orientation of neurons up to the time of olivary cell migration...before the end of the third month" of gestation. He notes that, in humans, the fetal thyroid forms about midgestation, and that maternal dietary iodine deficiency and associated hypothyroidism prior to the third trimester of pregnancy can result in endemic cretinism. Multiple possible causes for both transient and long-term maternal hypothyroidism are proposed, including dietary iodine deficiency, exposure to food-based antithyroid substances (particularly soy products and other foods with high levels of isoflavonoids), and other environmental antithyroid substances (herbicides, PCBs, mercury, and coal derivatives).

Colborn (2004) has also been outspoken in drawing an association between endocrine-disrupting synthetic chemicals and neurodevelopmental disorders such as AD/HD and autism spectrum disorders. Some environmental chemicals, e.g., perchlorate, which has sometimes contaminated water supplies, directly interfere with iodine uptake into the thyroid gland. Other chemicals interfere with thyroid hormone signaling; polychlorinated biphenyls (PCBs) have this effect. Bisphenol A (BPA), involved in the manufacture of plastics, also blocks thyroid action on glial cells.

As Zoeller (2005) notes, "a causal relation between (environmental) contaminants, thyroid hormone signaling, and cognitive development will be difficult to obtain given the fact that even small and transient thyroid hormone insufficiency

may be detrimental." If screening of pregnant women for elevated TSH levels and thyroid supplementation when indicated become routine, epidemiologic studies of autism in the children of these women will be informative. Meanwhile, there is not yet clear evidence to associate prenatal exposure to maternal hypothyroidism with autism spectrum disorders nor are there clear links from environmental toxins to maternal hypothyroidism to autism spectrum disorders, but the hypotheses presented are provocative and speak to the need for well-controlled study.

See Also

▶ Medical Evaluation in Autism

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Mathematics Disability

▶ Dyscalculia

May Institute

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Definition

The May Center for Child Development, part of the May Institute, is a school for students with an autism spectrum disorder (ASD). The school provides educational and behavioral services based on the principles of applied behavior analysis. Nearly half of the student population is provided residential services in one of the many community-based group homes. The May Center is staffed by doctoral-level professionals, board certified behavior analysts, and special educators.

Historical Background

May Institute was founded by Dr. Jacques May and his wife, Marie Anne May, in 1955. The first school for children with an autism spectrum disorder (ASD) was opened on Cape Cod. Dr. and Mrs. May had twin boys diagnosed with an ASD who were among the first students to attend the school. In 1978, Dr. Walter P. Christian was named the executive director of May Institute. Over the past three decades, May Institute expanded to include a number of schools for students with an ASD, a school for students with a traumatic brain injury, school consultation, adult services, and behavioral health services. May Institute now has over 200 service locations across the United States. The schools for individuals with an ASD are located in Randolph, MA, Woburn, MA, West Springfield, MA, and Santa Cruz, CA. Professionals at May Institute frequently publish research in peer-reviewed journals and present research findings at national and international conferences. The National Autism Center is May Institute's Center dedicated to promoting evidence-based practice and

was opened in 2005. The National Autism Center houses a diagnostic clinic specializing in the identification of an ASD throughout the life span. The following timeline provides a simple outline of only a few of the many notable events throughout May Institute's history.

1981 → First group home opens

1984 → First integrated preschool opens

1987 → May Center School opens in Braintree, MA

1988 → May Center School in Chatham, MA, named "School of Excellence" by US Department of Education

1990s → Services continue to expand across the USA

2003 → May Center School opens in West Springfield, MA

2005 → May Center for Child Development in Randolph, MA, opens. It is an 82,000 square foot state-of-the-art facility for students age 2.9–22 years.

Rationale or Underlying Theory

May Institute's services for individuals with an ASD are based on the science of behavior analysis. Behavior analysis focuses on how environmental variables affect behavior. Essentially, practitioners of behavior analysis, behavior analysts, make systematic changes to the environment to help people reach their full potential. The technology of behavior analysis is used in a variety of settings including public schools, hospitals, large corporations, and clinicians working with individuals. Much peer-reviewed research has identified applied behavior analytic techniques as effective in producing favorable behavior change in individuals with an ASD.

Goals and Objectives

It is the mission of May Institute to provide educational and rehabilitative services to individuals with an ASD and related disorders and their families. Individuals with an ASD often face challenges as they try to communicate and socially

interact with others. Many individuals on the autism spectrum experience difficulties successfully managing everyday situations or addressing their daily living needs. The professionals at May Institute develop individualized programs to decrease challenging behaviors of clients and increase adaptive, communication, social, and vocational skills.

School-aged children with an ASD undergo educational and behavioral assessments resulting in the development of Individualized Education Programs (IEPs). The professionals at May Institute work with school districts, and families of the children served to achieve the goals identified in the IEP. Adults with an ASD served at May Institute undergo assessment of vocational skills, self-care skills, and behaviors that could interfere with their successful participation in their community. The results of the assessments are compiled into an Individual Habilitation Plan (IHP). The development of individualized programs for individuals with an ASD is a collaborative process often involving an interdisciplinary team of professionals.

Treatment Participants

May Institute provides services to children and adults with an ASD, other developmental disabilities, brain injury, and behavioral health needs. Autism spectrum disorders are by definition on a "spectrum," meaning there is a wide range of strengths and behavioral needs among the ASD population across all of the setting in which they participate (e.g., school, home, community). May Institute provides academic, behavioral, and vocational services to individuals across the spectrum. The vast majority of individuals with an ASD benefit from behavior analytic technology.

Treatment Procedures

The treatment procedures used by professionals at May Institute for individuals with an ASD are grounded in the science of behavior analysis. The most basic principles of behavior analysis include

procedures to increase socially important skills through reinforcement and to decrease behaviors that interfere with successful participation in communities. Reinforcement has become a popular term that is often misused. Reinforcement is a technical term with very specific meaning in behavior analysis. Reinforcement procedures are used to increase appropriate behaviors. For example, if a parent wanted to increase how often their child says "please," she might provide praise or a pat on the head whenever the child naturally said "please." If the child uses the word "please" more with the passage of time, then parental praise and pats on the head are reinforcers. This simple example can be extended to most human behavior. Teaching a young child to play, a school-aged child to complete homework, or an adolescent to follow the rules of road as he learns to drive can all be increased through careful application of reinforcers. As a general rule, all behavior change should involve reinforcement of appropriate behaviors.

Inappropriate behaviors often need to be decreased or eliminated. This can often be addressed simply by providing a sufficient schedule of reinforcement for appropriate behaviors, and this should be the strategy that should be attempted first. Reinforcement of appropriate behavior must sometimes be paired with behavior reduction procedures, however. Behavior reduction procedures are used to decrease inappropriate behaviors. These procedures should avoid the infliction of pain or distress on an individual. For example, a parent blocking a child's entrance on to a busy street and firmly stating "stop" may, in fact, stop them in their tracks and ensure they are in a safe environment. Reinforcement and behavior reduction procedures serve as the foundation of behavior analysis. Although the science of behavior analysis may appear quite simple when explained in terms of basic principles, decades of research in laboratories and applied settings suggest the science of behavior is indeed complex.

Reinforcement procedures are used to increase adaptive behaviors such as communication, self-care skills, academics, and vocational skills. At May Institute, practitioners set behavioral goals for the individuals being served. The goals include training protocols and criteria to indicate when goals are

achieved. Students with an ASD may work on the goal several times a day or a few times a week.

The training protocols implemented at May Institute include a variety of techniques to teach behaviors that will increase independence and success at home, in school, or in the community. Discrete-trial teaching (DTT) is a technique frequently used by behavior analysts to teach new skills to individuals with an ASD. When using DTT, the practitioner breaks down a complex behavior into simple steps. Each step of the complex behavior is taught individually. Think about an instruction manual guiding an individual through the assembly of a toy car. Often, the steps are broken down, and each step is associated with a simple picture labeling the parts and the action one must take to complete the step. After an individual completes the last step, they have a little toy car which may have taken two hours to assemble! Now imagine the same individual practiced each step of the assembly process repeatedly. Over time, the individual would become quite fluent and efficient in the assembly of that fancy little toy car. This is one way to conceptualize how practitioners use DTT to teach individuals with an ASD. DTT can occur in any environment in which a child needs to learn new skills, such as a restaurant, a grocery store, or a classroom. Other procedures that use similar approaches to teaching complex behaviors include shaping and changing procedures.

Quality behavioral programs include a systematic approach to teaching appropriate and adaptive behaviors and teaching individuals with an ASD to demonstrate those behaviors independently. For example, a child may be taught to identify various colors using flashcards in a classroom setting. It is great to learn colors in the classroom setting but the child will spend most of her life outside the classroom! Therefore, it is of utmost importance to continue to teach the child to identify colors in all environments. Learning beyond the classroom setting is referred to as generalization of a skill. Generalization of skills is key to promoting independence for individuals with an ASD. Once generalization of a skill is achieved, the practitioner monitors the use of that skill to insure the individual with an ASD maintains the skill.

Efficacy Information

The literature supporting the use of applied behavior analytic strategies for individuals with an ASD spans the last several decades. Strategies such as discrete-trial teaching, shaping, chaining, functional communication training, and token economies are just a sample of the many techniques demonstrated to be effective behavior change strategies for individuals with an ASD. The National Autism Center, the May Institute's center for the promotion of evidence-based interventions for individuals with an ASD published findings of the National Standards Project in 2010. The National Standards Project included an analysis of 775 peer-reviewed studies of treatments for individuals with an ASD. Eleven treatments reviewed in the National Standards Project met criteria to for "established treatments." Essentially, "established treatments" are treatments for individuals with an ASD that were found to be beneficial. Most of these established treatments include the use of the basic principles of applied behavior analysis.

Outcome Measurement

Professionals at May Institute have contributed hundreds of studies to the scientific literature on ASD treatment. They have measured change both at the student level (e.g., communication gains, reductions in self-injury) and at the systems level (e.g., decrease absenteeism). A sample of recent articles identifying outcome measures is below.

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Qualifications of Treatment Providers

The professionals at the May Center for Child Development include doctoral-level psychologists, board certified behavior analysts, and special educators. Speech-language pathologists, nursing staff, an occupational therapist, a physical therapist, a consulting psychiatrist, and pediatrician are also available to students attending the May Center.

See Also

▶ Applied Behavior Analysis
▶ Behavior Analysis
▶ Lovaas Approach

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M-CHAT

▶ Modified Checklist for Autism in Toddlers (M-CHAT)

MCT

▶ Visual-Motor Integration, Developmental (VMI) Test

Mean Length of Utterance (MLU)

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Synonyms

Typical length

Definition

Mean length of utterance (MLU) is the average number of morphemes per utterance. It is an

Mean Length of Utterance (MLU), Table 1 Brown's stages of language development by mean length of utterance

Stage	MLU	Age	Linguistic characteristics
I.	1.0–2.0	12–26 months	Single-word and two-word utterances that express early semantic relationships, such as action-object and action-location
II.	2.0–2.5	27–30 months	Emergence of grammatical inflections, such as present progressive tense *-ing*
III.	2.5–3.0	31–34 months	Development of sentence types including declarative, interrogative, negative, imperatives
IV.	3.0–3.75	35–40 months	Emergence of sentence coordination using early conjunctions, such as *and*, *because*
V.	3.75–4.5	41–46 months	Continued development of complex sentences including coordination, complementation, and relativization
VI.	4.5 +	47+ months	Continued refinement

index of expressive language development used beyond the stage of single words, when a child uses two or more words together in an utterance. It is calculated in 100 spontaneous utterances by counting the number of morphemes in each utterance divided by the total number of utterances. MLU is used as a benchmark to assess individual differences and developmental changes in grammatical development in children in the early stages of language acquisition. Children with autism frequently demonstrate differences in MLU compared to non-autistic developmentally delayed children and typically developing children by producing shorter utterances with fewer grammatical morphemes. Recent research has acknowledged the use and utility of using MLU as an index for language development in children with autism (Condouris, Meyer, & Tager-Flusberg, 2003; Tager-Flusberg et al., 2009).

The use of MLU as a standard for measuring children's language development was initially described in 1973 when spontaneous language transcription and morpheme analysis methods were codified and subsequent stages of expressive language development were identified (Brown, 1973). Table 1 contains the six stages identified by Brown (1973), the corresponding MLU, and the linguistic characteristics of each stage.

See Also

▶ Communication Disorder/Communication Impairment
▶ Expressive Language
▶ Expressive Language Disorder

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Measles and Autism

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Birth of a Hypothesis

In 1998, Andrew Wakefield, a British surgeon, published a case series in the *Lancet* of eight children with autistic spectrum disorder; all had received the combination measles-mumps-rubella vaccine and all had lymphonodular hyperplasia of the small intestine. This study gave birth to the notion that MMR vaccine caused autism. To avoid autism, Wakefield suggested that the three vaccines in MMR vaccine should be given separately. The hypothesis that MMR caused autism was subsequently rejected by epidemiological studies (see section titled "MMR and Autism").

Wakefield's hypothesis that MMR vaccine caused autism was rooted in his studies examining the relationship between wild-type measles virus infections and inflammatory bowel disease. These studies set the stage for his notion that measles virus – either wild-type virus or attenuated virus – could cause intestinal disease. Using a monoclonal antibody, Wakefield and coworkers detected measles virus nucleoprotein in biopsy specimens from patients with Crohn's disease. However, this monoclonal antibody was subsequently found to detect a host, not measles virus, protein and bound to intestinal tissues obtained from patients with or without inflammatory bowel disease (IBD). Studies detecting measles virus genome by polymerase chain reaction also failed to detect measles virus in patients with IBD.

Wakefield's claim that autism could be avoided by separating the MMR vaccine into its three component parts was also born of studies of wild-type measles virus. Wakefield and coworkers performed a study of children born in England during a 1-week period in 1970 by evaluating the relationship between the timing of childhood infections and IBD. Wakefield observed an increased risk for IBD in children who were infected with measles and mumps virus within the same year. However, this study was limited in that (1) few patients were studied and (2) histories of infection were obtained 4–10 years after the event raising the question of recall bias.

Wakefield later stated that his claims that wild-type measles virus caused IBD were incorrect.

Measles-Mumps-Rubella (MMR) Vaccination

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Definition

In 1998, Dr. Andrew Wakefield and coworkers at the Royal Free Hospital in London published a paper in *The Lancet* titled "Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children." The paper detailed the stories of eight children: all had recently received the combination measles-mumps-rubella (MMR) vaccine and then developed signs and symptoms of autism spectrum disorder. By endoscopy, these researchers also found evidence for lymphoid hyperplasia in Peyer's patches of the small intestine. Wakefield and his coworkers reasoned that the measles vaccine component of MMR was traveling to the intestine, inducing intestinal disease, and allowing for entrance of encephalopathic proteins that traveled to the brain and caused autism.

Media coverage from this paper caused many parents to withhold MMR vaccine for their children. As a consequence, hundreds of children developed measles in England, the United Kingdom, and Ireland, and four children

died of complications from the disease. In the United States, parents of 125,000 children withheld the MMR vaccine accounting, in part, for a measles epidemic in 2008 that was larger than any in more than a decade.

The academic and public health communities in several countries responded by examining retrospectively children who either had or had not received MMR vaccine to determine whether autism was associated with vaccination. The results were clear, consistent, and reproducible. MMR vaccine was not associated with autism. Further, the physiological basis of Wakefield's contention was refuted when other researchers were unable to identify persistent measles vaccine virus genome in autistic children more frequently than in non-autistic children. Nor were the encephalopathic proteins posited by Wakefield ever identified.

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Measure

▶ Criterion

Measurement Error

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Synonyms

Bias; Error of measurement; Standard error of measurement

Definition

Measurement error is a statistical term that refers to the difference between the obtained value or score and the hypothetical "true" value. Psychological tests rarely, if ever, provide a perfect measure of a construct. The degree of uncertainty or variability surrounding the obtained value is referred to as measurement error. Measurement error can be divided into two parts: random error and systematic error. Random errors are statistical fluctuations (in either direction) in the measured data due to precision limitations of the measurement device. Random errors usually result from the experimenter's inability to take the same measurement in exactly the same way. Random error is variation due to a wide variety of uncontrollable and unpredictable factors and cannot be eliminated within a study or a test.

Systematic error, also called "bias," may occur in the sampling stage of an experiment as when the sample obtained differs systematically from the target sample. Systematic error can also occur at the pre-measurement, measurement, or calculation stage of an experiment as when an instrument is not used as the manual prescribes or when observer-expectancy or subject-expectancy effects are allowed. Systematic error can include discrepancies in measurement tools, observational bias, or shared environment effects. Systematic errors apply universally across the sample and are referred to as "bias" in social science research. Though difficult to prevent, systematic error can be eliminated once found. Bias in sampling, measurement, or calculation can be corrected.

Measurement error is negatively correlated with reliability. According to classical test theory, reliability is the ratio of true score variance to the sum of true score variance and error score variance. The higher the reliability coefficient of a test, the more confidence was have in making interpretations about any individual test score.

IQ testing, often part of the diagnostic procedure for ASD and other developmental disabilities, provides a good illustration of measurement error. Measurement error, the discrepancy between the obtained score and the true score on a test, results from both random and systematic error. If the same person were to take the same IQ test three separate times, they may well receive three different scores. Their scores would cluster around their "true" IQ score. This is the result of random error such as sometimes guessing correctly and sometimes incorrectly. A certain amount of random error is unavoidable in measuring any construct, including IQ. Test developers have taken care to limit systematic errors that may result from inconsistent administration of the test by carefully describing administration procedures. IQ test developers have also been diligent in minimizing systematic errors that may bias the test according to sex, cultural, racial, and ethnic differences.

See Also

▶ IQ Test

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Medial Frontal Negativity (MFN)

▶ Feedback-Related Negativity

Medial Temporal Lobe

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Synonyms

MTL

Definition

The medial temporal lobe (MTL) is a region within the cerebral cortex comprised of a system of anatomically related structures, including the hippocampal region and the adjacent entorhinal, perirhinal, and parahippocampal cortices. This system is involved in the creation of declarative memory (see Squire, 1991 and 2004 for a review) and also in the regulation of emotional reactions. The MTL has been discussed as one of the candidate neural substrates underlying the social deficits in autism. Evidence from monkey studies demonstrates that neonatal lesions to the MTL result in persistent socioemotional abnormalities later in life. Additionally, declarative memory seems to be affected in high-functioning individuals with ASD who were found to have deficits in episodic memory, with relatively intact semantic memory. Postmortem investigation of the brain in eight individuals with autism also revealed microscopic cytoarchitectonic abnormalities (increased cell density and small cell size) in MTL structures.

See Also

▶ Declarative Memory
▶ Episodic Memory
▶ Semantic Memory

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Mediated Learning Experience

▶ Dynamic Assessment

Medical Conditions Associated with Autism

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Synonyms

Genetic disorders; Nutritional issues; Pica; Seizures; Sleep disorders

Background

Children with autism spectrum disorders (ASD) including autism, Asperger's syndrome, and pervasive developmental disorder, not otherwise specified, have similar medical problems as children without disabilities. These children can have colds or ear infections as well as other typical illnesses of childhood and adolescence. Little research has addressed the medical problems of adults with autism. The primary care provider should monitor the health of individuals with ASD in the "medical home." The medical home describes a source of primary care that is accessible, continuous, culturally sensitive, and providing coordinated care. A recent report indicated that children with autism spectrum disorders were less likely than children with other special needs to receive their care in a medical home (Brachlow, Ness, McPheeters, & Gurney, 2007). This leads to more financial needs for the parents and more problems with access to care (Kogan et al., 2008). In addition to routine and disorder-specific anticipatory guidance, individuals with ASD need to be monitored for medical conditions for which they may be at higher risk including seizures, genetic abnormalities, sleep disorders, disordered eating/nutritional issues, pica, and GI issues.

Seizures

Seizures develop in approximately 10–25% of children with autism (Myers, Johnson, & American Academy of Pediatrics Council on Children with Disabilities, 2007). There is no one type of seizure that is more common than other seizure types. Children with ASD can have absence seizures (staring spells), tonic–clonic (grand mal seizures), myoclonic jerks, atonic seizures (drop attacks), or partial seizures (movements without loss of consciousness). The first peak time for onset of seizures in children with ASD is between 1 and 5 years of age. The second peak occurs in adolescence between 12 and 18 years of age (Myers et al., 2007). The anticonvulsant medications used for other individuals with

seizures are used to treat seizures in individuals with ASD.

Landau–Kleffner syndrome is a seizure disorder that may be considered in the differential diagnosis of ASD. This rare type of seizure has a characteristic EEG pattern and can cause a regression in language or aphasia (Kliegman, Behrman, Jenson, & Stanton, 2007). Landau−Kleffner syndrome is more common in boys, with regression in language and seizure onset in previously socially typical children at around age 5. This regression occurs later than that typically seen in ASD. Some of the behaviors can be similar to those seen in children with ASD including agitation, poor attention span, and irritability. In 70% of the children with Landau−Kleffner syndrome, there is another seizure type. Obsession and insistence on routine are not typically seen. Anticonvulsant medication may improve symptoms in Landau−Kleffner syndrome. Anticonvulsant medication may be useful for agitation or other behaviors in children with ASD in addition to seizure control, but it does not improve language.

In general, seizures are not a sensitive predictor of outcome in children with ASD. However, the prevalence of seizures is higher among individuals with moderate to severe intellectual disability and those with motor deficits. In children with severe intellectual disability and ASD, seizures may occur in up to 42%. In children without intellectual disability, etiologic or genetic diagnosis, or family history of epilepsy, the rate is only 6−8%. Individuals with autism plus epilepsy have on the average lower IQs and poorer adaptive, behavioral, and social outcomes than those without epilepsy. There are also higher rates of abnormalities on electroencephalography (EEG) without clinical seizures among people with ASD. The rate may be as high as 10−72%. The medical literature has not demonstrated benefit to treating these electroencephalographic abnormalities. There is currently not enough evidence to suggest routine screening EEGs without history or clinical evidence of seizures. Since the rate of seizures is higher in children with ASD, EEG should be considered whenever there are symptoms consistent with seizures (Myers et al., 2007).

Genetic Abnormalities

There is a 60−90% concordance rate of ASD in identical twins, which means that most of the time identical twins both have ASD. In fraternal twins, there is only a 30% concordance rate (Kliegman et al., 2007). Recent studies support that a strong genetic predisposition to autism is genetic, although there is a significant environmental impact as well.

No consistent genetic abnormalities are found in individuals with ASD, although the overall prevalence of genetic abnormalities on testing may be as high as 20%. The rate of fragile X is reported to be 0.045%, and the rate of abnormality on karyotype (or evaluation of the structure of stained chromosomes by microscopy) is 5% or less (Miller et al., 2010). A new genetic test called chromosomal microarray (CGH) compares the units of DNA in an individual to the composite normal to identify duplications (gain of material) or deletions (loss of material). Abnormalities on CGH microarray are seen in approximately 17–20% of the children with autism spectrum disorders who complete this testing (Shen et al., 2010). Not all of the abnormalities found on CGH microarray in individuals with ASD are associated with or cause autistic symptoms. In the most thorough and recent study, 9% of CGH abnormalities were considered abnormal or likely to be causative of the autism symptoms. Children with dysmorphic (or unusual) features and those with lower cognitive skills are more likely to have abnormalities on genetic testing.

Specific syndromes associated with ASD include X-linked intellectual disability, tuberous sclerosis, and Angelman syndrome among other disorders. Fragile X is the most common inherited cause of intellectual disability. These children have intellectual disability, macrocephaly, large pinnae, hypotonia, and joint laxity (Johnson, Myers, & American Academy of Pediatrics Council on Children with Disabilities, 2007). Roughly 20% of the children with fragile X also have ASD symptoms (Hatton et al., 2006). However, only 0.045% of children with ASD have fragile X (Shen et al., 2010). Children with tuberous sclerosis have hypopigmented skin areas, have brain and skin tumors (CNS hamartomas and fibroangiomata), are at a high risk for seizures, and have ADHD or autistic-like behaviors. Angelman syndrome is characterized by global developmental delays especially with language, a wide-based ataxic gait, and progressive spasticity with a particularly jovial personality. This is caused by various genetic abnormalities of chromosome 15 q11-13. Females with symptoms of ASD should be considered for Rett syndrome caused by the MeCP2 gene. Midline hand-wringing or patting behaviors will typically distinguish these children from those with ASD alone.

Sleep Disorders

Sleep problems are very common in children with autism spectrum disorders and can occur throughout childhood and adolescence. The sleep disorders are variable and can include difficulty settling to sleep, early rising, night wakening, sleep walking, or night terrors. The lack of sleep can affect daytime functioning including behaviors, cognitive skills, and memory. Frequent sleep problems greatly affect family stress and functioning.

Sometimes, there is a medical cause for the sleep problems such as gastroesophageal reflux, obstructive sleep apnea, or nutritional deficiency (e.g., decreased iron stores associated with restless leg syndrome). Children with GERD or gastroesophageal reflux disease can have some vomiting or discomfort during the night from stomach acid refluxing into the esophagus. Obstructive sleep apnea is a respiratory problem during sleep where the airway does not remain patent. This causes the person to awaken. With the interrupted sleep, children can be inattentive or agitated during the day (Myers et al., 2007).

The medical literature does not contain data at this time regarding the frequency of medical causes for sleep difficulties in people with ASD. History and physical exam are used to determine

the need to perform a medical workup for causes of sleep problems. In most children, behavioral measures are used to treat the sleep problems. Behavioral measures can include setting up a bedtime routine. Medications sometimes used include melatonin, alpha-adrenergic agonists (such as clonidine and guanfacine), and antihistamines (such as diphenhydramine). Further research needs to be done on the causes of sleep difficulties in people with ASD as well as effective treatments.

GI Issues

The prevalence of GI issues in children with autism spectrum disorders varies from 9% to 72%. The most common problems are chronic constipation or chronic diarrhea. One reason for the difficulty in assessing this problem is the communication difficulty children with ASD often have. Many children are nonverbal, and many of those who can communicate have difficulty with describing subjective feelings or isolating a source of pain. Some children will not have identifiable symptoms relative to the GI tract, but instead will have behavioral changes or changes in sleep patterns as evidence of GI issues. Careful evaluation including full physical exam and medical history are indicated anytime there are major changes in the behavior of an individual with ASD.

The common GI problems that are seen in other people can also be seen in people with ASD. An individual with constipation might have hard infrequent stools or might stool daily with distress. They might also have behavioral problems that are only clarified when physical exam palpates stool or an x-ray identifies significant constipation. Treatment might include a bowel regimen. Chronic diarrhea is also reported in people with ASD. The same etiologic workup entertained for other patients should be performed. Abdominal discomfort may be due to common problems such as lactose intolerance or less frequent medical disorders such as celiac disease. History and physical exam are important sources of information to the clinician in determining initial workup and appropriate referral to a gastroenterologist.

The evidence for autistic enterocolitis (leaky gut) is limited at this time. Prospective studies need to be done on the causes and treatments of the GI symptoms reported in individuals with ASD.

Nutritional Deficiencies

Food aversions are commonly reported in children and youth with ASD. In addition to self-restriction, dietary restriction for therapeutic reasons might occur.

The gluten-free and casein-free diet is a popular dietary treatment for the symptoms of autism. This involves removing all foods that contain gluten from wheat, barley, and rye, and casein, found in milk products. This diet may impact protein quality of food consumed (Arnold, Hyman, Mooney, & Kirby, 2003). It also requires provision of an alternate source of calcium and vitamin D than dairy products.

Children with ASD who have a limited food repertoire are at risk for consumption of an inadequate diet (Bandini et al., 2010). The impact of a limited diet on long-term health requires further study.

Pica

Pica is the ingestion and mouthing of nonfood objects. Chewing or mouthing toys and things in the environment is typical in children less than 12 months of age. Pica can persist because of sensory reasons, delay to a younger developmental level, anxiety, and may be due to nutritional deficiencies such as iron deficiency. Pica can also lead to increased lead levels from ingestion of lead dust in the environment or items manufactured with lead. It is advisable to continue monitoring lead levels in children who continue to have pica beyond the toddler stage when monitoring typically occurs (Myers et al., 2007).

Pathophysiology

There are a number of medical conditions associated with autism spectrum disorders (ASD).

Except for some genetic and neurologic abnormalities, medical conditions associated with ASD are not responsible for the symptoms of autism. Discomfort and medical illness can exacerbate behavioral symptoms. Medical and dental causes of new-onset behaviors should be considered.

Hypotheses have been generated associating GI pathology such as leaky gut or increased permeability with symptoms of ASD. More recent studies have not confirmed this association; however, the potential for disorders affecting brain and gut requires further study. There is no specific pathology identified to cause the constipation, diarrhea, or abdominal pain reported in children with ASD. Lymphonodular hyperplasia (lymph nodes in the intestine) may be a normal variant. Investigators are pursuing the possibility of immunologic differences in the intestine in children with ASD.

The etiology of the sleep difficulties of children and youth with ASD may be related to abnormal melatonin metabolism, atypical sleep architecture, restless leg syndrome, or behavioral sleep disorders. Etiologic and therapeutic studies are ongoing to address sleep in individuals with ASD.

See Also

▶ Gastrointestinal Disorders and Autism
▶ Genetics
▶ Intestinal Permeability Studies
▶ Leaky Gut Syndrome
▶ Physical and Neurological Examination
▶ Pica
▶ Seizure
▶ Seizure Disorder

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Medical Evaluation in Autism

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Definition

All children diagnosed with an autism spectrum disorder should have an evaluation by a medical professional to consider the potential causes of developmental disability and evaluate the individual for common co-occurring medical conditions. The medical evaluation includes a physical examination and neurological examination. Consideration of genetic causes requires laboratory testing most commonly using chromosomal microarray. Other genetic screening tests might include testing for X-linked intellectual disability, Rett syndrome, or other diagnoses suggested by the history and physical examination.

Historical Background

In 1941, Dr. Leo Kanner first described autism as a discrete disorder. Around the same time, Dr. Hans Asperger identified a similar disorder in Germany. While a similarity to childhood schizophrenia led many to consider autism a psychiatric disorder, Dr. Bruno Bettelheim in the 1950s attributed it to cold parenting. In the 1960s, Dr. Bernard Rimland proposed that there was a biologic basis for autism. The capacity to karyotype and see genetic abnormalities associated with disease states was developed in the1960s which led to the identification of genetic syndromes. Chromosome analysis was not routinely done on children with developmental differences until 1966. The biggest breakthrough in etiologic evaluation of developmental disability occurred when phenylketonuria or PKU was identified as a metabolic problem that could cause developmental delays and autism. This disorder resulted in ASD in 20% of untreated cases. Now, with newborn screening, it is a preventable cause of ASD. Similarly, prior to the introduction of the rubella vaccine, congenital rubella was a cause of autism that has been eliminated.

Advances in neuroimaging allow for investigation of central nervous system anomalies when indicated by history and physical examination.

Current Knowledge

The current recommendation for evaluation of children diagnosed with autism spectrum disorders is to start with a thorough history and physical exam. The clinician should obtain a three-generation genetic family history and full history including past medical history, developmental history, and behavioral history. The history often guides the rest of the evaluation. All children with language delays should have a hearing evaluation. In children who are school age and verbal, school hearing tests may suffice (Myers, Johnson &, American Academy of Pediatrics, Council on Children with Disabilities, 2007).

The next level of testing depends on the combined information from the history and physical exam. Routine EEG and neuroimaging are not recommended by the American Academy of Pediatrics at this time. MRI is indicated with recent or atypical regression, an abnormal neurologic exam, or a suggestive history for neurologic disease. EEG is indicated with recent or atypical regression or a history suggestive of seizures.

The current newborn screening in the United States will pick up many of the inborn errors of metabolism such as PKU, galactosemia, and congenital hypothyroidism. Maternal screening for rubella identifies pregnancies at risk for congenital rubella syndrome. If the newborn screening was not completed or is not available, then metabolic testing with quantitative amino acids should be considered in a child whose history and physical exam suggest possible inborn errors.

Comparative genomic hybridization microarray is considered the first-line genetic evaluation by the American College of Genetics. A recent study indicated that 17% of children with an ASD will have an abnormality on this testing (Shen, 2011).

However, most of these abnormalities are considered benign. Children with intellectual disability, female gender, or dysmorphic feature may be more likely to have a genetic etiology identified from these evaluations (Roesser, 2011). While comparative genomic hybridization (CGH) microarray can pick up a large number of duplications or deletions, there are some translocations that can only be seen on karyotype. Karyotype examination is often obtained when there is a family history of greater than 2 miscarriages or a specific diagnosis such as Down syndrome is suspected.

Genetic testing for Rett syndrome should be considered in girls diagnosed with ASD. They may demonstrate microcephaly or deceleration of head growth in early childhood. Other clinical markers of Rett syndrome include stereotypical hand movements and psychomotor regression. Patients with webbing of toes, mildly dysmorphic features, or failure to thrive could have Smith–Lemli–Opitz syndrome. In this case, 7-dehydrocholesterol level should be sent. A lipid panel may also pick up the extremely low cholesterol level. Children with ASD and seizures should have consideration of Angelman syndrome that has a characteristic chromosome 15 deletion.

Children with macrocephaly may be at increased risk of PTEN (phosphatase and tensin homolog) gene mutations. The PTEN mutations are tumor-suppressor genes associated with hamartomatous syndromes such as Bannayan–Riley–Ruvalcaba syndrome and Cowden syndrome. They are at risk for tumors in the thyroid, breast, and uterus. Any child with macrocephaly and family history of any of these cancers should have an evaluation for this.

Referral to a geneticist may be indicated for assessment of genetic workup, metabolic disease, dysmorphic syndromes, and genetic counseling. Children with regression, microcephaly, neurocutaneous lesions, midline facial defects, abnormalities in neurologic examination, or a history of seizures may require referral to a neurologist. MRI may be necessary. A screening MRI is not necessary for macrocephaly alone or single cafe au lait spot. EEG may be needed if there is suspicion of seizures. Seizures are seen in 25% of children with autism.

Lead testing is not part of the routine etiologic workup for autism, but could be considered for children with pica or for those at environmental risk if not previously obtained in the course of well-child care. Children with pica are at continued risk of lead poisoning at a much older age. Children with limited diets may benefit from nutritional evaluation to ensure adequate growth and development.

Future Directions

Over time, genetic diagnostics have become more accurate. Initially testing could only identify large abnormalities on karyotype analysis. Now, smaller abnormalities can be detected. The technology is emerging, so the clinical significance of some of these differences is not clear. In the future, the available knowledge about behavioral, medical, and other phenotypic information about these microdeletion and microduplication syndromes will increase. New genetic testing modalities may be developed. New uses for MRI, functional imaging, and brain spectroscopy will be evaluated and become more widely available.

See Also

▶ Lead Exposure and Autism
▶ Medical Conditions Associated with Autism
▶ Rubella
▶ Seizure

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Medulla

▶ Medulla Oblongata

Medulla Oblongata

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Synonyms

Medulla

Definition

The *medulla oblongata* is the lowest of the three structures of the brain stem (the pons and the midbrain are the other two), and as such, it participates in the brain stem's important role in serving as the modulator and integrator of any information exchange between the brain and the proprioceptive and exteroceptive systems of the human body. In the light of the fact that ASD is becoming recognized increasingly as a problem of the nervous system integrity involving many functions of

the brain, one might predict that the brain stem, in particular medulla oblongata, would have a significant share in the neuropathology of ASD. In fact, earlier postmortem and MRI structural imaging studies on the brain stem found all three structures significantly smaller in individuals with autism (Gaffney, Kuperman, Tsai, & Minchin, 1988; Hashimoto et al., 1993). These studies, however, suffered from the presence of confounding variables and were contradicted by concurrent and later studies, even though more recent volumetric studies of both white and gray matter continue to implicate the brain stem (Goldberg, Szatmari, & Nahmias, 1999; Rodier, 2002).

Neurochemical abnormalities in individuals with ASD have served as another link between medulla oblongata and autism. Serotonin is a neurotransmitter that is synthesized from tryptophan by neurons in the raphe nuclei of the brain stem reticular formation, which extends along all three structures of the brain stem. Autistic individuals have been found to have elevated whole-blood serotonin 5-HT levels and decreased tryptophan retention, both indicating a decrease in brain serotonin binding (Chugani et al., 1997; Carter et al., 2011; Kaluzna-Czaplinska, Michalska, & Rynkowski, 2010).

See Also

▶ Midbrain
▶ Serotonin

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Mellaril

▶ Thioridazine

Mellaril-S

▶ Thioridazine

Memantine

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Definition

Memantine: Memantine is a selective blocker of a specific glutamate receptor in the brain. It is approved for the treatment of dementia. It is also used in combination with the cholinesterase inhibitors such as donepezil. Memantine is presumed to have beneficial effects on Alzheimer's dementia because of its blockade of this specific glutamate receptor. It has not been well studied in children or adults with autism.

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Memory

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Synonyms

Recollection; Remembrance

Definition

The multifaceted process of encoding, storage, and retrieving knowledge of things that we have experienced, imagined, and learned. Memory is often measured using tasks associated with recall, retrieval, or recognition. There are a wide range of memory abilities in individuals with autism spectrum disorder (ASD), with some showing significant impairments across multiple types of memory, and others showing "savant" skills. Most commonly, individuals with ASD have a profile of strengths and weaknesses that vary across specific subtypes of memory.

See Also

▶ Declarative Memory
▶ Episodic Memory
▶ Explicit Memory
▶ Free Recall
▶ Memory Assessment
▶ Memory Development
▶ Recognition Memory
▶ Retrieval of Information
▶ Rote Memory
▶ Semantic Memory
▶ Short-Term Memory

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Memory Assessment

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Definition

The assessment of memory in ASD is carried out by researchers attempting to delineate the pattern of strengths and weaknesses in memory and learning in ASD generally and to understand the psychological, neurobiological, and etiological correlates of the atypical memory profiles delineated. Memory assessment may also be carried out by practitioners to delineate and understand atypical patterns of learning and memory in individuals with ASD with the aim of developing effective intervention strategies. Very little assessment of the neurobiological and etiological correlates of atypical memory and learning in ASD has been carried out, and what follows relates exclusively to the psychological assessment of memory.

Current Knowledge

Memory is involved in the acquisition, storage, retrieval, and everyday use of associations, habits, skills, perceptual images, words, facts, and personal experiences. It is therefore a critical component of all kinds of learning. People with ASD across the spectrum show certain atypical patterns of memory and learning, including some outstanding strengths as well as certain limitations. In lower functioning individuals with ASD, moderate or severe memory limitations contribute to clinically significant learning disabilities. At the same time, memory strengths in both lower and higher functioning individuals may be utilized in compensatory learning. It is therefore practically as well as theoretically important to characterize the pattern of memory strengths and weaknesses in people with ASD and to understand how and why uneven memory profiles occur, both generally and individually. This in turn requires that appropriate investigative procedures are developed and used by researchers and that appropriate assessment tools are available to practitioners. A representative selection of experimental research procedures and clinical assessment tools is outlined below.

Experimental Assessment Procedures

The Assessment of Implicit, or Non-declarative, Learning

Many associations, habits, skills, and perceptual images are acquired "implicitly," that is to say, without conscious awareness or control of what is being learned, although there may be an intention to learn. Moreover, what has been learned implicitly is not generally available to report – hence the term "non-declarative." For example, babies work hard at learning to walk, oblivious of the increasingly well-entrenched changes in brain activity and muscle coordination that are occurring every time they struggle to their feet and stagger a step or two. Similarly, they unconsciously learn the sound system and grammatical rules of their native language without awareness of the rules and regularities they are acquiring. Because implicit learning takes many forms, it can be experimentally assessed in many ways. A few examples, all of which have been used in investigative studies of people with ASD, are given below:

- Conditioning. When used with vulnerable people, a typical conditioning test might consist of shining a dim light into an individual's eye just before delivering a small puff of air onto the eyeball (as in a standard test used by opticians) which produces a reflexive blink, and measuring how many repetitions of this procedure are needed before the dim light elicits a reflexive blink in the absence of a puff of air.
- Category Formation. Basic-level categories relating to common objects, actions, or qualities are largely acquired implicitly from the first weeks of life onward. There are various theoretical models of how this is achieved. One well-authenticated model involves the (unconscious) acquisition of a prototype (e.g., the most typical form of a "dog" or a "tree"). A commonly used category formation task involves showing the examinee pictures of an imaginary creature (e.g., a "moodle") defined by a particular set of probabilistic features (e.g., a longish and somewhat crooked nose, a shortish tail) and contrasting moodles with "non-moodles" (which in some ways resemble moodles, but which lack their prototypical features) by sorting into two piles. Examinees are then asked to try to sort a different set of moodles from the non-moodles with correction from the tester. A critical measure of category formation is whether or not representations of a prototypical moodle are correctly sorted.
- Sequence Learning (as, e.g., in acquiring motor skills, habitual routines, or other forms of "procedural" learning). A serial response task is commonly used to assess implicit sequence learning. In this task, a stimulus (e.g., an asterisk) appears in one of several locations on a computer screen in a repeating sequence, and participants respond to each appearance by pressing a corresponding key. Learning is demonstrated by a decrease in response time on trials when the locations follow the sequence and by an increase in response time on trials when locations do not follow the sequence.

The Assessment of Explicit, or Declarative, Memory and Learning

Words and their meanings, factual knowledge, and the content of personal experiences are at least potentially available to conscious awareness during learning and potentially available to subsequent report, hence the term "declarative." The content of declarative memory may broadly be described as "things that we know that we know," even if we need some prompting to recover the memory.

Whereas experimental tests of implicit learning in people with ASD are currently mainly directed toward answering the question "Can people with ASD do this?", the peaks and troughs of explicit memory in people with ASD are already quite well established (Boucher, Mayes, & Bigham, in press). In brief, the most able individuals with ASD have good vocabularies (even though words may not always be used in entirely typical ways); they have excellent ability to acquire factual knowledge, especially relating to topics of special interest; but they have some difficulties in recalling personal experiences, especially the more subjective elements, such as how they themselves were feeling at the time. Less able individuals with ASD may have across the board difficulties with declarative memory. Because profiles of declarative memory abilities across the spectrum are relatively well established, experimental assessments of explicit learning are mainly directed toward answering questions concerning *why* the patterns of memory peaks and troughs occur and differ across the spectrum.

Declarative memory tests may be designed to investigate critical differences in the *kinds of things* examinees can or cannot easily remember. Critical differences that have been investigated in people with ASD include:

- The complexity of the material to be remembered (e.g., comparing the ability to recall lists of unrelated words, as opposed to related words, sentences, or stories; and pictures of single objects, as opposed to scenes)
- The social connotations of the material (e.g., comparing the ability to recognize pictures of faces as opposed to buildings)

- The extent to which the examinees themselves played a role in the action or event to be remembered (e.g., comparing memory for actions they themselves have carried out as opposed to those the tester carried out)
- The modality of the material to be remembered (e.g., comparing memory for spoken as opposed to written words)

Other tests are designed to investigate differences in the *learning and recalling conditions* that may contribute to memory peaks as opposed to memory troughs. For example:

- "Learning over trials" as opposed to "single trial learning."
- "Intentional" as opposed to "incidental" learning, that is, tests in which the examinee is instructed to try to remember the pictures they will be shown or the gist of the story they will hear as compared with tests in which they are simply shown some pictures or read a story and then unexpectedly tested for memory of what they have seen or heard.
- Computer-based as opposed to person-led learning.
- Recognition tests (which of these pictures did you see just now?) as opposed to free recall tests (what objects did you see in the pictures you saw just now?) and "free recall" as compared to "cued recall" tests (one of the pictures was of a kind of fruit/began with the sound "b").
- Immediate as opposed to delayed memory tests.

Yet another group of experimental memory tests focuses on the *processes* that may underlie memory peaks as opposed to memory troughs in ASD. For example:

- Tests of encoding biases, such as tendencies to encode (register into memory) details of a scene rather than the scene as a whole; or the sound rather than the meaning of heard words
- Tests of retrieval processes (i.e., the processes by which what has been unconsciously learned or consciously memorized becomes accessible for use) and especially difficulties that people with ASD may have in effortful and strategic forms of memory search where few or no cues or prompts are available as opposed to associatively triggered memories or recall in response to informative cues or leading questions

The Assessment of Working Memory

"Working memory" involves the ability to maintain information in short-term memory while simultaneously operating on it in some way. Maintaining information in short-term memory is not by itself a major problem for people with ASD, as is evident from their good rote memory ability. However, the simultaneous maintenance and manipulation of information involve executive control and may be problematic. Experimental assessment of working memory in people with ASD is at the stage of delineating the kinds of working memory tasks on which people with ASD reliably succeed as compared with those they find significantly difficult.

Some experimental assessments of working memory that have been used with people with ASD are described below:

- Backward Digit Span. In this task, the examinee must register and maintain in short-term memory a serially presented list of, for example, seven digits, and subsequently report the sequence in reverse order.
- "N-back Tasks." In this kind of task, the examinee might be asked to name individual letters successively presented on a screen and to press a response key if the letter on the screen is the same as the last-but-one letter presented or the same as the last-but-two letter presented.
- Self-ordered Pointing Tasks. In this type of task, the examinee might be shown a set of line drawings of, for example, nine everyday objects located on a 3×3 grid. The set is reproduced nine times with no object appearing in the same location twice. The examinee is shown each reproduction in turn and instructed to point to a different item each time, requiring them to hold in mind a cumulative list of items already responded to.
- Prospective Memory Tasks. "Prospective memory" involves "remembering to remember" to do something, for example, remembering to take swimming things to school on a Wednesday, to post a birthday card to

grandma tomorrow, and to take the saucepan off the hob at a certain time. Experimental tests of prospective memory generally involve giving an instruction such as "remember to press the red button whenever you see an animal on the screen/once a minute" and then giving the examinee some other task to be getting on with, such as sorting pictures on the screen by their color. The measure of prospective memory ability is the number of times the original instruction is acted on, either in response to the "event cue" (an animal occurring on the screen) or in response to the "time" cue (an internal estimate of 1 min).

Clinical Assessments

Most clinical assessments of memory have been developed for use with adults with medical conditions known to be associated with memory impairments or anomalies, such as head injury, stroke, Alzheimer's disease, or posttraumatic stress disorder. Some of the best-known of these clinical assessments are designed to test a broad range of memory abilities. Others have been designed to assess in greater detail some specific form of memory. Versions of some assessment procedures developed for adults have subsequently been developed for use with children. Other procedures have been developed specifically for use with children and are not suitable for use with adults. A representative selection of clinical assessment procedures, all of which have been used for the assessment of memory in people with ASD, is listed below:

- *The Wechsler Memory Scale, 3rd edition* (Wechsler, 1997). This widely used test consists of subtests assessing immediate auditory and visual-spatial memory and subtests assessing story recall, verbal paired-associate learning, face recognition, and recall of the content of pictures of family scenes, this latter group of subtests being assessed in both immediate and delayed recall conditions.
- *The Rivermead Behavioural Memory Test, 3rd edition* (Wilson et al., 2008). This test is designed to assess memory using materials

and situations resembling everyday situations. So, for example, prospective memory is assessed, as is memory for a route, and learning to associate a name with a face. There is a children's version of this test: *Rivermead Behavioural Memory Test for Children* (Wilson, Ivani-Chalian, & Aldrich, 1991).

- *The Doors and People Test of Visual and Verbal Recognition and Recall* (Baddeley, Emslie, & Nimmo-Smith, 1994). This test, as its name indicates, is designed to assess person-related as compared to object-related memory, visual as opposed to verbal memory, and recognition as opposed to recall. It can be used with children as well as adults.
- *The California Verbal Learning Test-II* (Delis, Kramer, Kaplan, & Ober, 2000a). This test assesses memory for word lists in a variety of conditions, including comparisons of single trial versus multiple trial learning, immediate versus delayed recall, free recall versus recognition versus cued recall, and "old list" versus "new list" learning. There is a children's version of this test: *The California Verbal Learning Test for Children-II* (Delis, Kramer, Kaplan, & Ober, 2000b).
- *The Autobiographical Memory Interview* (Kopelman, Wilson, & Baddeley, 1990). This test uses a structured interview format to probe the ability to recall facts and specific incidents from the individual's past life, from childhood to recent time.
- *The Benton Face Recognition Test* (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). In this test, each test item consists of a black and white photograph of a face set above a choice of six other black and white photographs of faces in a variety of orientations, and examinees must indicate whether one or more of these are of the person in the target picture.
- *The Rey-Osterrieth Complex Figure Copying and Memory Test* (Osterrieth, 1944). As the name of this test suggests, examinees are first asked to copy a complex abstract figure. This is then removed, and the examinee is immediately asked to draw the figure again, this time from memory. Following a delay, they are again asked to draw the figure from memory.

Tests developed specifically for use with children include:

- *The Wide Range Assessment of Memory and Learning* (Sheslow & Adams, 1990). The content of this test broadly corresponds to the content of the adult-targeted Wechsler Memory Scale (see above).
  - *The Children's Memory Scale* (Cohen, 1997). The content of this test also corresponds broadly with that of the Wechsler Memory Scale. More specifically, it is described as assessing verbal and visual memory; short delay and long delay memory; recall, recognition, and working memory; and the role of attentional factors in memory.
- *The Children's Nonword Repetition Test* (Gathercole & Baddeley, 1996). This test of immediate short-term memory assesses the ability to repeat accurately a series of made-up words of increasing length.

The above list represents only a small selection of clinical assessment procedures, and many more are available and have potential value for better understanding the nature and causes of uneven memory abilities in ASD. A comprehensive list of assessment procedures can be found in Lezak, Howieson, and Loring (2004).

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Memory Development

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Definition

The concept of *Memory Development* may appear to require few introductions, but closer

inspection reveals certain complexities that are important to note. For one, the notion of development must not be misunderstood as referring exclusively to the changes in behavior and cognition that accompany infancy and early childhood. Although this early stage of development is of key interest, important changes also take place later in life, and since adults come to be the way they are through their developmental history, they must not be overlooked as a rich source of information about developmental processes. Just as the archeologist is able to infer what events took place in a distant past from the study of ancient treasures, so the developmental psychologist can make certain inferences about the principles of development by taking a close look at adult behavior. What also renders the concept of memory development complicated is the fact that "memory" is far from the transparent phenomenon that our common usage of the term may have us believe. Whether we forget the name of a person we have just been introduced to, the capital of a country we once visited, the location of our car in a car park, or a certain sequence of key strokes on the piano, we are always quick to blame our *memory* for our failures. Yet, decades of research have shown that such instances of forgetting are not the result of the failures of a single memory system or process but of the imperfections of a number of such systems and processes that each contributes in specific ways to our ability to learn from the past. It is beyond the scope of this entry to provide a summary of the various approaches that have been taken to carving the nature of memory at its joints (for overviews relevant to the study of autism, see Gardiner, 2008 and Mottron, Dawson & Souliéres, 2008), but two distinctions require a brief comment. The first is the division between *procedural* and *declarative* memory. Procedural memory describes memory for sequences of motor behaviors that can be learned and expressed without the necessary involvement of conscious awareness. Declarative memory, by contrast, describes memory for information that is learned and retrieved under the influence of conscious awareness. This entry will only concern issues relating to declarative memory development since the vast majority of research in autism has addressed this domain. The second distinction is based on the observation by Tulving (1985) that not all of our declarative memories are associated with the same kind of conscious experience. The memory of the name of our childhood primary school, for instance, is qualitatively different from that of our first day there. The former is associated with a *noetic* sense of awareness (knowing) that is relatively void of a feeling of personal belonging. It characterizes retrieval from our *semantic memory system* that constitutes a store of impersonal facts and knowledge about the world. *Autonoetic* awareness (remembering), by contrast, accompanies retrieval from our *episodic memory system*, which encompasses all those memories that revolve around our "self" in the past. These distinctions are critical when considering how memory develops since the lack of language during the earliest stages of development makes it impossible for infants to "declare" what they remember and how they remember it. As a result, the study of memory development in very young children is complicated, and when language development follows an atypical trajectory, such as in the case of autism, matters become even more intricate. It is thus perhaps not surprising that the study of memory development in autism has adopted the archeological route of focusing on adults as a source of information. The patterning of memory strengths and weaknesses in older groups has provided important clues about what role disturbances in memory development may play in the origin and/or maintenance of the clinically defining manifestations of autism, and together with advances in the methods for studying how memory matures during the first few years of life, these clues are beginning to open promising new research avenues for the near future.

Historical Background

Memory research in autism has a long history that begins with the seminal work of Beate Hermelin and Neil O'Connor in the 1960s

(Hermelin & O'Connor, 1970). At that time, cognitive approaches and associated computer analogies of the mind/brain relation dominated the field of psychology, and autism was finally beginning to be accepted as a neurodevelopmental disorder rather than the consequence of pathological parenting. In the context of these developments, Hermelin and O'Connor set about to determine how the autistic mind *processed* and *stored* information, and they soon made a discovery that remains valid up to the present day. In a series of experiments, they demonstrated that children with autism did not benefit from "meaning" when trying to remember sets of stimuli. For instance, whereas typically developed children would remember grammatically correct sentences far better than random sequences of words, children with autism would remember both sets of stimuli equally well. Similarly, children with autism did not demonstrate a mnemonic advantage for meaningfully related as compared to unrelated words or pictures, while children without autism reliably did. Together these findings led Hermelin and O'Connor (1970) to conclude that autism was characterized by an impairment in processing information meaningfully and numerous subsequent studies have lent support to this suggestion. Another early discovery was the observation that tests of free recall pose disproportionate difficulties for individuals with autism. Free recall relies almost exclusively on the operations of the episodic memory system and requires the retrieval of previously learned information with only minimal support (e.g., "Tell me all the words you can remember"). Boucher and Warrington (1976) showed that children with autism were significantly impaired in recalling namable pictures, written words, and spoken words despite performing similarly to comparison children when retrieval cues were provided at test (e.g., "Can you remember something you sit on" for the item "stool"). Importantly, this pattern highlighted a parallel with patients who suffered damage to an area of the brain known as the hippocampus, leading Boucher and colleagues to conclude that this medial temporal lobe (MTL) structure was likely to play a critical role in the neurodevelopmental origins

of autism (see Mayes & Boucher, 2008 for a recent review of the relevant evidence).

As ahead of their time as these early pioneers were, their insights and discoveries were soon to fall by the wayside in favor of other conceptual developments in the field. The discovery that children with autism lacked a "theory of mind" (Baron-Cohen, Leslie & Frith, 1985) began to dominate the search for the developmental origins of the disorder during the 1980s and the formulation of the weak central coherence (WCC) theory around the same time soon appeared to provide an elegant explanation for the findings by Hermelin and O'Connor (1970) in terms of a detail-focused rather than a holistic and meaning-focused processing style in autism (e.g., Shah & Frith, 1993). In addition, it was thought that the kind of memory difficulties experienced by individuals with autism could not possibly contribute causally to the development of the disorder since the memory processes relevant to these difficulties (i.e., primarily episodic processes) were widely thought not to mature until the age of 3–4 years in the course of typical development. In other words, there was a widespread conviction that memory difficulties emerged after the clinically defining symptoms of the disorder. For the next 20 years, therefore, the dominant topic of discussion was the nature of the relationship between the detail-focused processing style of individuals with autism and their difficulty in understanding the minds of others. Research on memory merely continued at the fringes of scientific awareness. Today, however, developments in both the autism memory literature and the mainstream memory development literature are beginning to draw attention to the possibility that atypical learning and memory processes may play a much more important role in the development of autism than originally thought.

Current Knowledge

In order to understand why interest in the learning and memory difficulties of individuals with autism is growing, it is necessary to provide an

overview of the developments in two distinct literatures – that concerning the patterning of memory strengths and weaknesses in autism and that concerning how memory typically develops during the first years of life.

Memory Strengths and Weaknesses in Autism

As already alluded to, our current knowledge about memory function in autism stems primarily from studies of children, adolescents, and adults who have sufficient language and general intellectual abilities to cope with the demands of declarative memory tasks. Work with these relatively high-functioning individuals generally confirms the original conclusions by Hermelin and O'Connor (1970) and Boucher and colleagues (e.g., Boucher & Warrington, 1976) that individuals with autism experience difficulties in drawing on meaning to facilitate memory and that their performance on free recall measures is disproportionately attenuated compared to supported test procedures such as cued recall and recognition. Close scrutiny of these phenomena in recent years, however, has led to a more refined understanding of why a difficulty in drawing on meaning should coincide with disproportionate difficulties in free recall, and three sets of observations have proven particularly informative in this context. First, it is now widely accepted that autism is characterized by impairments in episodic memory that go beyond a disproportionate difficulty with free recall procedures. For instance, when individuals with autism are asked to describe the quality of their memories on tests of recognition memory (e.g., "Have you seen X before?"), they are less likely than comparison participants to recollect specific details about the study episode (e.g., Bowler, Gardiner & Gaigg, 2007). Individuals with autism also struggle to recall contextual details such as when, where, and how they learned something when they are directly tested for such details (e.g., Bowler, Gardiner & Berthollier, 2004; Poirier, Martin, Gaigg & Bowler, 2011), and they often adopt a third-person rather than a first-person perspective when recalling autobiographical events (Lind & Bowler, 2010). The second influential discovery is that, contrary to the original

conclusions by Hermelin and O'Connor (1970), individuals with autism appear to draw on "meaning" to facilitate memory under several circumstances. For instance, conceptual relations between words (e.g., crop-grain) have been shown to promote memory in autism as much as in comparison groups when recognition procedures ("Did you see the word apple earlier?") rather than free recall procedures ("What words did you see earlier?") are used (e.g., Bowler, Gaigg & Gardiner, 2008) or when attention is drawn to such relations during study (Gaigg, Gardiner & Bowler, 2008; Mottron, Morasse & Belleville, 2001). In addition, individuals with autism are as likely as comparison participants to experience false memories of words that are meaningfully related to a set of studied words (e.g., night, pillow, tired, bed, dream...for a false memory of *sleep*) (Bowler, Gardiner, Grice & Saavalainen, 2000; Hillier, Campbell, Kiellor, Phillips & Beversdorf, 2007), which suggests not only that the concept of "meaning" is too broad to capture what individuals with autism do not process effectively in the service of memory but also that memory difficulties in this disorder are unlikely to be a reflection of a local processing style as proposed by the WCC theory. The third development that has contributed to our understanding of the patterning of memory strengths and weaknesses in autism is the complex information processing framework developed by Minshew and colleagues (see Williams, Minshew & Goldstein, 2008), which notes that memory difficulties in this disorder become more pronounced as tasks become informationally more complex. For instance, Minshew and Goldstein (2001) found that individuals with autism demonstrate a progressively more pronounced memory difficulty for materials that increase in semantic and syntactic complexity from sequences of letters to sequences of words and sentences. Although these observations are consistent with Hermelin and O'Connor's original observations, Minshew and Goldstein (2001) also found that when asked to learn the path through a maze, individuals with autism compared to those without performed progressively worse as the number of choice points in the maze increased, and this finding is less amenable to an explanation in terms of "meaning." Taken together, therefore, these

findings favor the view that it is "complexity" rather than "meaning" that lies at the root of the memory difficulties in autism, which is also consistent with neuropsychological evidence implicating the frontal lobes in autism (see Williams et al., 2008 for a review). But what is the metric for complexity? How can it be measured and defined, and how does the concept of complexity account for the episodic memory difficulties outlined above? The answer to these questions lies in the mainstream memory literature where a distinction between *item-specific* and *relational* processes (e.g., Hunt & Einstein, 1981) will lead back to a developmental consideration of the role memory abnormalities may play in the ontogenesis of autism.

The Mainstream Literature

Around the time of the first systematic investigations of memory in autism, Hunt and Einstein (1981) proposed that the efficacy of memory is principally dependent on the processing of two types of information – item-specific information and relational information. *Item-specific* information is information specific to the individual elements of a to-be-remembered set of materials such as the fact that a banana is yellow, that it is sweet, that it is soft textured, and that it belongs to the category of fruit. *Relational* information, by contrast, is information that defines the relations between elements such as the fact that a banana is similar to a prune. Critically, relational information presupposes item-specific information. One can only relate banana and prune if relevant item-specific knowledge about the banana and prune is available. In other words, the processing of relational information is computationally more complex because it requires (1) the retrieval of item-specific information about elements of experience and (2) the formulation (not necessarily explicitly) of a relation between elements on the basis of such item-specific knowledge.

Bowler and Gaigg (2008) have argued that a definition of Minshew's "complexity" in terms of item-specific (simple) and relational (complex) information provides a powerful tool for explaining the patterning of memory strengths and weaknesses in autism (see also Bowler,

Gaigg & Lind, 2011 for an up-to-date review). For one, the distinction between relational and item-specific processing is widely thought to parallel that between episodic and semantic memory. More importantly, the distinction also helps to resolve the complex pattern in which "meaning" modulates memory in autism. The observations from memory illusion paradigms are particularly well suited to illustrate this point. In such paradigms, participants study lists of words of meaningful associates of one nonpresented item (e.g., night, pillow, tired, bed, dream... for *sleep*). Individuals with autism tend to recall fewer words from to-be-remembered lists in such tasks, but they nevertheless also fall prey to erroneously recalling the nonstudied target words (Bowler et al., 2000). This apparent paradox is explained by the fact that veridical recall of list items depends on the effective processing of the relations between the items on the list, which, as noted earlier, also involves the bringing to mind of item-specific information about each individual word. False recall of the critical item, on the other hand, is largely the result of it being brought to mind by each of the studied words on the list. The critical word, in other words, constitutes part of the item-specific knowledge one has about the list items. Although this interpretation may seem contrived, it receives support from direct tests of the hypothesis that relational but not item-specific processing is compromised in autism (e.g., Gaigg et al., 2008) and from the neuroscientific literature (see Eichenbaum, 2004; Mayes & Boucher, 2008; Williams et al., 2008 for relevant reviews).

As noted earlier, until the 1980s, it was widely assumed that children were unable to form long-lasting declarative memories until the age of around 3–4 years. This view was mainly based on the fact that adults can rarely remember events from the first years of life, which seemed to suggest that no such event memories (i.e., episodic memories) are formed during early childhood. Just as archeologists can make mistakes in inferring the origin of certain artifacts, however, so developmental theorists can draw erroneous conclusions about developmental processes on the basis of adult behavior, and the domain of memory development provides

a case in point. As it turns out, infants as young as 9 months can remember a surprising amount when tested with appropriate procedures (see Bauer, 2006), and the most relevant to the study of autism is the observation that typical infants between 9 and 18 months rapidly acquire abilities that are indicative of relational memory processes. For instance, between 9 and 18 months, infants become increasingly proficient at deferred imitation tasks. In such tasks, an experimenter typically demonstrates a random sequence of actions such as banging a metal ring on a stick, then spinning the ring, and finally balancing it on a block. Following a delay of hours or even weeks, the infant who observed this sequence is presented with the same objects and encouraged to use them. Strikingly, by age 9 months, infants not only imitate the actions but they imitate them significantly above chance in the order in which they were demonstrated. Since the ordering of events in memory is widely regarded as a product of episodic memory and relational processes (in this case temporal relations are processed), this provides strong support for the idea that relational memory processes begin to develop toward the latter stages of the first year of life (Bauer, 2006). Additional evidence for this suggestion stems from intricately designed eye-tracking studies that assess novelty preferences in infants through visual paired comparison tasks. In such tasks, infants are first presented with a series of pictures, and after a short delay, they view the same pictures again alongside new and unfamiliar ones. In standard versions of this task, infants as young as 6 months demonstrate novelty preferences by visually exploring the novel picture for longer which indicates that they recognize the familiar one. Importantly, 6–9-month-olds do not demonstrate novelty preferences when tested in a different room to that in which the pictures were first seen. Such context dependence is thought to reflect a relative immaturity in relational processing since memory representations of the pictures are inflexibly bound to the memory representations of the context in which they were presented. The great advantage of mature relational processes is that they endow us with the ability to flexibly combine and recombine elements of past experiences, and this flexibility begins to emerge by about 12 months when infants begin to show novelty preference irrespective of context changes (see Jones & Herbert, 2006; Jones, Pascalis, Eacott & Herbert, 2011 for further details). Importantly, the first reliable behavioral markers of autism are not evident until around 18–24 months, considerably later than the period during which relational processing capacities emerge in typical development.

Future Directions

The above overview is incomplete and oversimplified but nevertheless demonstrates that it is conceivable that memory atypicalities in autism emerge before the clinically defining features of the condition. In itself, this does not necessarily indicate that memory abnormalities are causally responsible for the clinical features of autism, but it is a hypothesis that is in desperate need of empirical evaluation. The growing mainstream literature on relational memory development provides ample methodologies that can readily be adapted for this purpose, but in addition, there are other research directions that a relational processing hypothesis of autism invites. These directions are informed by a growing literature, which suggests that relational memory processes are not merely important for what we may narrowly consider to constitute "memory." For instance, it is now well established that episodic memory and associated relational processes are not only important for dwelling on the past but also for imagining, predicting, and planning for the future (Schacter, Addis & Buckner, 2008). Relational processes are also well established to be critical for a form of reasoning known as *transitive inference*, which allows us to make inferences such as "Paul is taller than Bob" given that "Paul is taller than Mark" and "Mark is taller than Bob," and to infer relations among objects or subjects that share a common relation with a third object/subject (e.g., Susan knows Mary because Susan is Bill's wife and Mary is Bill's aunt) (Eichenbaum, 2004). Relational processes are also critical for our ability

to navigate three-dimensional environments (Eichenbaum, 2004), and recent evidence also suggests that relational processes are important for certain forms of category learning (Zeithamova, Maddox & Schnyer, 2008), analogical reasoning (Hummel & Holyoak, 2003), symbolic and conceptual thinking (Kumaran, Summerfield, Hassabis & Maguire, 2009), and, most importantly, understanding false belief (Bowler, Briskman, Gurvidi & Fornells-Ambrojo, 2005 and see Bowler, Gaigg & Lind, 2011). In short, there is absolutely no doubt that a disturbance in the typical development of relational processing capacities could have widespread repercussions on other areas of cognition, some of which have already been implicated in autism, others await closer scrutiny.

See Also

▶ Episodic Memory
▶ Explicit Memory
▶ Memory
▶ Semantic Memory

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Menarche

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Synonyms

First "period"

Definition

Menarche is the medical term for the onset of menstruation, which is the periodic shedding of the uterine lining in females of reproductive age. Menarche is a hallmark of puberty and is often colloquially referred to as the first "period." It typically follows thelarche (breast development) by approximately 2 years. In general, females must have at least 17% body fat in order for menarche to occur. The average age of menarche in the United States is between 12.1 and 12.6 years, with some variations across ethnic groups. African American females have a lower average age of menarche. The average age of menarche has been declining in developed countries over the last 150 years, likely as a result of improved adolescent nutrition. Low body weight and poor nutrition can delay menarche. Anovulatory cycles and irregular menses often occur in the first few months following menarche (Joffe, 2006).

Girls on the autism spectrum may reach menarche later than the general population, but the reasons for this delay are unclear. Proposed mechanisms include the role of elevated body mass index as well as increased exposure to androgen hormones during the prenatal period, though this hypothesis is controversial (Whitehouse, Murray, Hickey, & Sloboda, 2010). Children with autism often experience worsening symptoms during puberty (Knickmeyer, Wheelwright, Hoekstra, & Baron-Cohen, 2006). Autistic girls may be at increased risk for mood and behavioral disturbances around menstrual periods. More research is needed regarding the use of oral contraceptive pills (OCPs) for treatment of mood disturbances related to menses in this population (Burke, Kalpakjian, Smith, & Quint, 2010). Medications that are commonly used to treat aggression and mood disturbances in children with autism can cause menstrual irregularities. For example, atypical antipsychotic medications can be associated with weight gain and elevated prolactin levels which in turn can impact the menstrual cycle.

The association between maternal early life factors and autism spectrum disorders is a subject of ongoing research. Maternal factors such as early menarche (age of menarche 10 years or less) and

late adolescent obesity (body mass index greater than 30) are possibly linked to autism spectrum disorders (Lyall, Pauls, Santangelo, Spiegelman, & Ascherio, 2010).

See Also

▶ Antipsychotics: Drugs

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Meningitis

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Synonyms

Meningococcal disease: a specific form of meningitis that is caused by the bacteria *Neisseria meningitidis*

Definition

The brain and the spinal cord are surrounded by three membranes that are collectively termed meninges. *Meningitis* is inflammation of the meninges that is typically caused by infectious agents such as viruses, bacteria, fungi, and parasites. There are also noninfectious causes of meningitis, including certain drugs, malignancies, and autoimmune diseases. Classic clinical signs of meningitis are fever, headache, neck stiffness, light sensitivity (photophobia), and alterations in consciousness. These symptoms may be absent or difficult to appreciate in infants and very young children. Meningitis can also be associated with nonspecific systemic symptoms such as irritability or loss of appetite. Seizures and focal neurologic deficits can occur as well. The gold standard for diagnosis of meningitis is the lumbar puncture procedure, during which a sample of the cerebrospinal fluid (the fluid encircling the brain and spinal cord) is removed for analysis.

Viral meningitis is relatively more common than other forms and usually resolves without specific medication treatment. Bacterial meningitis is less common than viral meningitis, but is associated with higher morbidity and mortality and requires antibiotic therapy. The most common bacterial causes of meningitis are *Escherichia coli* and group B streptococcus in neonates, *Streptococcus pneumoniae* and *Haemophilus influenzae* type b in older children, and *Neisseria meningitidis* in adolescents. The incidence of bacterial meningitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* has decreased since the introduction of a vaccination program against these bacteria. It is advised that children receive a series of vaccinations against *Streptococcus pneumoniae* and *Haemophilus influenzae* between the ages of 2 months and 15 months. Routine vaccination against *Neisseria meningitidis* is recommended at the 11–12-year-old well-child visit. Older children who have not yet received this vaccine should be vaccinated at the earliest opportunity. Unvaccinated or incompletely vaccinated children are at higher risk of acquiring bacterial meningitis as are children who are immunocompromised. Intellectual disability,

seizure disorders, hearing loss, developmental delays, and behavioral disturbances can all be sequelae of bacterial meningitis.

See Also

► Measles-Mumps-Rubella (MMR) Vaccination

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Meningococcal Disease: A Specific Form of Meningitis That Is Caused by the Bacteria *Neisseria Meningitidis*

► Meningitis

Mental Age

► Age Equivalents

Mental Flexibility

► Cognitive Flexibility

Mental Health Interventions

► Child Psychotherapy

Mental Health Practitioner

► Clinical Social Worker

Mental Retardation

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Synonyms

Cognitive delay; Developmental disability (Ontario); Intellectual disability; Learning disability (UK)

Definition

The condition associated with subaverage intellectual functioning has undergone many changes in name and definition since it was first recognized (circa 1493; Scheerenberger, 1983). In fact, the term "mental retardation" is no longer current; "intellectual disability" is the currently accepted term. Although a complete history of terminology and classification of intellectual disability is outside the scope of this entry, the highlights of the past quarter century follow. The term *mental retardation* replaced the term *mental deficiency* in 1987, and the condition underwent several minor definition changes during the following 25 years. Perhaps the most significant change to the definition occurred in 1992 when the concept of support was introduced as a fundamental aspect of the classification system. The current diagnostic criteria for intellectual disability (Schalock et al., 2010) is based on three criteria: *significant limitations in both intellectual functioning and adaptive behavior expressed in conceptual, social, and practical adaptive skills and age of onset before the age of 18*. Once a diagnosis of intellectual disability is

made, planning and providing support is critical to teaching the skills and behaviors needed to successfully participate in all aspects of daily life.

Throughout history, people with intellectual disabilities have been devalued and whatever term is associated with this condition acquires the stigma of the condition and is used pejoratively in common vernacular. Earlier terms such as feebleminded, idiot, moron, imbecile, and mentally deficient each acquired social stigma and became offensive and hurtful to people with intellectual disability and their families. In recent years, the term mental retardation has acquired a derogatory connotation. For this reason, self-advocates, parents, and administrators sought an acceptable substitute. Rosa's Law, signed into effect on October 5, 2010 by President Obama, changed the official federal terminology from mental retardation to intellectual disability. This law was preceded by the American Association on Intellectual and Developmental Disabilities who made the name change in 2007 and the state of Maryland who made the change in 2009. The change from mental retardation to intellectual disability was a change in name only; there was no change in the diagnostic criteria, which allowed individuals receiving services under the term mental retardation to continue receiving the same services without interruption after the name changed to intellectual disability.

See Also

▶ Developmental Disabilities

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Mental Retardation (Former Term)

▶ Intellectual Disability

Merycism

▶ Rumination

Mesencephalon

▶ Midbrain

Mesibov, Gary

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Name and Degrees

Gary B. Mesibov

Stanford University, AB Psychology, 1967

University of Michigan, MA Developmental Psychology, 1968

Brandeis University, PhD Psychology, 1974

Major Appointments (Institution, Location, Dates)

2000 – Present Fellow, Frank Porter Graham Child Development Center, University of North Carolina at Chapel Hill

1987 – Present Professor of Psychology Emeritus, Department of Psychiatry, University of North Carolina at Chapel Hill

1987 – Present Clinical Professor Emeritus, Department of Psychology, University of North Carolina at Chapel Hill

1992–2010 Director, Division TEACCH (Treatment and Education of Autistic and Related Communication-Handicapped Children), University of North Carolina at Chapel Hill

1988–1992 Codirector, Division TEACCH

1981–1987 Associate Professor of Psychology, Department of Psychiatry, University of North Carolina at Chapel Hill

1983–1987 Associate Director, Division TEACCH

1979–1982 Coordinator of Adolescent and Adult Services, Division TEACCH

1975–1981 Assistant Professor of Psychology, Department of Psychiatry, University of North Carolina at Chapel Hill

1975–1979 Psychologist, Division for Disorders of Development and Learning, University of North Carolina at Chapel Hill

1974–1975 Postdoctoral Fellow, Clinical Child Psychology, Division for Disorders of Development and Learning, University of North Carolina at Chapel Hill

Major Honors and Awards

1982 President, Society of Pediatric Psychology (Section 5 of the American Psychological Association Division of Clinical Psychology)

1982 Certificate of Appreciation for Contributions to Developmentally Handicapped Citizens of North Carolina (Awarded by Orange County, NC Association for Retarded Citizens)

1984 Fellow Status, American Psychological Association Divisions 37, 12

1989 Distinguished Professional Contribution Award, Society of Pediatric Psychology, American Psychological Association

1990 First recipient of Mesibov Award, given annually by Residential Services, Inc. for excellence in community-based residential service system for developmentally handicapped children and adults in Orange County, NC

1994 Opleidingscentrum (Belgium) International Award for contributions translating theory into effective practice in autism

1994 Mary G. Clarke Award from the North Carolina Psychological Association given annually to a psychologist in North Carolina for outstanding contributions spanning several years. Contributions must reflect qualities of dedication, competence, high ethical standards, advocacy for the field of psychology, and sensitivity

1995 MAPP (International organization to help More Able Autistic People) Award for invaluable service to the organization and to high-functioning people with autism

l997 Distinguished Professional Contributions Award for Public Service, American Psychological Association

2000 "Doctor Honoris Causa" (Honorary Degree) from the University of Mons-Hainaut (Belgium) for contributions to improving the quality of life for people with autism throughout the world

2000 Emily and Frank Puzio Award from the Eden Institute's Princeton Lecture Series for leadership in improving the quality of life of individuals with autism

2006 UNC Chancellor's Award for Excellence for meritorious accomplishments clearly above and beyond what is expected in human relations

2006 NC State Employees Award for Excellence representing outstanding performance. This is the highest award an NC state employee can receive

2010 Danish National Autism Society Professional of the Year for doing the most to advance treatment and education of people with autism spectrum disorders

2010 American Association on Intellectual Developmental Disabilities Award for service to people with disabilities.

2010 Autism Society of America Founders Award for career substantive contributions to the field of autism spectrum disorders

2011 Honorary Degree from the University of Northampton (UK) for contributions to the education of children and adults on the autism spectrum

Landmark Clinical, Scientific, and Professional Contributions

Gary B. Mesibov has dedicated his career as a psychologist to autism. His contributions include a major assessment instrument; a book series; a comprehensive program of educational, vocational, residential, and family support services; and a unique training program for other professionals. His reputation among students, families, and professional colleagues is one of wisdom, generosity, compassion, and amazing productivity. He brings intellectual rigor to his professional activities and combines it with gentleness and respect for all clients and their families. His influence began in North Carolina and has spread throughout the world.

Short Biography

Gary B. Mesibov defended his doctoral dissertation in psychology at Brandeis University in the spring of 1974. Shortly thereafter, he arrived at the University of North Carolina at Chapel Hill as a postdoctoral fellow in the Division for Disorders of Development and Learning (DDDL). Gary's time at the DDDL marked the beginning of his professional identification with the field of developmental disabilities. Recognized as a gifted and prolific psychologist, after only 18 months, Gary was asked to accept a staff position at the DDDL with an appointment as an Assistant Professor of Psychology in the Department of Psychiatry. Gary's quiet passion for understanding and serving people with developmental disabilities soon led to professional involvement with newly developing service models in North Carolina, including group homes, sheltered workshops, limited guardianship, and social skills training, as well as service on a human rights committee at the regional residential facility for people with severe/profound intellectual disabilities. Gary conducted research, introduced students to the rewards and fascinations of developmental disabilities, and worked closely with clients and families. At the same time, he was teaching in the Department of Psychology, supervising interns and postdoctoral fellows in the Department of Psychiatry, and devoting considerable time and effort to the development of the Society of Pediatric Psychology (Section 5 of the American Psychological Association's Division 12).

Chapel Hill had long been a center of excellence in the field of developmental disabilities. In addition to the DDDL's broad-based training program in developmental disabilities, a small, psychoanalytically oriented program on autism had functioned for some years within the Department of Psychiatry. In 1966, this program was expanded and refocused by Eric Schopler and Robert Reichler on the assumptions that autism was a neurobiological disorder and that parents and professionals could work as cotherapists to help children with autism develop. In 1972, that program was renamed TEACCH (Treatment and Education of Autistic and Related Communication-Handicapped Children) and funded by the North Carolina General Assembly as the nation's first statewide autism program.

Eric recruited Gary in 1979 to assume the new position of Coordinator of Adolescent and Adult Services at TEACCH. Four years later, Gary became Associate Director; 5 years later, codirector; and in 1992, with Eric Schopler's semiretirement, Director of Division TEACCH. Gary served in this position for 18 years until his retirement in 2010. This was a formative period for the organization as it grew to nine regional centers across the state of North Carolina, serving thousands of individuals on the autism spectrum. It was also a period of both broadening and deepening TEACCH's philosophical underpinnings

and, as a result, its approach to intervention for individuals with autism. Eric had first understood the importance of using structure to help children with autism focus and learn; Gary elaborated on the principles of structured teaching and applied them to classroom, vocational, and residential settings. He also emphasized the importance of improving the quality of life for individuals on the autism spectrum, not merely addressing "deficits" or "behavior problems." In 2004, Gary coauthored *The TEACCH Approach to Autism Spectrum Disorders* as an introduction to the TEACCH philosophy, structured teaching, and its application across a wide range of contexts.

From 1983 until 1998, Gary and Eric coedited the "Current Issues in Autism" series for Plenum Press. These books were based on the yearly TEACCH conference held in Chapel Hill each May. The conference has drawn noted autism experts such as Margaret Bauman, Eric Courchesne, Geraldine Dawson, Christopher Gillberg, Temple Grandin, Cathy Lord, Sally Ozonoff, Michael Rutter, Oliver Saks, Wendy Stone, and Lorna Wing. Conference speakers uniformly, and quite independently, speak with affection and admiration for Gary's contributions. Throughout the years, he has demonstrated a remarkable capacity to maintain warm, personal relationships with professionals around the world.

Like most respected academics, Gary began to be asked to give talks or provide training outside his hometown. In the late 1970s, his talks were in rural North Carolina, with occasional well-timed presentations at the Atlantic coast in the summer. By the 1980s, he was accepting invitations to Kentucky, Ohio, Georgia, Florida, and Oregon. During this time, he was also developing a unique, weeklong, multimodal training program for teachers and other professionals working with students with autism. Gary and a training team would arrive at a location on Sunday, set up a model classroom with local students with autism on Monday morning, and take turns giving didactic lectures and operating the classroom. The trainees would observe trainers working with the students and then take over themselves, designing and presenting teaching activities that put into practice the principles

they had been hearing in the lectures. After the local students went home for the day, there would be small-group and large-group debriefings of what trainees had tried, what had worked, and what had not worked. This model classroom has been presented every summer since 1985, training more than 2,000 teachers of students with autism. Gary and his teams have also presented the classroom and other types of training in Australia, Belgium, China, Denmark, England, France, Germany, Hong Kong, India, Italy, Japan, Kuwait, Mexico, New Zealand, Northern Ireland, Norway, Pakistan, Qatar, Russia, Saudi Arabia, Singapore, Sweden, and Venezuela.

Gary was also involved in developing the Adolescent and Adult Psychoeducational Profile (AAPEP), an assessment instrument for adolescents and adults with autism. In 2007, he and his colleagues issued a major revision of the instrument, renamed the TEACCH Transition Assessment Profile (TTAP), in order to assess more accurately the skills needed for successful employment in community settings and to promote independent functioning in the home, workplace, and community. Gary's vision and leadership have been the impetus behind TEACCH's Supported Employment Program, which continues to be one of the most successful such programs in the nation for adults with autism.

Gary served for 10 years as editor of the *Journal of Autism and Developmental Disorders* and on the editorial boards of the *Journal of Pediatric Psychology, Journal of Clinical Child Psychology*, and *Journal of Cognitive Rehabilitation*, in addition to being a guest reviewer for almost a dozen other journals. Over his career, Gary has earned a reputation as someone who can translate basic research into everyday practice. In recent years, he has helped the autism community think carefully about "evidence-based practice" and how this concept can be applied to specific autism interventions and to broad-based program models.

Gary's many professional awards demonstrate his commitment to advancing the science and practice of psychology while maintaining a clear focus on improving quality of life for

individuals with autism across the lifespan. For example, he received the 1997 American Psychological Association's Distinguished Professional Contributions Award for Public Service. He has received honorary doctoral degrees from the University of Mons-Hainaut (Belgium, 2000) for "contributions to improving the quality of life for people with autism throughout the world" and from the University of Northampton (United Kingdom, 2011) "for his contribution to the education of children and adults on the autism spectrum." In 2006, Gary received the University of North Carolina at Chapel Hill Chancellor's Award for "meritorious accomplishments" on behalf of the university. In 2010, he was named "Professional of the Year" by the Danish Autism Society for "doing the most to advance treatment and education of people with autism spectrum disorders." Also in 2010, Gary received the Autism Society of America Founders Award for "career substantive contributions to the field of autism spectrum disorders." These are just the highlights from a career marked by recognition from parents and professionals alike.

Since stepping down as director of Division TEACCH, Gary has found a bit more time for his grandchildren, but he has not lost his passion for improving the quality of life for individuals with autism, particularly for adolescents and adults. He continues to inspire the TEACCH staff and the autism community at large to embrace "the culture of autism" as a metaphor for understanding the unique qualities of the children, adolescents, and adults they serve.

See Also

▶ TEACCH Transition Assessment Profile (TTAP)

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Mesoridazine

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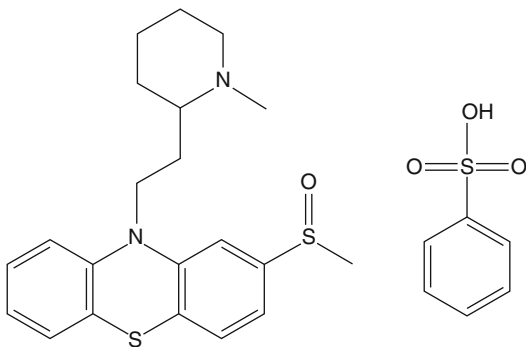[1]Christian Sarkine Autism Treatment Center, Indianapolis, IN, USA
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Synonyms

Mesoridazine besylate; Serentil

Definition

Mesoridazine is a prescription drug in the group of piperidine phenothiazines in the family of first-generation antipsychotics whose active ingredient mesoridazine besylate has the chemical formula $C_{27}H_{32}N_2O_4S_3$. This drug was initially FDA-approved for medical use in the year 1970 and was produced by the company Novartis, but the production of this drug has been discontinued. This compound has relatively low potency compared to the other first-generation antipsychotics, and its mechanism of action is thought to involve anticholinergic binding. This drug is FDA-approved for the treatment of schizophrenia and can be used to treat aggressive symptoms. Observed side effects include drowsiness/sedation, Parkinsonism, akathisia, orthostatic hypotension, tachycardia, electrocardiogram (ECG) abnormalities, anticholinergic effects, sexual dysfunction, galactorrhea, and weight gain.

See Also

▶ Antipsychotics: Drugs

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Mesoridazine Besylate

▶ Mesoridazine

Messages

▶ Vocabulary

Metabolic Testing

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Description

Definition

Metabolic testing is the laboratory evaluation looking for inborn errors of metabolism. Inborn errors of metabolism are genetic or inherited conditions due to the lack of a necessary enzyme or biochemical process that results in the inability to convert substrates into the appropriate biologic product in the body. Some inborn errors of metabolism result in toxic accumulations of substances that cannot be metabolized, and others have symptoms that result from a deficit in production of necessary biochemical compounds.

Specific biochemical tests are used to examine the metabolism of compounds such as amino acids, carbohydrates, fatty aldehydes, organic acids, peroxisomes, lysosomes, and others.

Background

Inborn errors of metabolism are seen in the general population at a rate of 0.1−0.4%. They may be identified in children on the autism spectrum 3−5% of the time. However, each type of error is extremely rare. Over time, more and more inborn errors of metabolism have been identified. Categories of errors include metabolism of carbohydrates or sugars, problems with processing protein or amino acids, mitochondrial disorders, storage disorders, disorders of steroid metabolism, and many other disorders.

Metabolic testing may be ordered to look for rare causes of developmental disability in the presence of a history of regression, a family history, specific symptoms, or findings on neurologic exam. Metabolic testing is performed through newborn screening in every state in the United States.

Different panels are included in newborn testing in each state. Some allow families to refuse. Newborn screening takes a few drops of blood dried on a filter paper that are then evaluated using very specific methodology. Most states include PKU, galactosemia, biotinidase deficiency, congenital adrenal hyperplasia, maple syrup urine disease, tyrosinemia, and other nonmetabolic disorders like hypothyroidism, sickle cell syndrome, and cystic fibrosis.

The symptoms of inborn errors of metabolism can occur at birth, sometime in the first 3 years of life, or later. Some disorders like phenylketonuria occur when the placenta no longer compensates for the metabolic error. In other situations, decompensation occurs during a serious illness or major stressor. Others are progressive such as infantile ceroid lipofuscinosis, biotinidase deficiency, and Sanfilippo syndrome.

Abnormalities on newborn screening typically require additional testing. Specific tests are used for each of the identified metabolic disorders. A specialist such as a geneticist or child neurologist often must consult to help guide the evaluation.

The first inborn error of metabolism to benefit from widespread newborn screening was phenylketonuria or PKU. It is due to an absence of the enzyme that metabolizes the amino acid phenylalanine into tyrosine. Without this enzyme, a toxic metabolite builds up and results in neurologic impairment. This is the most common of the inborn errors of metabolism and is seen in 1 in 10,000 live births. The treatment for this is diet by limiting intake of Phe. Untreated children with PKU developed intellectual disability and often autism. The prevalence of autism in PKU has dropped from 20% to 5.7% due to early detection and treatment with diet. If this abnormality is identified early, the child will have few if any severe problems. Newborn screening in all US states and Canada typically detects PKU, so these problems can be avoided. However, children born in areas that do not have newborn screening might still be evaluated for this disorder (Baieli, Pavone, Meli, Fiumara, & Coleman, 2003).

An increasing number of metabolic disorders have interventions that improve outcome. Another

example is galactosemia. While the following are not associated with ASD, they are causes of developmental disability. Children with galactosemia, which is a disorder of sugar metabolism, will develop cataracts, kidney failure, liver failure, and brain damage. Galactosemia can be treated with dietary elimination of galactose. Children with biotinidase deficiency can have variable presentation but, if left untreated, can have developmental delays, vision or hearing loss, seizures, ataxia, hair loss, and/or candidiasis (a fungal infection). This is treated in some cases with oral biotin and avoiding raw eggs, which decreases absorption of biotin. Tyrosinemia is another disorder of protein metabolism and causes mental retardation and kidney and liver damage and is treated with low-protein diet and liver transplant if needed. The most severe forms of maple syrup urine disease cause vomiting, dehydration, hypotonia, seizure, brain injury, pancreatitis, coma, and ultimately death.

Other inborn errors may be seen in children with nonspecific symptoms, and many are without specific treatments. Many disorders of metabolism are not included in newborn screening programs. The mitochondrial disorders do not have accurate screening tests. It has been suggested that there is an increased rate of mitochondrial abnormalities among children with ASD. Mitochondria are small organelles that are involved in producing energy in each cell of the body. These organelles contain their own genetic code that is separate from the genetic code in the nucleus. The mitochondria are contained in the egg, but not in the sperm, so all mitochondria and their DNA are inherited from the mother. However, the mother might have fewer and less intense symptoms, or possibly more symptoms, depending on the number of functional mitochondria that are inherited. Symptoms suggestive of mitochondrial disorders are excessive fatigue, severe hypotonia, cyclic vomiting, visual problems, hearing problems, poor growth, and/or seizures. Specialized testing including muscle biopsy may be necessary to identify mitochondrial disorders. Specialists in metabolic genetics or child neurology are consulted.

Treatment Goals

Metabolic testing includes an array of specific biochemical analyses ordered as part of a medical workup of an individual with a history and physical examination suggesting evaluation of a specific category of metabolic disorders.

The goal of the metabolic testing is to identify a specific inborn error of metabolism. Some of these inborn errors of metabolism have identified dietary or vitamin treatments that can help limit or improve the symptoms. Many inborn errors of metabolism do not have a known effective treatment. New therapies are under study for many disorders that range from dietary modification, pharmacologic replacement of enzyme, and gene therapy. Diagnosis of an inborn error of metabolism helps families understand the etiology of the developmental disability or other symptoms present in the child and allows for counseling regarding heritability.

Metabolic testing is not routinely done to evaluate the nutritional status of children with limited diets.

Clinical Uses

The level of metabolic testing indicated varies from child to child and situation to situation.

All children should have some form of newborn screening to identify the most common and most treatable types of inborn errors of metabolism.

Children diagnosed with autism should have a thorough history and physical exam done by a medical professional with experience in autism spectrum disorders. Additional testing for metabolic disorders is not required in every child with an autism spectrum disorder (Myers, 2007). Children with a history of regression, especially unusual regression or regression with illness, should be considered for metabolic disorders. Children with autism and history of severe seizures especially those resistant to treatment may also be considered for underlying metabolic etiologies. Unusual gastrointestinal disturbances, especially cyclic vomiting or frequent vomiting with mild illness, may indicate a mitochondrial myopathy or another metabolic disorder. Children with prominent

hypotonia, ataxia, movement disorders, or motor regression may also be considered for metabolic testing based on history and physical examination.

For many of these children, referral to a geneticist or metabolic expert is the most efficient way to approach the metabolic evaluation. For most patients, a tiered level of testing is done. The least invasive tests indicated by the symptoms that are most likely to give information are ordered first and then work up based on the history to more invasive testing like skin or muscle biopsy.

See Also

▶ Inborn Errors of Metabolism
▶ Medical Evaluation in Autism

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Metachromatic Leukodystrophy

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Synonyms

MLD; Scholz's disease; Sulfatide lipidosis; Sulfatidosis

Short Description or Definition

Metachromatic leukodystrophy (MLD) is a rare genetic disorder that worsens over time. Symptoms are primarily neurological and related to white matter degeneration, although other organs can also be affected. Psychiatric symptoms often occur. In the early stages, MLD may be confused with autism.

Categorization

Metachromatic leukodystrophy (MLD) is a degenerative white matter disease, which is also classified as a lysosomal sphingolipid storage disease. Given the sudden neurological regression associated with MLD, early stages of this disease can sometimes be confused with autism spectrum disorders, including childhood disintegrative disorder and Rett disorder. As MLD progresses, the pronounced neurological symptoms distinguish it from autism spectrum disorders.

Epidemiology

MLD is classified as rare, with an estimated prevalence ranging from 1:40,000 to 1:100,000 among individuals of European decent. However, higher prevalence has been recorded in several small ethnic groups such as Navajo Indians in the United States and Habbanite Jews and Arabs in Israel.

MLD is caused by a deficiency of arylsulfatase A, a lysosomal enzyme that helps degrade cerebroside sulfate. As a result, sulfatide builds up intracellularly. This occurs primarily in Schwann cells and oligodendrocytes, causing demyelination and decreased white matter.

Over 100 mutations have been identified as a cause of MLD, making it genetically quite heterogeneous. Among Caucasian patients affected by MLD, 2 alleles are common, A and I. Together, these account for roughly 50% of cases. Furthermore, there is a well-documented genotype-phenotype correlation in MLD. Homozygosity for

null alleles such as I, which do not yield any enzyme activity whatsoever, always produces the most severe form of the disease, with late infantile onset and rapid progression. In contrast, homozygosity for alleles such as A that allow low levels of enzyme activity is typically associated with adult onset and gradual progression. Heterozygosity for both types of alleles typically produces an intermediate form of MLD, though there is significant overlap between juvenile- and adult-onset forms.

There are three onset patterns of MLD, described in more detail in the next two sections. Between 40% and 50% of cases are classified as "late infantile," 30–40% as "juvenile," and around 20% as "adult."

Natural History, Prognostic Factors, Outcomes

There are three main forms of MLD, differentiated according to age at onset. Further differentiation can be made according to the pattern of progression and symptoms. Late infantile MLD arises in the first 2 or 3 years of life. Progression is typically rapid; patients succumb to the disease within 5–6 years. In this form, neurological symptoms are usually the first sign, though early stages of MLD can cause behavioral changes such as social regression and withdrawal. In adult-onset MLD, it is more common for psychological and behavioral symptoms to appear first, with neurological impairment appearing slightly later on. Early on, this form of MLD can be confused with schizophrenia, though the emergence of neurological symptoms clearly distinguishes the two. In contrast to late infantile MLD, progression in the adult form is much more gradual. This type of MLD typically emerges early in adulthood, though some cases have described onset as late as 50–60 years of age. Juvenile-onset MLD begins between the ages of 3 and 16, with widely variable progression. Symptoms can develop as rapidly as the late infantile form, yet some patients can survive into early adulthood.

Clinical Expression and Pathophysiology

The ultimate phenomenology of all forms of MLD is thought to result from demyelination of neurons, triggered by an accumulation of sulfatide in oligodendrocytes, Schwann cells, and neurons. This accumulation is caused by a deficiency of the enzyme arylsulfatase-A, which is responsible for degrading sulfatide. Although the accumulation of sulfatide appears to trigger demyelination, the mechanism is not yet clear.

As mentioned above, MLD has several patterns of onset. Initial symptoms vary both across and within the subtypes of MLD. Here we focus on the early infantile- and juvenile-onset forms, which, when accompanied by a pronounced regression, may initially be difficult to distinguish from regressive ASDs, such as childhood disintegrative disorder and Rett disorder, but also may have subtle enough initial onset patterns to be mistaken for a previously "unrecognized" ASD. Dramatic regressions of the type seen in both childhood disintegrative disorder and Rett disorder are most commonly associated with the late infantile form of MLD. Generally this form of MLD is accompanied by neurological signs, including gait disturbances, and abnormal movement patterns. It can also be accompanied by a more general loss of developmental milestones, including speech, cognition, and self-help skills. Abnormal movement patterns may be interpreted as the hallmark repetitive behaviors of other ASDs. When coupled with developmental losses, these changes may be interpreted as an ASD. However, a careful neurological exam may reveal other changes, e.g., depressed deep tendon reflexes, positive Babinski sign, and muscular hypotonia, not consistent with ASD (although Rett disorder is also accompanied by neurological changes). Early infantile MLD progresses rapidly, however, to severe neurological signs, including spastic quadriplegia and severe dementia, and ultimately death. The juvenile onset of MLD can manifest more subtly in changes in school performance, psychiatric symptoms, etc. Sometimes the first neurological signs can be as subtle as clumsiness and poor coordination. Once again, when subtle, it is easy to imagine that this constellation of symptoms could

be interpreted as a previously unidentified ASD. These symptoms may be static for an extended period, sometimes even years. However, a neurological exam may reveal the changes described above. Once the disease begins to declare itself in clear neurological signs and symptoms, the progression generally becomes more rapid and similar to early infantile MLD.

Evaluation and Differential Diagnosis

The majority of signs and symptoms of MLD are neurological. Thus, a detailed neurological exam is an essential first step in evaluating suspected MLD, or for that matter, any deterioration of adaptive skills. Subtle neurological signs which point to the early stages of MLD may be picked up on exam, even if there are no obvious neurological deficits. The disease can sometimes first be manifested in behavioral changes. Therefore, it is important that any workup for a developmental derailment, as commonly seen in the ASDs, includes MLD on the differential. However, with the progress of MLD, dramatic neurological disturbances are inevitable and will be obvious both clinically and on exam. Neuroimaging, in particular MRI and MRS, may be a powerful tool in establishing a diagnosis. Areas of T2 hyperintensity (see fMRI section), initially in the periventricular areas but spreading from there, may be the first sign. Other findings are common. For a review of this topic, please see Kim et al. (1997) or Gieselmann and Krägeloh-Mann (2010). Laboratory testing is important. Both blood and urine will show evidence of MLD. The level of arylsulfatase enzyme activity can be tested in the blood leukocytes. Elevated urinary excretion of sulfatide over a 24-h period is also a sensitive marker. There are limitations to genetic testing for MLD due to the large number of mutations that can underlie the disease. Prenatal diagnosis of MLD can be done using cells from chorionic villi. The differential diagnosis for MLD includes a number of psychiatric disorders during the early stages, including attention disorders and psychotic disorders. Later, degenerative neurological disorders, including other leukodystrophies such as Krabbe disease, dominate the differential.

Most relevant to this discussion, the combination of developmental derailment, including social changes and the loss of adaptive milestones, coupled with subtle neurological signs can suggest an ASD. Any evaluation of new ASD should include MLD on the differential, with heightened suspicion in cases of regressive ASD.

Treatment

Therapeutic options for MLD are limited. In some cases, hematopoietic stem cell transplantation can be beneficial, but only under a limited set of conditions (see Gieselmann and Krägeloh-Mann, 2010). A number of experimental therapies are being explored currently, including enzyme replacement therapy and gene therapy. However, at this point, there is no cure for MLD.

See Also

▶ Childhood Disintegrative Disorder
▶ Magnetic Resonance Imaging
▶ Regression

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Metallothionein

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Definition

Metallothioneins are proteins that bind metals, controlling the levels of these metals in the body

and preventing toxic effects (Owens, Summar & Aschner, 2008). Some hair and urine analysis studies have shown that levels of heavy metals are increased in children with autism (Owens, Summar, & Achner). Animal studies have demonstrated that mice with dysfunctional metallothioneins are at increased risk for heavy metal (specifically, mercury) poisoning but do not show baseline behavioral sequelae. Additionally, there are natural differences in metallothionein genetics, which may lead to the creation of faulty metallothionein proteins, predisposing an individual to heavy metal sensitivity. The hypothesis that children with autism have faulty metallothionein proteins and are therefore more sensitive to metals from the environment and potentially vaccines, has been proposed as an explanation for the cause of autism. However, there are no peer-reviewed studies showing an association between metallothionein abnormalities and autism. Despite this lack of support, some scientists and clinicians have attempted to treat autism by increasing metallothionein function. However, no peer-reviewed clinical trials have provided any evidence to support this treatment (Owens, Summar, & Aschner).

See Also

- ▶ Chelation
- ▶ Hair Analysis
- ▶ Lead Exposure and Autism
- ▶ Measles-Mumps-Rubella (MMR) Vaccination
- ▶ Thimerosal
- ▶ Toxicology
- ▶ Vaccinations and Autism

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Metaphor

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Definition

A metaphor is a type of figurative language in which two objects or ideas are implicitly compared in a way that is not literal, as in "She has a heart of gold." There are a number of different types of metaphors, and they are a commonly used stylistic element in speech and writing. Metaphors can be used as a persuasive tool or to facilitate understanding by relating one concrete idea to another more abstract concept.

Metaphorical understanding in typically developing children typically begins between 4 and 5 years of age (Ozcaliskan, 2005). Children with autism, however, often take language very literally and thus demonstrate challenges with the comprehension and interpretation of metaphor (Rundblad & Annaz, 2010) and other types of figurative language. This is likely due to deficits on another level with theory of mind – the ability to attribute mental states to self and others and challenges with cognitive flexibility. Yet, some children with autism will exhibit their own unique metaphorical use of language, making associations between objects or experiences that have private meanings (Twachtman-Cullen, 1998). To facilitate understanding, familiar communication partners may make sense of these utterances through probing and cues from the child.

See Also

- ▶ Cognitive Flexibility
- ▶ Figurative Language
- ▶ Metaphoric Language

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Definition

Individuals with Autism Spectrum Disorders (ASD) may produce speech that appears to be irrelevant to the current communicative context. For example, Kanner (1946) described a child with ASD who would yell, "Don't throw the dog off the balcony!" whenever he was about to throw something. His parents reported that several years earlier, they had been staying in a hotel with a balcony and warned the child not to throw his stuffed toy dog over the railing. Kanner emphasized that this "metaphorical language" was not irrelevant or meaningless. Rather, individuals with ASD attach unique meanings to these "figures of speech" based on specific past experiences.

See Also

▶ Figurative Language
▶ Idiosyncratic Language

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Metaphoric Language

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Synonyms

Idiosyncratic language

Methylphenidate

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Synonyms

Ritalin

Definition

Methylphenidate: Methylphenidate is also a stimulant medication. Although it also enhances release and blocks reuptake of dopamine, it is less potent than the amphetamines. There are many preparations with methylphenidate including immediate-release compound in which the tablet is rapidly absorbed and the duration of action is approximately 4 hours. When using the immediate-release compounds, it is likely that the dose will have to be repeated twice or even three times per day. There are also long-acting formulations marketed under several different trade names. These long-acting formulations do not have to be repeated throughout the day. However, various products may only come in particular strengths. Therefore, becoming familiar with the different brands of medications is important for using these long-acting formulations of methylphenidate in the clinic. Methylphenidate also comes in a transdermal skin patch. The skin patch can be worn for 8–9 h per day and replaced with a new patch each day. The skin patch comes in several strengths and may require some trial and error in that the oral dose of methylphenidate may not immediately translate to the dose of the skin patch. One drawback of the current skin patch preparations is their high cost.

The immediate-release formulation of methylphenidate was studied in a large-scale, multisite trial in children with autism spectrum disorders (Research Units on Pediatric Psychopharmacology, 2005). The study included three doses of methylphenidate (low to high) and placebo in a crossover trial (each subject received the study treatments in random order under double-blind conditions). All active dose of methylphenidate was superior to placebo in this short-term study. In contrast to the benefits observed in typically developing children with attention deficit/hyperactivity disorder, however, in children with autism spectrum disorders who were hyperactive, impulsive, and distractible, the beneficial effects were modest. The study in children with autism spectrum disorders showed that doses that are well tolerated in typically developing children with attention deficit/hyperactivity disorder were less well tolerated in children with autism spectrum disorders. Intolerable adverse effects included irritability, insomnia, loss of appetite, and increased stereotypic behavior. These results suggest that when treating children with autism spectrum disorders accompanied by hyperactivity and impulsiveness, the low-to-medium doses are likely to produce modest benefit. However, attempts to achieve a greater benefit by pushing the dose upward are likely to encounter dose-limiting adverse effects.

See Also

▶ Stimulant Medications

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M-FUN

▶ Miller Function and Participation Scales

Microcephalic

▶ Microcephaly

Microcephalus

▶ Microcephaly

Microcephaly

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Synonyms

Microcephalic; Microcephalus; Nanocephaly

Definition

The term "microcephaly" is used to indicate a head circumference (HC) with two standard deviations (SD) below that expected for age, sex, and race. Some authors consider microcephaly when the HC is 3 SD below. A small skull suggests, in most cases, a small brain. Given that 55% of the brain is cortex, a small brain means less cerebral cortex and it is generally associated with mental retardation. We distinguish two forms of microcephaly: primary and secondary. When it appears before the first 32 weeks of gestation, it is considered as primary microcephaly, and when it appears after birth, it is considered as secondary microcephaly. Most neurons are generated during the first 21 weeks of gestation, and neuronal connections after birth. Therefore, in cases of primary microcephaly there is often a lack of neurons, whereas in the secondary cases, the initial neuronal production is usually normal, producing few neural connections or subsequent neuronal death. The causes of both primary and secondary microcephaly may be genetic, secondary to prenatal infections, or metabolic diseases among others.

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Micrographia

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Definition

Micrographia is abnormally small handwriting or handwriting that becomes progressively smaller and harder to read. Micrographia is a common feature of Parkinson's disease, possibly reflecting difficulties with scaling and controlling the amplitude of movement (Rao et al., 2003). Micrographia, however, can develop as a sign of focal neurological lesions that disrupt the cortico-subcortical loop involving the putamen, thalamus, premotor cortex, and sensorimotor cortex (Denes, Signorini, & Volpato, 2005; Kim, Im, Kwon, Kang, & Lee, 1998). Difficulties in handwriting have been documented in children with autism spectrum disorders (ASD), including problems with forming letters (Fuentes, Mostofsky, & Bastian, 2009) and macrographia (Beversdorf et al., 2001), but not micrographia.

See Also

▶ Apraxia
▶ Gross Motor Skills
▶ Macrographia

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Midbrain

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Synonyms

Mesencephalon

Definition

The midbrain is a component of the brain stem that plays a role in a number of central nervous system functions. It contains the substantia nigra, which has an important role in motor function. It also plays a role in vision, hearing, and arousal. Gaffney et al. (1998) found that the entire brain stem to be significantly smaller in a group with autism. Other groups have replicated the finding and extended it to the midbrain in particular. Hashimoto et al. (1992) found that the midbrain and pons (another component of the brain stem) were significantly smaller in a group with autism in comparison to a control group. Furthermore, several studies have found functional abnormalities in the brain stems of subjects with autism (Maziade et al., 2000; Thivierge, Bédard, Côté, & Maziade, 1990).

See Also

▶ Midbrain Raphe

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Midbrain Raphe

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Synonyms

Midbrain raphe nuclei; Nuclei of raphe; Raphe nuclei

Definition

"Midbrain raphe" refers to two nuclei found in the reticular formation of the midbrain: the superior central nucleus and dorsal raphe nucleus. Other raphe nuclei are also found in the medulla and pontine reticular formations. The common element between all raphe nuclei is that they form a seam, or ridge, along the medial aspect of the brain stem,

making up the most medial aspect of the reticular formation, a phylogenetically ancient part of the brain. The primary purpose of all raphe nuclei appears to be to release the neurotransmitter serotonin to other areas of the brain, including areas responsible for social information processing. They are also thought to play a fundamental role in regulating circadian rhythm (For a discussion of the role of serotonin in autism, please see the *serotonin* section of the encyclopedia. For a more general discussion of the midbrain, please see the *midbrain* section of the encyclopedia.)

See Also

▶ Midbrain
▶ Serotonin

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Midbrain Raphe Nuclei

▶ Midbrain Raphe

Middle Ear Infection

▶ Otitis Media

Milestone

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Synonyms

Developmental milestones; Indicator; Marker

Definition

Skills that are indicative of development. Examples are taking a first step, smiling for the first time, and waving "bye-bye." Children reach milestones in how they play, speak, learn, behave, and move (Center for Disease Control [CDC] 2010). There is a standard pattern and age range for how and when most children achieve these milestones. Children with autism are typically delayed in their acquisition of communicative and social developmental milestones and also in their development of skills such as using eating utensils, drawing, dancing, rhythm, and music (Jones & Prior, 1985).

See Also

▶ Developmental Milestones

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Milestones

▶ Objective

Milieu Teaching

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Definition

Milieu teaching (Hart & Risley, 1975) includes a group of procedures, derived from the behaviorist

tradition, that were developed to teach language skills to children by embedding learning opportunities within the child's everyday (i.e., natural) environment and by taking advantage of a child's interest in and motivation to gain access to materials. According to Goldstein (2002), incidental teaching represents the key component of milieu teaching. Incidental teaching episodes begin with spontaneous child-initiated communication acts as the child attempts to gain access to preferred materials, objects, or events within the natural environment. These child communication acts serve the pragmatic function of requesting (or manding). In addition to incidental teaching, two other well-known milieu language teaching procedures (described below) are mand model and time delay.

Because they are embedded in the natural environment, milieu language teaching procedures are often taught to parents who can then incorporate milieu language procedures into the child's everyday routines and activities.

There are now many variants of the milieu teaching approach including prelinguistic milieu teaching, which focuses on teaching preverbal children to use nonverbal communication skills such as gestures, eye gaze, and vocalization; and enhanced milieu teaching, a more comprehensive approach to naturalistic language intervention, that includes environmental arrangement, responsive interaction techniques, and milieu teaching procedures.

According to Gilbert (2008), the following components are characteristic of milieu teaching:
1. Training in everyday environments
2. Arranging the environment to promote spontaneous requesting by the child
3. Offering preferred toys and activities to reinforce child communication
4. Building predictable turn-taking routines
5. Use of time delay (i.e., expectant waiting) to encourage communication
6. Waiting for the child to initiate by gesturing or indicating interest in an object or activity
7. Providing models of more advanced communication following a child initiation
8. Rewarding communication with access to the desired object/activity rather than unrelated reinforcers

Historical Background

Classic behavioral approaches to early language intervention made use of imitation procedures and tangible rewards for imitation. These methods have several drawbacks including communication that is passive or prompt dependent or which does not generalize to contexts outside of those in which the communicative behavior was taught. In addition, children who have not yet acquired the understanding that communicative bids can be used to affect the behavior of other people (i.e., who do not understand the instrumental function of communication as a means to a desired end) may have difficulty acquiring basic communication skills.

In response to these drawbacks of discrete trial interventions, behavioral interventionists began to develop methods that were based upon the strengths of behavioral programming (e.g., predictable structure, use of task analysis, attention to antecedents and consequences of behavior). These methods addressed the need to establish basic communicative behavior and to generalize communicative acts beyond the training setting. These developments also included the use of the natural environment as the context for learning, planning of contingencies carefully engineered to elicit spontaneous communicative acts that could be shaped toward more conventional and functional language, and the inclusion of parents as intervention agents.

Rationale or Underlying Theory

The rationale that led to the emergence of milieu teaching approaches is that it is important for children to learn to communicate within the everyday context within which their communication behaviors will be used. In addition, by arranging the environment to provide objects, actions, and events in which children have an interest, the child will be motivated to direct a request for access to the desired object or activity to the communicative partner who can then model more advanced and conventional forms of communication.

Goals and Objectives

The broad goal of milieu teaching is to increase the child's use of specific requesting behaviors. Related goals include teaching related grammatical forms and vocabulary. According to Hancock and Kaiser (2007), milieu teaching emphasizes reciprocity, turn taking, following the child's lead, meaningful and contingent feedback for child communication, and expansion of child utterances to model more advanced forms.

Treatment Participants

Responsive education/prelinguistic milieu teaching is designed for children at developmental levels between 12 and 18 months who have not yet become clear and frequent communicators. If children use more than 10 words or signs, or understand more than 75 words, then they should be enrolled in an intervention that places more of an emphasis on expressive vocabulary. Children for whom RE/PMT is appropriate should produce less than two acts of intentional communication per minute during play interactions with a caregiver.

Children enrolled in enhanced milieu teaching should be verbally imitative, have at least 10 expressive vocabulary words, and should have a mean utterance length of 1.0 to 3.5 words.

Treatment Procedures

Incidental teaching, time delay, and mand modeling have been identified as major components of the milieu language teaching procedure.

In the mand-model procedure, the teacher, clinician, or parent arranges the environment to include objects/actions/events that the child is motivated to request access to. When the child approaches the materials, the adult provides a mand, asking: "What do you want?" If this question elicits the child's production of a word or word approximation, the adult expands by providing a semantic or grammatically more advanced version of the child's production.

If the child does not respond to the mand, the clinician provides a model: Say, I want truck. If the child does not respond, the teacher provides one more model and provides the child with access to the desired material.

The time delay procedure is a prompt fading strategy used to encourage children to use vocabulary that they do know, but may not frequently produce spontaneously. Time delay is similar to "fill in the blank." Again, desired materials are available to the child. The teacher holds an item (e.g., a puzzle piece of a cow) and says, "I want the _____."

Incidental teaching is a technique in which the adult uses child initiations during ongoing activities to provide language input. Incidental teaching requires that the environment be arranged to include materials and activities that are highly motivating to the child such that the child will initiate to gain access to the materials. Incidental teaching is child-directed in that the adult follows the child's lead and allows the child's current focus of interest to guide the teaching episodes.

Efficacy Information

According to the American Speech-Language-Hearing Association, there is a large body of empirical support for more contemporary behavioral approaches using naturalistic teaching methods that demonstrate efficacy for teaching not only speech and language but also communication. The following specific intervention strategies have been found to promote initiation and generalization: arrange the environment to provide opportunities for communicating with preferred materials, encourage child initiations and follow the child's attentional focus and interest, intersperse preferred and nonpreferred activities, use embedded instruction in the natural environment, offer choices and encourage choice making, use natural reinforcers that follow what the child is trying to communicate, and use of time delay.

There are only a few studies, all using single-subject design, that have compared traditional

discrete trial with naturalistic behavioral approaches. These studies have reported that naturalistic approaches are more effective at leading to generalization of language gains to natural contexts.

Outcome Measurement

Outcome measures used in studies of milieu teaching will typically consist of measures of the rate or frequency of child nonverbal or verbal communication acts, measures of utterance length (mean length of utterance in words), measures of use of grammatical morphemes (mean length of utterance in morphemes), and vocabulary use (lexical diversity, number of different words). Other measures may include parent use of targeted strategies or number of milieu teaching episodes.

Qualifications of Treatment Providers

Individuals who teach parents must have skills in the delivery of milieu teaching procedures but must also have skills in interacting with parents in ways that support parent learning. Professionals must have skills in providing coaching and feedback to parents and must be able to model desired parent behaviors within the context of a parent-child interaction without disrupting the interaction or overwhelming the parent.

See Also

▶ MacArthur-Bates Communicative Development Inventories, Second Edition

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Milk Protein

▶ Casein

Miller Assessment for Preschoolers (MAP)

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Synonyms

MAP

Description

The Miller Assessment for Preschoolers is designed to evaluate the developmental status of children aged 2 years 9 months to 5 years 8 months across a broad range of areas including behavioral, motor, and cognitive functioning. The MAP test items are categorized into five performance indices. The foundations and coordination indices assess sensory motor abilities involving basic gross and fine motor tasks, awareness of sensations, and oral motor skills. The verbal and nonverbal indices assess cognitive skills required for language development, problem solving, memory, and perception. And the complex task performance index measures sensorimotor abilities in conjunction with cognitive abilities that require the interpretation of visual-spatial information. For children with severe developmental problems, the MAP can be used to provide a developmental overview and to clarify strengths and weaknesses. The MAP may be administered and scored by a wide range of professionals including psychologists, occupational therapists, physical therapists, speech pathologists, nurses, or special education teachers. Scores are obtained through direct testing, and subjective aspects of performance are included in the behavior during testing checklist as well as in supplemental observations that do not contribute to a child's total score. Total scores and performance index scores are expressed in percentile ranks. Item percentiles can be used to interpret the performance of at-risk or borderline cases.

Historical Background

The Miller Assessment for Preschooler was the culmination of 10 years of research involving 4,000 children and 800 test items. Each item was field tested with small samples of preschoolers, and 530 items were chosen for the MAP tryout edition. It is from this sample that the 27 items that constitute the MAP were selected. The MAP was first published in 1982 and then revised in 1988. The theoretical information that contributed to the development of the MAP comes from a broad range of literature in child development, education, psychology, language development, physical and occupational therapy, and medicine.

Psychometric Data

The MAP was standardized on a sample of 1,200 preschoolers, representing all nine continental geographic regions of the United States. Approximately equal numbers of children in each region were tested, and the sample was stratified by age, sex, race, size of residential community, and socioeconomic factors.

Reliability

Reliability of the MAP was determined using interrater agreement, test-retest reliability, and internal consistency of the total test.

Interrater reliability was calculated on 40 children. Correlation coefficients were calculated on a sample of 40 children who participated in the interrater reliability study. Scores ranged from .84 to .99 for the total test and the performance indices and are suggestive of a high level of interrater agreement.

Test-retest reliability was calculated on a group of 81 children randomly selected from the standardization sample. The two tests were administered between 1 and 4 weeks after initial testing. Retest stability is reported in percentages and ranged from 72% to 94% for the total score and the five performance indices.

Internal reliability was calculated from the item raw scores for the total sample using split

half method and the average item to test correction. Both methods produced internal consistency values around .80.

Validity

Three methods were used to support the validity of the MAP: content, criterion-related, and construct validity.

Content validity of the items was established by experts from a number of specialty areas who were asked to rate the content validity within their fields of expertise. A content specifications by item table supports the content validity of the test.

Criterion-related validity was established using concurrent and predictive validity. MAP scores were correlated with one of the four standardized instruments including the Wechsler Preschool and Primary Scale of Intelligence (WPPSI), the Illinois Test of Psycholinguistic Abilities (ITPA), the Southern California Sensory Integration Tests (SCSIT), and the Denver Developmental Screening Test (DDST). Correlations of the complex task index and the WPPSI verbal and performance IQ approached statistical significance. Correlations were significant for the ITPA and the MAP total score, the coordination index, and the nonverbal index. One significant correlation was found between the MAP foundation index and the SCSIT score. In comparison to the DDST, 72% of the sample was similarly grouped by both instruments; however, the MAP identified 24% more children in the at-risk categories.

Evidence of predictive validity was obtained from a study of children tested 4 years after initial testing with the MAP. Results suggest that performance obtained on the MAP in the preschool years is predictive of intelligence, motor skill acquisition, and school achievement 4 years later.

Clinical Uses

The MAP may be administered and scored by a wide range of professionals including psychologists, occupational therapists, physical therapists, speech pathologists, nurses, or special education teachers. The purpose of the MAP is to identify developmentally delayed preschool children who need further evaluation and to provide a comprehensive structure clinical framework for identifying a child's strengths and weaknesses. The intent is to identify difficulties in children in the preschool age group (that typically go undiagnosed) that cause them to fall behind their peers in one or more areas of development. The MAP can also be used with children who have more severe developmental problems to provide a developmental overview or strengths and weaknesses when comprehensive standardized evaluations cannot be administered.

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Miller Function and Participation Scales

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Synonyms

M-FUN

Description

The Miller Function and Participation Scales (M-FUN) is a developmental assessment for children ages 2.6–7.11, designed to assist therapists in determining how a child's motor capacities affect participation in home and school environments. Based on the World Health Organization's International Classification of Function, Disability and Health (ICF; WHO, 2001), the M-FUN addresses the mandate of occupational therapists to evaluate the whole child and determine how a child's motor problems might be affecting his or her functional abilities. The scales consist of a performance component, which includes workbook activities to tap visual motor abilities and play-based activities that tap gross and fine motor abilities. The performance component is comprised of three subscales: gross motor, fine motor, and visual motor. In addition, there is a participation component, which consists of three observation checklists that rate a child's participation at home, school, and during the testing session. Among the abilities examined in the M-FUN observation checklists are mobility, postural control, sensory discrimination and modulation, social skills and communication, object manipulation, and participation in daily routines.

Several indicators of a child's performance can be derived from the M-FUN including standard scores, percentile ranks, and age equivalents for each subscale. Criterion-referenced scores are derived for home observation, classroom observation, and test observation checklists. The scales can be used to determine if a child has a developmental delay, or for children older than 7.11 years who have known motor delays, the test can be used to measure progress or to plan treatment. Unique to the M-FUN is the Neurological Foundations Profile, which facilitates the identification of underlying impairments affecting the child's ability to perform tasks and serves as a guide for treatment planning. Additionally, the M-FUN provides information about growth in the child's visual motor, fine motor, and gross motor abilities. Following intervention, the child can be retested using the M-FUN, and progress scored can be derived that reflects the acquisition of new skills even if he or she is not progressing at the same rate as age-ability peers.

Historical Background

The M-Fun was developed out of the need for a functional motor evaluation of skills and abilities that underlie participation in school. Based on the model from the ICF (WHO, 2001) and OT Practice Framework (AOTA, 2002), the M-FUN employs a competency model rather than a deficit model to assess children.

Psychometric Data

Normative data was collected from over 400 children from four geographic regions of the United States (West, South, North Central, and Northeast). The standardization sample closely

matches the demographic characteristics of children ages 2.6–7.11 by sex, race/ethnicity, and parent education level reported the 2002 United States census. The standardization sample also included children in each age group (5–7% of total) who were diagnosed with a motor delay or impairment.

The reliability of the M-FUN was examined using test-retest reliability, internal consistency, and interrater reliability. Retest of 27 children from the standardization sample was conducted with 0–21 days of initial testing. Moderately high reliability was found across time for all ages with scores ranging from .77 to .82. Internal consistency reliability supports the homogeneity of the items in the scale with the average reliability coefficients ranging from .85 or the visual motor subscale to .90 for the fine motor subscale and .92 for the gross motor subscale. Reliability coefficients for the clinical group on each subscale were similar to those reported for the normative sample. In addition, reliability coefficients for all three observation checklists were excellent, ranging from .87 to .98. Interrater reliability was computed for 29 children with the average decision agreement 93–96% for each subscale.

Validity data was collected for test content, internal structure, relationship to other variables, and diagnostic accuracy.

Content validity was based on ICF, the OT Practice Framework, a review of the literature, and focus group experts. The internal structure was analyzed by examining patterns of scaled score intercorrelations. Coefficients were between .47 and .55 suggesting that each subscale measures a different motor construct/ability. Concurrently validity was examined in order to determine the M-FUN's relatedness with other instruments designed to measure similar constructs. One study compared scores on the Miller Assessment for Preschoolers (MAP) to scores on the M-FUN in a sample of 15 children. Correlations ranged from .47 to .83 suggesting that the two tests supply complementary information about a child's abilities. A study of discriminant validity revealed that the M-FUN subscales discriminate between children with clinically

diagnosed delays and those who are typically developing at a meaningful and statistically significant level. Classification analysis to assess the clinical utility of the M-FUN produced moderate to excellent sensitivity and specificity. For cutoff scores of 1 standard deviation below the mean, the sensitivity was between .69 and .89, and the specificity was between .80 and 1.00.

Clinical Uses

The M-FUN may be administered by a variety of qualified professional including occupational therapists, physical therapists, special education or adaptive physical education specialists, and early childhood interventionists who are interested in determining how a child's motor abilities affect their participation in home and school. Examiners should have experience in test administration, scoring, and interpretation, as well as knowledge of sensory processing and motor development in preschool and school-aged children.

The M-FUN can be used for a variety of purposes:
• To determine a child's eligibility for intervention services to address gross motor, fine motor, and visual motor delays
• To document delays in motor development (gross motor, fine motor, visual motor)
• To determine motor readiness/preparedness for school – strengths and needs in the area of motor abilities that may impact on the child's ability to participate fully in school and home routines
• To make recommendations for optimizing the child's functioning at school and home (least restrictive environment)
• To assist in the development of treatment planning through use of the neurological foundations profile
• To identify underlying neuromotor deficits affecting functional abilities – to identify fine motor, visual motor, and gross motor skill areas that might affect a child's school success

To measure progress over time following a course of intervention

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Mindblindness

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Definition

"Mindblindness" is a term coined by autism researcher Simon Baron-Cohen (1990). It also is the title of the essay containing work from his doctoral dissertation (Baron-Cohen, 1997). In that essay, Baron-Cohen theorized that humans have evolved to be able to "mindread" or to effortlessly, automatically, and unconsciously assess the behavior of others. This is critical because mindreading forms the basis of the ability to successfully engage in social interactions requiring the minute-by-minute interpretation and prediction of the behavior of one's interaction partners. Baron-Cohen goes on to propose that persons with autism have a selective impairment in mindreading.

The concept of mindblindness is rooted in the fields of both evolutionary biology and cognitive science. It is Baron-Cohen's contention that natural selection favored species and individuals from those species with greater social intelligence which included mindreading abilities. Mindreading abilities enabled primates to cohesively bond together in organized social hierarchies to achieve common goals. Those who were more adept at playing social chess through excellent mindreading skills (forward planning, plotting, counterplotting, strategic problem solving to achieve one's goals) ended up at the top of such social hierarchies. Given the importance of mindreading abilities to survival, in this view, such abilities are believed to be a discrete component of cognition or a "module."

The human mindreading system is thought to have four separate components. The first – the intentionality detector (ID) – is a perceptual device that interprets approach and avoidance in terms of goals and desires. For example, it enables one to interpret the motion of a mouse toward cheese as reflecting the mouse's desire to eat. ID is the first mechanism human infants use. It can be cued by all forms of sensory input (i.e., seeing or hearing something). The second mechanism is the eye direction detector (EDD), which works through the visual system and computes whether eye-like stimuli are directed toward or away from something, including whether the eyes are directed at the organism itself or toward another organism. The third component – the shared attention mechanism (SAM) – builds triadic representations which specify relations among the agent, the self, and another object or agent. For example, the SAM would compute that Johnny and I are both looking at the cheese (or mom). Finally, the theory of mind mechanism (TOMM) is a system for inferring the full range of mental states from behavior or for employing a "theory of mind." Theory of mind is a shorthand term for the capacity to attribute mental states to oneself and others and to interpret behavior in terms of mental states.

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Mineral Treatments

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Definition

Dietary minerals are chemical elements needed for mammals to maintain basic physiologic functioning. Minerals that are needed in larger amounts to maintain health (macrominerals) include calcium, phosphorous, magnesium, sodium, potassium, phosphorous, chloride, and sulfur. Lesser amounts of iron, manganese, copper, iodine, zinc, cobalt, fluoride and selenium, and molybdenum are necessary for cellular functioning (trace minerals). Minerals are absorbed from dietary sources. The dietary reference index (DRI) publishes the required intake of minerals for age and gender. If a person with autism ingests a very restricted diet because of food aversions or is given a restricted diet as a proposed intervention for symptoms of autism, they might be at increased risk for diminished intake of minerals. For example, removal of dairy products from the diet eliminates the major source of calcium in milk products. Mineral supplementation in individuals with autism might be indicated if there is deficient nutritional intake. Another conventional medical intervention that would require mineral supplementation might be decreased iron status. Iron deficiency will ultimately lead to low blood counts or anemia. Prior to that point, lowered iron stores may lead to fatigue and sleep disruption/restless leg syndrome, among other neurobehavioral symptoms. Iron supplementation would be recommended after laboratory documentation of deficiency.

In addition to physiologic replacement of necessary nutrients, a number of controversial therapies provide minerals at amounts greater than recommended by the DRI to target symptoms of autism. Minerals included in novel therapy regimens include magnesium (given with vitamin B6) and zinc. Blood and hair measurement of minerals has been used without scientific support to date to determine if individuals with autism have altered metabolic requirements for minerals or mineral levels purported to be associated with neurologic symptoms. Laboratory measurement of minerals in blood or hair is not currently a conventional component of the etiologic workup of individuals with autism. Testing for specific minerals may be necessary with suspected toxic exposures such as environmental lead exposure. Chelation is a medical procedure used in individuals with autism without support of the scientific literature to increase excretion of heavy metals (a type of mineral) like mercury that some believe are associated with symptoms of autism. This practice increases excretion of other minerals from the body as well and may impact the availability of minerals necessary for routine physiologic processes. Practitioners who prescribe chelation will prescribe supplements containing minerals and trace minerals that may be excreted along with the lead or other metal of concern.

See Also

▶ Chelation

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Minimal Brain Damage

▶ Attention Deficit/Hyperactivity Disorder

Minimal Brain Dysfunction

▶ Attention Deficit/Hyperactivity Disorder

Minimal Speech Approach

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Definition

The minimal speech approach was developed by Potter and Whittaker (2001) to enable communication in children with autism. This approach requires the caregiver or interventionist to use simple speech, consisting of one to three words, usually nouns, which are paired with nonverbal communication. The nonverbal communication can consist of a picture, an object, or a gesture, which help to facilitate comprehension. For example, using the minimal speech approach, the therapist might say "lunch" and point to a picture communication symbol of a lunch box rather than saying "All right, choice time is over now. We need to put everything away and get ready for lunch. Let's go."

In order to create a communication-enabling environment, key characteristics of this approach include reducing the use of speech in all situations, appropriate mapping of single words, giving information in nonverbal ways, minimizing running commentary, delaying the use of speech when teaching new tasks, and avoiding a focus on relative and temporal terms (Potter & Whittaker, 2001).

Children with autism often experience confusion when excess speech occurs during communicative interactions. This can lead to anxiety and distress. The simplification of language aims to avert social disengagement and challenging behaviors by facilitating understanding. Potter and Whittaker (2001) found that when a minimal speech approach is used consistently and appropriately, children are more socially responsive and demonstrate more spontaneous communication.

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Mirror Mechanisms

▶ Frontal Lobe Findings in Autism

Mirror Neuron System

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Structure

Mirror neurons are a unique subset of neurons located in motor areas of the brain, which are

thought to play a central role in social communication and imitation. They are active not only during the execution of movements but also during the passive observation of movements made by others. It has been hypothesized that the activity of mirror neurons during observation of movement might represent an internal "motor simulation" of the observed movement. Such a simulation may then be used as a basis for imitating the observed movement or as a gateway for accessing the intentions, goals, and emotions associated with the movement in the mind of the observer. According to the hypothesis, the observer then attributes these intentions and emotions to the observed person in order to interpret their behavior. Individuals with autism have difficulties understanding the intentions, states, and emotions of people around them. It has been suggested that these social difficulties may be caused by the development of abnormal mirror neurons. Despite the large amount of attention that this hypothesis has received in the popular and scientific literatures, the evidence supporting it has been weak and inconsistent. Below is a general overview of mirror neuron research in monkeys and in humans followed by a description of the research related specifically to autism.

Function

Monkey Mirror Neurons

In 1996, Gallese et al. (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996) discovered that about 10% of neurons in ventral premotor area F5 of the macaque monkey respond not only when the monkey executes a particular movement – as expected in this cortical motor area – but also when the monkey passively observes the experimenter performing that very same movement. These visuomotor neurons were named "mirror neurons" because their activity in the brain of the passively observing monkey seems to mirror that of motor neurons active in the person actually executing the movement. Following this initial finding, in 1998, Fogassi et al. (Fogassi, Gallese, Fadiga, & Rizzolatti, 1998) reported that mirror neurons also exist in the inferior parietal lobule

(IPL) of the macaque and established the idea of a "mirror system" composed of these two cortical areas.

In these and further studies (Caggiano, Fogassi, Rizzolatti, Thier, & Casile, 2009; Ferrari, Gallese, Rizzolatti, & Fogassi, 2003; Ferrari, Rozzi, & Fogassi, 2005; Fogassi et al., 2005; Kohler et al., 2002; Umilta et al., 2001), mirror neurons were identified based on two critical response characteristics: First, mirror neurons respond in a selective manner to a particular preferred movement such that some neurons respond, for example, only to grasping with the whole hand while others respond only to gripping with the fingertips. In this manner, mirror neuron responses distinguish between different movements in an analogous manner to primary visual cortex neurons that distinguish between different visual stimulus orientations. Second, mirror neurons respond similarly to their preferred movement regardless of whether it is being passively observed or actively executed; thus, the same mirror neuron that responds when the monkey grips with the fingertips also responds when the money passively observes someone else gripping with the fingertips. These unique characteristics distinguish mirror neurons from the many other visual, motor, and visuomotor neurons that comprise about 90% of the neurons in areas F5 and IPL of the monkey and are involved in a multitude of visuomotor processes needed for the coordination of movement (Castiello, 2005).

The discovery of mirror neurons generated much excitement regarding their possible role in mechanisms of movement understanding and imitation. When we observe someone performing a movement, such as waving their hand to indicate "hello," how do we instantaneously understand that their intention is to greet us? According to the "simulation theory," we covertly and unconsciously simulate ourselves performing the movement, then access our own associated intentions and goals for that particular movement and assign them to the person we are observing (Rizzolatti & Craighero, 2004). This chain of neural computations supposedly enables us to both understand and ascribe intentionality to

others. Mirror neurons have, therefore, been proposed as the physiological mechanism that enables a critical step in this process: precise visual to motor mapping (Rizzolatti & Sinigaglia, 2010). Specifically, according to the theory, whenever you observe someone performing an action, particular movement-selective mirror neurons embedded in your motor system are activated, enabling you to simulate yourself performing that movement and to access your own associated intentions and goals (probably through activity of other brain areas, including the limbic system). Taken a step further, mirror neurons can be thought of as a sensorimotor gateway for forming an internal representation of the observed person's intentions and emotions based on their body language, facial expressions, actions, and so on (Rizzolatti & Craighero, 2004; Rizzolatti & Sinigaglia, 2010).

It has also been suggested that the same act of motor simulation facilitates imitation and thereby underlies our ability to learn new movements by imitating others (Buccino et al., 2004b; Iacoboni et al., 1999). In this case, covert simulation, which involves activating the precise motor neurons that encode the proper kinematics and dynamics necessary for the execution of the observed movement, may be followed by overt imitation, which involves activating the same neurons along with additional motor neurons that actually command the appropriate muscle contractions.

It is important to note two rather surprising points regarding mirror neuron research in nonhuman primates. First, all of the described mirror neurons responded only to object-oriented movements such as grasping or ripping an object. Thus, while the macaque monkey does display several social and communicative movements (e.g., friendliness by lip smacking or threatening by exposing teeth), there have been no reports of mirror neurons responding to such movements as one might have expected if this system was to mediate the representation of other's intentionality. This lack of evidence argues against the suggestion that mirror neurons enable the monkey to understand the intentions and emotions of other monkeys. Second, although macaque monkeys clearly possess mirror neurons, this species does not naturally learn by imitation, except for, perhaps, a very short period at infancy (Ferrari et al., 2006). The absence of imitative behavior in the macaque challenges the hypothesis that mirror neurons enable imitation.

Human Mirror System

The excitement regarding the possible role of mirror neurons in social cognition drove many investigators to search for the human homologue of the monkey mirror system. Early neuroimaging studies utilizing positron emission topography (PET), functional magnetic resonance imaging (fMRI), electroencephalograph (EEG), and magnetoencephalograph (MEG) have applied three types of protocols to elicit mirror neuron responses in humans: passive movement observation, active movement execution, and imitation (simultaneous observation and execution). This section will focus on the fMRI studies because this technique offers the best spatial resolution and offers the strongest evidence regarding the cortical location of responsive neural populations. The discussion below, however, is just as applicable to studies using the other neuroimaging techniques that have generally used the same experimental protocols and the same underlying logic.

In the first protocol, subjects passively viewed images or video clips of movements, such as a smiling face or a hand grasping an object, and their neural responses were compared against a rest condition, following the logic that mirror neurons respond during movement observation and not during rest (Buccino et al., 2001; Buccino et al., 2004a; Iacoboni et al., 2005). In the second protocol, responses during movement execution were recorded to first isolate cortical motor areas and then assess responses to movement observation within these predefined areas (mirror neurons are expected to respond both during observation and execution of a movement). In the third protocol, an imitation condition was added and the responses during imitation were compared with responses during observation and during execution with the logic that mirror neurons should be more active during simultaneous observation and execution than during execution

or observation alone (Buccino et al., 2004b; Carr et al., 2003; Grezes, Armony, Rowe, & Passingham, 2003; Iacoboni et al., 1999; Leslie, Johnson-Frey, & Grafton, 2004; Tanaka & Inui, 2002).

These fMRI studies consistently reported that two cortical areas respond during movement observation, execution, and imitation: the anterior intraparietal sulcus (aIPS) and the ventral premotor (vPM). Most of the studies proposed that these areas compose the human "mirror system," implicitly suggesting that they contain mirror neurons. Further neuroimaging studies have attempted to characterize the responses of the human "mirror system" during observation, execution, and imitation of different movements. For example, comparing mirror system responses to hand movements that have a goal versus movements that do not (Iacoboni et al., 2005) or in which movements are made by a human arm versus by a robot arm (Gazzola, Rizzolatti, Wicker, & Keysers, 2007). The majority of these studies interpreted stronger mirror system responses to particular conditions as evidence of mirror neuron preference for particular types of movements rather than others.

There are two concerns with these early experiments and the interpretation of their results. The first is that these experiments were unable to measure exclusive mirror neuron activity. For example, the typical results of passive movement observation and imitation experiments reveal strong responses in many cortical areas, including areas that are not believed to contain mirror neurons (e.g., primary visual cortex). This is clear evidence that many other neurons (e.g., visual neurons) in diverse cortical areas respond strongly during these tasks. Limiting the analysis to cortical areas that respond during movement execution (by masking out areas that do not) does focus the analysis on more meaningful brain areas but does not solve the problem. As mentioned above, 90% of neurons in "mirror system" areas are not mirror neurons but are rather visual neurons that respond only during movement observation, motor neurons that respond only during movement execution, or visuomotor neurons that respond during both but do not respond

selectively to movement identity (e.g., neurons selective for object rather than grasp type (Murata, Gallese, Luppino, Kaseda, & Sakata, 2000). Since neuroimaging methods record the average response of very large neural populations, how can one know if the reported responses were generated by the activity of mirror neurons or by the activity of any of these other intermingled neural populations? For example, if a study reports that mirror system areas exhibit stronger fMRI responses during observation of movements with goals than movements without goals (e.g., Iacoboni et al., 2005), does it necessarily mean that mirror neurons responded more strongly? Or could it be that visual neurons responded more strongly because video clips of movements with goals contain richer visual stimuli than video clips of movements without goals?

The second, and perhaps more important concern, is that these studies did not assess movement selectivity. Movement selectivity is a defining physiological signature of mirror neurons in the monkey and is of central importance for the hypothesis that mirror neurons play a role in mapping perception to action. If mirror neurons indeed enable understanding and/or imitation of movements, subpopulations of mirror neurons must distinguish between different movements such that particular mirror neurons must respond selectively to particular movements (Dinstein, 2008; Dinstein, Thomas, Behrmann, & Heeger, 2008b). Without clear response selectivity across observation and execution, the mirror neuron theory falls apart. Imagine, for example, a situation where you observe someone executing a "thumbs up" movement. In order to properly understand that movement by simulation, it is critical that you activate the correct motor neurons encoding that particular movement. If you accidently activate another group of motor neurons that encode the "thumbs down" movement, you will arrive at the wrong conclusion regarding the intention of the person you are observing. Assessing movement selectivity in mirror system areas is, therefore, a crucial step for confirming or refuting the mirror neuron theory (Dinstein, 2008; Dinstein et al., 2008b).

A common method for assessing neural selectivity using fMRI takes advantage of the fact that

sensory neurons adapt/habituate when their preferred stimulus is presented repeatedly (Grill-Spector, 2006; Grill-Spector & Malach, 2001; Krekelberg et al., 2006). Cortical areas containing mirror neurons may, therefore, exhibit reduced fMRI responses when the same movement is presented repeatedly (a single neural population responds repeatedly and adapts) in contrast to when different movements are presented (different neural populations respond and there is no adaptation). Mirror neurons may be expected to adapt during trials where the same movement is repeatedly observed, repeatedly executed, observed and then executed, or executed and then observed (cross-modal adaptation). Showing such response selectivity in mirror system areas would be strong evidence for the existence of mirror neurons and would also offer a tool for further characterizing their selectivity for particular types of movements. For example, does adaptation occur across different movements that share a common goal (waving "hello" with either left or right hand) but not across different movements that do not (waving "hello" with left hand and waving "come here" with right hand). Such results would offer important evidence regarding the movement characteristics that are encoded by human mirror neurons.

Several recent studies have used fMRI adaptation protocols to assess response selectivity for different hand movements. These studies have reported visual (Dinstein et al., 2007; Hamilton & Grafton, 2006; Shmuelof & Zohary, 2005), motor (Dinstein et al., 2007; Hamilton & Grafton, 2009), and cross-modal (Chong et al., 2008; Kilner et al., 2009; Lingnau et al., 2009) adaptation in mirror system areas during observation and execution of different hand movements. While some of the studies used object-oriented hand movements (e.g., pulling, gripping, and grasping objects) (Hamilton & Grafton, 2006; Kilner et al., 2009; Shmuelof & Zohary, 2005), others used symbolic or gestural hand movements (e.g., thumbs up, rock, paper, scissors) (Chong et al., 2008; Dinstein et al., 2007; Hamilton & Grafton, 2009; Lingnau et al., 2009). A consistent finding across all studies was that mirror system areas exhibited visual adaptation when the same movement was observed repeatedly and motor adaptation when the same movement

was executed repeatedly. Such adaptation could hypothetically take place in two independent neural populations, one visual and the other motor, or in a single neural population of mirror neurons. While these results do not prove the existence of mirror neurons in humans, they do suggest that neurons with visual and motor movement selectivity are intermingled within mirror system areas in humans. This is somewhat encouraging because a fundamental feature of cortical organization is that neighboring neurons are strongly connected and perform common computations. The existence of neighboring intermingled neurons with movement selectivity, therefore, does suggest the existence of some form of mirror mechanism in humans. More persuasive is a recent study using object-oriented hand movements, which reported visual and motor adaptation as well as both forms of cross-modal adaptation in mirror system areas (Kilner et al., 2009). Cross-modal adaptation could only take place in a mirror neuron population that adapts when observing and then executing or when executing and then observing the same hand movement. Taken together, this evidence suggests that mirror neurons do exist in humans and that, similarly to mirror neurons found in the macaque monkey, they respond selectively to movements involving objects. It is not clear whether there are mirror neurons in humans that respond selectively to gestural and/or communicative movements.

Another method for assessing neural selectivity using fMRI involves the comparison of voxel-by-voxel response patterns using different classification techniques. This analysis is particularly useful in situations where subpopulations of neurons with different selectivity are distributed unevenly within multiple neighboring voxels. In such cases, each subpopulation is expected to generate a unique fMRI response pattern that appears in trials containing its preferred stimulus and is distinct from the pattern generated by neighboring subpopulations in trials containing their preferred stimuli. This technique was successfully used, for example, to study the selectivity of human visual cortex neurons to visual orientations (Kamitani & Tong, 2005), visual motion (Kamitani & Tong, 2006), and visual categories (Haxby et al., 2001).

Two recent fMRI studies have used this technique to assess selectivity for different hand movements in mirror system areas during both observation and execution. The main difference between the studies was that in the first, subjects observed and executed symbolic hand movements (rock, paper, or scissors), while in the second, movements were oriented toward objects (grasping or pulling objects). The first study reported that classification of the fMRI response patterns in aIPS enabled accurate identification of the movement observed or performed on each trial. This shows that each movement was associated with a unique spatial response pattern generated by a unique and selective neural subpopulation (Dinstein, Gardner, Jazayeri, & Heeger, 2008a). If aIPS were to contain only mirror neurons, an identical fMRI response pattern would be expected during observation and execution of the same movement. This, however, was not the case as accurate movement identification by response pattern was possible only within the visual or motor modality but not across modalities. The second study, using object-oriented movements, did report accurate movement classification in aIPS both when assessing responses within each modality as well as across the two modalities (Oosterhof, Wiggett, Diedrichsen, Tipper, & Downing, 2010). These results seem to suggest a dissociation between responses to symbolic hand movements and object-oriented hand movements. Again, clear evidence supporting the existence of mirror neurons in humans seems to exist when considering object-oriented movements rather than gestural movements.

To conclude, the adaptation and classification studies seem to present converging evidence suggesting that, like the monkey, humans have mirror neurons that respond selectively to different movements involving object manipulation. The case for mirror neurons selective for gestural and communicative movements seems less clear and is somewhat at odds with the mirror system hypothesis suggesting that mirror neurons enable social communication. Proper social communication is mostly based on correct interpretation of body language, gestures, and expressions rather than interpretation of object-oriented movements such as grasping or pulling.

Pathophysiology

Mirror System Dysfunction in Autism?

Impaired social interaction is one of the three core behavioral symptoms of autism (DSM-IV-TR, 2000). Impaired imitation may also be a characteristic of autism, although there is controversy regarding its consistency (Hamilton, Brindley, & Frith, 2007). According to the "dysfunctional mirror system theory of autism," these behavioral problems are caused by dysfunctional mirror neurons that impair the individual's ability to simulate observed movements/actions (Williams, Whiten, Suddendorf, & Perrett, 2001). The idea is that inaccurate simulation or perhaps even a complete lack of simulation disrupts the ability to appropriately interpret the goals, intentions, and emotions associated with observed hand gestures, facial expressions, and body language of others. This theory has received an extraordinary amount of attention in both the popular press (Blakeslee, 2006; Ramachandran & Oberman, 2006) and the scientific press (Buccino & Amore, 2008; Iacoboni & Dapretto, 2006; Iacoboni & Mazziotta, 2007; Keysers & Gazzola, 2006; Le Bel, Pineda, & Sharma, 2009; Oberman & Ramachandran, 2007; Perkins, Stokes, McGillivray, & Bittar, 2010; Rizzolatti & Fabbri-Destro, 2008, 2009; Rizzolatti, Fabbri-Destro, & Cattaneo, 2009; Williams, 2008; Williams et al., 2001). The empirical evidence supporting it, however, has been remarkably sparse and inconsistent.

Evidence in support of the dysfunctional mirror system theory of autism has come from several EEG/MEG (Honaga et al., 2010; Martineau, Cochin, Magne, & Barthelemy, 2008; Nishitani, Avikainen, & Hari, 2004; Oberman et al., 2005) and fMRI (Dapretto et al., 2006; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2007; Schulte-Ruther et al., 2011) studies that have reported significantly weaker responses in mirror system areas of individuals with autism, as compared to controls, during passive observation or active imitation of hand movements or facial expressions. Weaker mirror system responses in autism have been interpreted as evidence for weak mirror neuron responses that are unable to complete the proper simulation processes supposedly needed to understand the

meaning of the observed movements or imitate them. There have been, however, a similar number of EEG/MEG (Avikainen, Kulomaki, & Hari, 1999; Fan, Decety, Yang, Liu, & Cheng, 2010; Oberman, Ramachandran, & Pineda, 2008; Raymaekers, Wiersema, & Roeyers, 2009) and fMRI (Dinstein et al., 2010; Marsh & Hamilton, 2011; Williams et al., 2006) studies that have reported equivalent mirror system responses in autism and control groups and one fMRI study that has even reported significantly stronger mirror system responses in autism as compared to controls during the observation of hand movements (Martineau, Andersson, Barthelemy, Cottier, & Destrieux, 2010). As a side note, it is interesting that all of the studies above, regardless of the reported response strength in autism, used gestural hand movements, finger tapping, or facial expressions rather than object-oriented movements. The mixed results were, therefore, not a consequence of using different movements.

Numerous methodological issues could have generated the heterogeneous results described above. For example, it is difficult to control the behavior of subjects during EEG and fMRI experiments. When subjects are asked to imitate a movement, delays in the timing or length of movement execution may greatly impact the estimated brain response. If subjects with autism imitate the movement later or more slowly than controls, their estimated brain responses will seem weaker because of a temporal mismatch between the expected and actual brain response. In such a situation, reduced mirror system responses would have little to do with mirror system abnormalities in autism and a lot to do with a different choice of behavioral response in autism. Regardless of the true reason underlying the reduced responses, the results discussed above clearly show that individuals with autism can exhibit normal mirror system responses under some experimental conditions (Avikainen et al., 1999; Dinstein et al., 2010; Fan et al., 2010; Marsh & Hamilton, 2011; Martineau et al., 2010; Oberman et al., 2008; Raymaekers et al., 2009; Williams et al., 2006). This argues against the claim of a generally dysfunctional mirror system in autism.

As discussed previously, perhaps the biggest concern with the interpretation of the studies above is their lack of ability to isolate mirror neuron responses and their lack of ability to assess movement selectivity. With this in mind, the reports above actually say very little about mirror neuron integrity in autism. Weak, normal, or excessive fMRI responses in mirror system areas could be generated by different combinations of visual neuron responses during observation and motor neuron responses during imitation. There is, therefore, no reason to assume that any of the reported differences in fMRI responses between autism and control groups were due to differences in mirror neuron responses. Furthermore, these studies do not offer any evidence for determining whether neural subpopulations in mirror system areas exhibit normal or abnormal movement selectivity in autism. The "dysfunctional mirror system theory of autism" would predict weak or even a complete lack of movement-selective responses in autism, which would be expected to yield an impaired simulation process. Is this indeed the case?

A recent fMRI adaptation experiment attempted to address this particular question and reported that mirror system responses in individuals with autism exhibited equivalent movement selectivity to that found in controls (Dinstein et al., 2010). In this study, individuals with autism exhibited not only strong mirror system responses during the observation of symbolic hand movements (e.g., rock, paper, scissors, thumbs up), but they also exhibited adaptation in trials where the same movement was repeatedly observed or repeatedly executed. These adaptation results were interpreted as evidence for typical movement selectivity in mirror system areas of individuals with autism. Since selectivity is one of the two defining characteristics of mirror neuron responses, these data offer strong evidence against a general mirror system dysfunction in autism. All of the high-functioning individuals with autism who participated in this study exhibited ADOS scores that were well above the criteria for autism rather than the milder diagnoses of PDD-NOS and Asperger's syndrome. These results, therefore, cannot be attributed to less severe behavioral symptoms in the participating subjects. Note that this study, like all other mirror system studies

in autism, used gestural hand movements rather than object-oriented movements. Since cross-modal adaptation is a key signature of mirror neurons, which seems to be apparent only in responses to object-oriented movements, it would be important to also determine the integrity of such responses in autism.

Finally and more generally, it is important to consider how useful it is to describe autism as a disorder of one particular neural population such as mirror neurons. Most of the symptoms associated with autism do not seem related to mirror neurons at all. These include the core diagnostic symptoms of repetitive behaviors and language impairments (DSM-IV-TR, 2000) as well as the commonly described secondary symptoms, which include sensory hypo/hypersensitivities (Jones, Quigney, & Huws, 2003; Kanner, 1943; Minshew & Hobson, 2008; O'Neill & Jones, 1997), sleep problems (Cortesi, Giannotti, Ivanenko, & Johnson, 2010; Richdale & Schreck, 2009), and gastrointestinal problems (Buie et al., 2010a, b). Furthermore, much of the research into autism suggests that multiple neural abnormalities exist in many brain areas. fMRI studies have reported abnormally weak neural responses in autism not only in mirror system areas but also in superior temporal sulcus (Pelphrey & Carter, 2008), face processing areas (Dawson, Webb, & McPartland, 2005), "mentalizing" areas (Marsh & Hamilton, 2011), and cingulate cortex (Chiu et al., 2008), among others. Reports of abnormal functional (Minshew & Keller, 2010) and anatomical (Courchesne et al., 2007) connectivity have suggested that neural communication and synchronization may be altered (mostly decreased) across multiple brain areas in autism. Developmental studies have reported early overgrowth of gray and white matter in frontal cortex, temporal cortex, and cerebellum, which is followed by arrested growth during adolescence (Courchesne, Redcay, & Kennedy, 2004). Genetic studies have reported numerous mutations, deletions, and single-nucleotide polymorphisms that may increase the risk of developing autism. Most of the associated genes are involved in general cellular development including dendritic growth and synaptic maturation (Geschwind & Levitt, 2007). Such genetic abnormalities would be expected to create widespread excitation-inhibition imbalances (Rubenstein & Merzenich, 2003) as well as abnormalities in the neural architecture and connectivity of multiple brain areas, thereby, impacting multiple behaviors (Bourgeron, 2009). Finally, individuals with autism have abnormally high chances of developing epilepsy throughout life. It is estimated that 20–30% of individuals with autism have epileptic seizures at some point in life and that up to 60–70% may exhibit abnormal epileptiform-like EEG recordings (Tuchman & Rapin, 2002). When considering this larger breadth of evidence, it seems that describing autism as a disorder of mirror neurons may not be particularly useful in capturing the multitude of behavioral and physiological elements associated with the disorder.

To conclude, despite its surprising popularity (Iacoboni & Dapretto, 2006; Iacoboni & Mazziotta, 2007; Rizzolatti & Fabbri-Destro 2008, 2009; Williams et al., 2001), at present, the evidence supporting the "dysfunctional mirror system hypothesis of autism" seems rather sparse, inconsistent, and controversial (Baird, Scheffer, & Wilson, 2011; Dinstein et al., 2008b; Hamilton, 2009; Hamilton et al., 2007). Further assessment of response selectivity in autism using adaptation and classification techniques is warranted in order to reveal useful data that will support or refute the hypothesis. The integrity of mirror system selectivity in autism should be tested with gestural hand movements and facial expressions, which seem particularly relevant to the social symptoms of autism, as well as with object-oriented movements, which seem to be the most effective movements for generating mirror neuron activity in both monkeys and humans.

See Also

▶ Cerebral Cortex
▶ Superior Temporal Sulcus Region

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Mirtazapine

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Synonyms

Remeron

Definition

An antidepressant medication. Mirtazapine exerts its antidepressant effect by inhibiting alpha-2 adrenergic presynaptic receptors, resulting in increased levels of serotonin and norepinephrine. This is an alternate mechanism to that used by SSRI medications. Additionally, mirtazapine blocks H-1 histamine receptors, which may contribute to its sedating effects. Mirtazapine is also associated with increased appetite, higher risk of weight gain, dry mouth, and constipation.

See Also

▶ Antidepressants

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Mismatch Negativity

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Definition

The mismatch negativity (MMN) is an event-related potential (ERP) evoked in response to a perceived change in sensory stimuli. It is commonly elicited in an oddball paradigm in which a standard stimulus is paired with a deviant stimulus, the standard being presented the majority of instances. It generally occurs 150–250 ms after the presentation of the deviant stimulus, though in children its latency is delayed to between 200 and 300 ms. The MMN is typically evaluated by calculating a difference wave, computed by subtracting the ERP in response to the standard stimulus from the ERP to the deviant stimulus.

Historical Background

Electrophysiology provides an avenue to examine mental functioning that may not be manifested behaviorally. It allows for the investigation of aspects of cognition, perception, and other biological bases for behavior. This is especially useful in assessing infant and clinical populations that may lack the requisite capacities for expression.

Electroencephalography (EEG) consists of recording the brain's electrical activity. In humans, this is accomplished by placing electrodes at various locations on the scalp. Electrical surface recordings are limited in terms of spatial resolution, in that it is difficult to precisely identify the source of electrical fields in the brain. However, electrical recordings can provide excellent temporal resolution, revealing the brain's response effectively in real time.

Event-related potentials (ERPs) are electrical activity time-locked to a particular event. ERPs are commonly utilized to assess the brain's processing of external stimuli. In order to demonstrate that the recorded response is related to the target event and not to extraneous influences, a series of trials are averaged together to create a composite waveform. Waveforms can be averaged across trials within a single subject, as well as across individuals and groups.

The mismatch negativity (MMN) was first described by Näätänen and colleagues in a 1978 paper examining negative potentials via EEG in response to deviations in tone frequency. The MMN refers to an automatic neurological response to a change in auditory stimuli, represented by a peak difference generally observed 150–250 ms poststimulus. The degree of variance between the stimuli required to elicit the neural MMN response is approximately the difference required for behavioral discrimination.

ERPs such as the MMN are assessed in terms of amplitude – power or voltage, and latency – timing.

MMN amplitude has been associated with degree of deviant contrast and accuracy of discrimination, with increases in amplitude associated with greater contrast and greater discrimination, and decreases in amplitude associated with reduced contrast and reduced discrimination. Earlier latency has also been associated with greater stimulus contrast.

The MMN has been demonstrated in response to wide variety of stimuli. These include computer-generated sounds such as sinusoidal tones and musical chords, as well as human speech sounds such as vowels and consonant phonemes. Among these stimuli, the MMN has been shown to be sensitive to changes in frequency, pitch, intensity, duration, and presentation order. More recently, researchers have begun to explore MMN equivalents in response to visual and olfactory stimuli.

The MMN has been consistently elicited independent of directed attention. Further, it has been demonstrated in the context of multiple-competing auditory streams. However, competing auditory stimuli can diminish MMN amplitude. Competing visual stimuli generally do not impact the MMN. Conversely, variations in background noise which elicit the MMN response can impact attention, reorienting a person to an anomalous environmental stimulus.

This highlights an important developmental and operational function of the MMN. The MMN represents the brain's perception of an anomalous event. It is often followed by a positive peak occurring between 250 and 300 ms. This positive potential, known as the P3a, is an electrophysiological marker of novelty and represents the automatic reorienting of attention. Thus, the MMN is a functional precursor, evidencing the automatic perception of a deviant stimulus, leading to the actual reorienting of attention as evidenced by the P3a (for review, see Friedman, Cycowicz, & Gaeta, 2001).

The source of the MMN appears to be in the auditory cortex, as evidenced by scalp distribution data, studies of magnetic encephalography, intracranial recordings, and cases of brain lesions. Additional data reveal the frontal lobe as a contributing generator. It is suggested that the frontal lobe involvement may be related to attentional switching associated with the MMN (Alho, 1995). Other studies have evidenced that the MMN response elicited by speech sounds is primarily sourced in the left temporal lobe, whereas MMN in response to nonspeech sounds is primarily sourced in the right temporal lobe (Kujala, 2007).

Various studies have demonstrated the effects of training on the MMN. Individuals, who at the beginning of a session could not behaviorally discriminate between divergent stimuli and failed to exhibit a corresponding MMN, later learned through exposure to behaviorally discriminate between the stimuli and exhibited a parallel MMN response. This further demonstrates the value of the MMN as a real-time index of learning and discrimination.

Current Knowledge

As an electrophysiological index of auditory perception that closely matches behaviorally observed capabilities, the MMN provides a valuable tool in the biological assessment of language and associated capacities. It has accordingly been utilized in the scientific examination of autism spectrum disorders (ASD). Given that deficits in language and social orienting are prominent features of autism spectrum disorders, a contributing factor in these impairments may be an inability to perceive and process contrasting auditory stimuli, especially speech sounds. Thus, the MMN provides a potential method for exploring auditory processing in ASD.

A limited number of studies have examined the MMN in ASD. Results from these studies have not been entirely consistent, though a variety of studies have demonstrated MMN and other ERP differences in ASD subjects as compared with controls. These have included differences in amplitude, latency, and hemispheric distribution. Divergent findings may be due to differences in paradigm design, participant characteristics, and diagnostic inclusion criteria.

A series of studies have shown enhanced MMN in ASD (Ferri et al., 2003; Jansson-Verkasalo et al., 2003; Kujala, Tervaniemi, & Schröger, 2007; Kujala et al., 2010; Lepisto et al., 2005, 2006; Lepisto, Nieminen-von Wendt, von Wendt, Näätänen, & Kujala, 2007; Lepistö et al., 2008).

The most common finding among these studies is an increase in amplitude, particularly over the right hemisphere. Some studies have also evidenced shorter latencies (Ferri et al., 2003; Jansson-Verkasalo et al., 2003; Kujala et al., 2007; Lepisto et al., 2005, 2007). This is consistent with behavioral findings indicating heightened auditory discrimination abilities in ASD (Gomot, Giard, Adrien, Barthelemy, & Bruneau, 2002). Enhanced perceptual ability may in fact adversely impact language learning, reflecting an inability to ignore irrelevant stimuli.

Other studies have failed to show MMN or shown diminished MMN amplitude in ASD (Dunn, Gomes, & Gravel, 2008; Kuhl, Coffey-Corina, Padden, & Dawson, 2005; Lepisto et al., 2005, 2006). These findings are generally interpreted to evidence reduced discrimination, with obvious implications for language deficits.

In a noteworthy study, Kuhl et al. (2005) examined MMN and behavioral speech preferences in a sample of school-aged children with and without ASD. The paradigm involved an auditory preference task, assessing a child's preference for speech or nonspeech stimuli, and an ERP task, assessing MMN responses to changes in consonant-vowel speech sounds. On a group level, children with ASD exhibited a preference for nonspeech sounds and failed to exhibit MMN. Typically developing controls, chronologically and mentally age-matched, exhibited a preference for speech sounds and exhibited a typical MMN response. Interestingly, when the ASD group was subdivided based on speech preference, the children with ASD who preferred speech sounds exhibited MMN responses similar to typical controls. According to the authors, this finding provides evidence for a relationship between phonetic learning and social interaction, suggesting that social interest may have a direct impact on language learning. This further substantiates the MMN as a neural correlate of broader language capacities with potential social implications.

Another study replicated previous findings demonstrating diminished MMN amplitude in ASD subjects in response to unattended stimuli. However, when subjects were instructed to attend to the stimuli, the MMN for ASD subjects was similar to controls (Dunn et al., 2008). This indicates that auditory processing that occurs automatically in typical individuals may require attention to be operative in ASD. This presents a significant disadvantage noting that direct attentional capacities are inherently limited, and thus processing capability may suffer in complex environments. This study also provided an explanation for discrepant findings in previous literature, noting that a prominent study that failed to show MMN differences in ASD had procedurally instructed participants to attend to the stimuli.

MMN may change over time in ASD. Two studies were conducted utilizing the same experimental paradigm with adults and children respectively, diagnosed with Asperger's. MMN responses were recorded to changes in duration and pitch. Both samples demonstrated enhanced MMN to pitch changes. However, duration changes showed a diminished MMN in children and an enhanced MMN in adults (Lepisto et al., 2006, 2007). These findings imply that MMN may have a complex developmental course in ASD.

Many studies revealed differences in hemispheric distribution in ASD as compared with control samples (Gomot et al., 2002; Jansson-Verkasalo et al., 2003; Kujala et al., 2007, 2010; Lepisto et al., 2006, 2007). As a trend, these included enhanced responses over the right hemisphere and diminished responses over the left hemisphere. Whereas control groups often exhibited no hemisphere dominance for the MMN, ASD groups exhibited right hemisphere dominance (Kujala et al., 2007; Lepisto et al., 2006, 2007). These abnormal patterns of MMN lateralization may reflect impaired interhemispheric processing.

Future Directions

Some of the difficulties in interpreting the multiplicity of findings with regard to the MMN in ASD are likely related to varying diagnostic criteria across studies. This is an issue that affects ASD research across the board, given the etiological and clinical heterogeneity of ASD.

Utilizing instruments that involve standardized behavioral observation and standardized interviewing, in conjunction with expert clinical judgment, can better constrain research populations ensuring more consistent ASD samples.

Though increased amplitude and shorter latency are associated with greater discrimination, when an increase in amplitude is coupled with extended latency or, conversely, when a decrease in amplitude is coupled with shorter latency, the specific implication with regard to discrimination is unclear. Though differences in amplitude and latency in ASD manifest "abnormal processing," future research may be able to determine more precisely how variations in electrophysiological components relate to global processing.

The MMN can be recorded in young infants reliably between 3 and 5 months. Some studies have even elicited MMN correlates in fetuses. As more specific clinical electrophysiological profiles emerge, MMN may be a promising tool for revealing clinical disorders early in development, leaving open the prospect of increasingly early intervention.

Training and learning have been shown to improve MMN responsiveness. This may indicate an opportunity for intervention in clinical disorders. In ASD specifically, directed attention has been shown to positively impact the MMN (Dunn et al., 2008). Future research could focus on the evaluation of intervention effects in clinical populations using the MMN as a marker. This may provide information that can be translated into evidence-based intervention methodologies, as well as general information about the nature of auditory processing deficits in these populations.

Researchers have also begun exploring methods for assessing MMN at the single-subject level. Currently, the MMN provides a reliable tool for examining group differences in clinical populations. As this methodology progresses, it may be able to reliably indentify an individual's auditory discrimination capacity. Such an electrophysiological marker could have useful implications for diagnosis and intervention in ASD.

See Also

▶ Auditory Discrimination
▶ Auditory Potentials
▶ Auditory Processing
▶ Neurophysiology

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Mitochondrial Deficits/Disorders

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Synonyms

Electron transport chain disorders; OXPHOS disorders; Respiratory chain disorders

Short Description or Definition

Mitochondria are small organelles which sit in the cell cytoplasm and are thought of as the "powerhouse" of cells. They are the site of cellular respiration which ultimately provides energy (adenosine triphosphate, ATP) for the cell's activities through a metabolic pathway known as oxidative phosphorylation, utilizing a series of reactions known as the electron transport chain. This comprises five multiprotein complexes (I–V) of which complex I is the largest and most complex. Cells which have high energy needs such as muscle, liver, and brain have more mitochondria than cells in tissues with less energy demand, such as skin cells. Neurons are particularly dependent on ATP synthesis by this mitochondrial respiratory chain.

Not only do mitochondria have this crucial role in energy production, but they are also the only organelle to have their own genome containing mitochondrial DNA (mtDNA). The mitochondrial genome is a small circular genome which encodes some of the proteins and enzymes required by the respiratory chain to produce energy. It is inherited exclusively down the maternal line. However, most mitochondrial components are encoded by genomic DNA (gDNA) from the nuclear genome within the cells. Mutations and other genetic abnormalities arising in both mtDNA and gDNA may therefore give rise to mitochondrial dysfunction. Mitochondrial mutations arise relatively more frequently than genomic ones, and more than 100 mtDNA deletions and over 150 mtDNA mutations have been identified so far (Hass et al., 2007) as well as 40 known nuclear genes involved in mitochondrial disease. The phenotypic effects of these are highly variable. Symptoms include poor growth, loss of muscle coordination, muscle weakness, visual problems, hearing problems, learning disabilities, mental retardation, heart disease, liver disease, kidney disease, gastrointestinal disorders, respiratory disorders, neurological problems, autonomic dysfunction, and dementia. There are more than 40 known different nuclear genes associated with mitochondrial disease, and they can present very differently from individual to individual. In 1985, Coleman and Blass suggested that autism may be due to mitochondrial dysfunction, and since then autism has become a well-recognized feature of childhood mitochondrial respiratory chain disease. Autism is a heterogenous disorder and is likely the result of several underlying pathophysiological mechanisms including altered neurite morphology, synaptogenesis, and cell migration abnormalities. There is growing evidence that

mitochondrial dysfunction is an additional patho-genetic basis for a subset of individuals with autism.

Epidemiology

The prevalence of mitochondrial dysfunction is probably underestimated. The minimum birth prevalence in the general population has been estimated at ~0.01% (Skladal, Halliday, & Thorburn, 2003). The prevalence in autistic spectrum disorder has recently been estimated at 5.0% (Rossignol & Frye, 2011).

Clinical Expression and Pathophysiology

Mitochondrial dysfunction has been implicated in several psychiatric and neurological disorders, including schizophrenia (Prabakaran et al., 2004), bipolar disorder (Konradi et al., 2004), Alzheimer's disease (Ohta & Ohsawa, 2006), and Parkinson's disease (Martin, 2006). In 1985, Coleman and Blass reported elevated lactic acid levels in some patients with autism, and subsequently Lombard in 1998 suggested the possibility that disorders of oxidative phosphorylation (OXPHOS disorders) may be implicated in some cases of autism. Since then, numerous lines of evidence support this theory. Firstly, the co-occurrence of mitochondrial disorders and autism is more than would be expected from the incident population figures for mitochondrial disease and autism alone (Haas, 2010). Secondly, numerous case reports and retrospective case series studies have described mitochondrial deficits and/or genetic mutations associated with autism. Thirdly, preliminary clinical studies have identified a possible "mitochondrial autism" phenotype, and fourthly, biomarker and postmortem brain studies have provided evidence for mitochondrial dysfunction in some cases of autism.

Evidence for Co-occurrence
Since 1998, there have been numerous case reports of mitochondrial dysfunction co-occurring with autistic spectrum disorders. Several of these have identified the genetic mutation responsible for the mitochondrial dysfunction as well as measuring peripheral biochemical markers of mitochondrial dysfunction (e.g., Graf et al., 2000; Filiano et al., 2002; Filipek et al., 2003; Pons et al., 2004; Weissman et al., 2008), whereas others have relied on biochemical evidence (e.g., Filipek, Juranek, Nguyen, Cummings, & Gargus, 2004; Poling, Frye, Shoffner, & Zimmerman, 2006; Tsao and Mendell, 2007).

Haas (2010) makes the point that with a 1:2,000 population incidence of definite mitochondrial disease and a 1:110 population incidence of ASD, only 1 in 2,000 ASD cases would be expected to have mitochondrial disease, and only 1 in 110 mitochondrial diseases would be expected to have autism. He argues that the co-occurrence of both is higher than this. Mitochondrial dysfunction is the most common metabolic abnormality associated with autism (Rossignol & Frye, 2011). This is supported by a school-based epidemiological study (Oliveira et al., 2005) of nearly 60,000 school children in Portugal which identified 120 children with ASD. Of these, 69 had further biochemical investigations, including plasma lactate, a marker for impaired mitochondrial function, and some had muscle biopsies. Definite mitochondrial respiratory chain disease, primarily complex I and IV deficiencies, was identified in approximately 7% of children with ASD. A recent meta-analysis conducted by Rossignol and Frye (2011) estimated the prevalence of mitochondrial disease in ASD to be 5%, although outline several methodological reasons why this is likely to be an underestimate.

More recently, investigators have been able to study mitochondrial function in postmortem brain tissue from ASD individuals. Chauhan et al. (2011) found a reduction in several of the electron chain complexes and an increase in markers of oxidative stress in some brain regions from children with autism compared to controls.

The Autism Phenotype in Mitochondrial Disorder
Several studies have compared the phenotypic characteristics of ASD + mitochondrial disorder to both the general ASD population and the

mitochondrial disorder population. Of the 25 ASD cases Weissman et al. (2008) reviewed with a known mitochondrial disorder, 24 had one or more major clinical abnormalities uncommon in idiopathic autism. Many of these individuals had other CNS symptoms such as epilepsy, hypotonia, gross motor developmental delay, hearing deficits, and multiple regressions. It is often the case that metabolic decompensation associated with neurodegeneration in primary metabolic disease occurs following infection (Edmonds et al., 2002). This can resemble the regression seen in some cases of autism. Autistic regression followed by an ASD has been documented in children with fever and infection. Some of these children have subsequently been shown to have primary mitochondrial disease (Shoffner et al., 2010; Weissman et al., 2008). Although regression has been reported to occur in approximately one third of autistic children, typically before age 3 years, 40% in the Weissman sample demonstrated unusual patterns of regression: either repeated regressions, regressions involving losses of gross motor function, or regressions after age 3 years. Children in this sample also had a high frequency of nonneurological disorders affecting other organs and tissues, such as gastrointestinal symptoms, cardiovascular abnormalities, oculomotor abnormalities, and muscle fatigue. They also point out that the sex ratio of ASD in children with primary mitochondrial disease is 1:1, unlike the male preponderance seen in idiopathic autism. Weissman et al. (2008) argue that the ASD seen in mitochondrial disease is so different to idiopathic autism and have suggested the term "mitochondrial autism" for these cases. The underlying pathophysiological mechanisms responsible for the ASD seen in mitochondrial dysfunction are not known, but Hass (2010) argues that it is likely to involve neuroinflammation, glial activation, and cytokine release. No specific mitochondrial deficiency or disorder appears to be particularly associated with the presence of ASD. Rossignol and Frye's meta-analysis (2011) identified a deficiency of mitochondrial complex I as the most common deficiency in 53% of ASD patients with concomitant mitochondrial disorder.

When comparing the phenotypic characteristics of ASD and mitochondrial dysfunction to those with just mitochondrial dysfunction, interestingly, those with both diagnoses appear to have higher rates of ataxia, fatigue, GI abnormalities, and elevated lactate (Rossignol & Frye, 2011).

Genetic Studies

Despite an estimated prevalence of mitochondrial disease in 5–7% of ASD cases, when autism populations have been screened for known mtDNA mutations, the results have largely been negative, e.g., only 2 individuals out of 810 ASD individuals screened for four known mtDNA mutations had one of these mutations (Serajee, Zhang, & Huq, 2006). This is probably not that surprising given that only four mutations were analyzed.

Even when individuals with ASD and known mitochondrial dysfunction have been investigated, only a minority have an identifiable genetic or chromosomal abnormality (Graf et al., 2000; Pons et al., 2004; Weissman et al., 2008). However, it is entirely possible that there are as yet unidentified genetic mutations and polymorphisms which cause, or contribute to, mitochondrial dysfunction.

Association studies of genomically encoded mitochondrial genes have been more successful, with several studies providing evidence for association between the SLC25A12 gene, which encodes a mitochondrial aspartate/glutamate carrier, and ASD (e.g., Palmieri et al., 2010; Ramoz et al., 2004; Segurado et al., 2005). However, several other studies have failed to replicate these findings, possibly as a result of small sample sizes and clinical as well as genetic heterogeneity. It is also possible that in some cases, other genetic risk factors, as well as environmental risk factors in addition to certain mtDNA mutations, contribute to the development of autism.

Chromosomal abnormalities have also been identified in children with both ASD and mitochondrial disorder, but whether the chromosomal abnormality underlies either of the disorders is not clear. Filipek et al. (2003) identified two unrelated children with ASD and chromosome 15q11-q13 inverted duplications. Both had abnormal muscle mitochondrial enzyme assays. A recent case report by Ezugha et al. (2010)

described a child with autism and mitochondrial disease, who also had epilepsy, leg weakness, and mental retardation. Buccal swab electron transport chain analysis revealed a severe decrease in complex IV and mild deficiency in complex I activity, and subsequent microarray analysis had discovered a deletion at 5q14.3. It is assumed that genes that either encode or regulate the expression or assembly of electron chain transport proteins are located within these deleted regions.

Summary

Although a few individuals with ASD and mitochondrial dysfunction have identifiable mutations or deletions in their mitochondrial or nuclear DNA, the vast majority have no such identifiable pathology. It is still unclear whether there is a specific "mitochondrial autism," as suggested by Weissman et al. (2008), or a continuum of mitochondrial dysfunction of differing severity in ASD, as suggested by studies demonstrating a correlation between mitochondrial dysfunction and ASD symptom severity (e.g., Minshew, Goldstein, Dombrowski, Panchalingam, & Pettegrew, 1993). It is also still unclear to what extent the mitochondrial disorder/dysfunction is responsible for the ASD.

Evaluation and Differential Diagnosis

How Are Mitochondrial Disorders Diagnosed?

The diagnosis of mitochondrial disorder can be challenging, partly because these disorders can impact on so many different systems and because there is a high degree of phenotypic heterogeneity both between different mitochondrial disorders and within the same disorder. Additionally, a family history is often not present. There are several well-characterized mitochondrial syndromes such as Leber's hereditary optic neuropathy, Leigh syndrome, myoclonic epilepsy with ragged red fibers (MERFF), and mitochondrial myopathy, encephalomyopathy, lactic acidosis, stroke-like symptoms (MELAS). Other mitochondrial disorders are often classified as predominantly muscular

or CNS or multisystem presentations. Although there are many different genetic causes of mitochondrial disorder, the endpoint of impaired mitochondrial function is common to them all. As a result, a number of mitochondrial metabolites can be measured to screen for possible mitochondrial disorder: high plasma lactate levels are one of the commonest, but pyruvate, alanine, carnitine, and urinary organic acid levels and ratios are also potential indicators of mitochondrial dysfunction. However, mitochondrial deficiencies may not always be detected by metabolite screening, whether autism is present or not: Tsao and Mendell (2007) identified two girls with ASD and normal lactate levels with diagnosed mitochondrial electron transport chain deficiencies. Similarly, in the series of Weissman et al. (2008) of 25 ASD cases with co-occurring mitochondrial disorder, 76% had raised serum lactate levels. Rossignol and Frye (2011) conducted a meta-analysis of six studies measuring lactate and found an overall prevalence of elevated lactate of only 31%. They also noted that as a group, ASD individuals were more likely to have abnormal biochemical values of mitochondrial function compared to controls and that there was considerable variability in these biochemical markers in the ASD population. The vast majority of children with both disorders are diagnosed with the ASD first and the mitochondrial disorder subsequently.

Importantly, plasma lactate levels may also be caused by many other disorders other than primary mitochondrial dysfunction and are therefore not diagnostic. For most individuals, the diagnosis is made through measurement of electron transport chain activity, but an underlying nuclear or mitochondrial mutation that might account for the deficiency/dysfunction is rarely identified (Debray, Lambert, & Mitchell, 2008).

Treatment

There is no known cure for mitochondrial disorders. General treatment is aimed at reducing further damage to mitochondria and treating any systemic organ damage that may have resulted from the mitochondrial disorder. More specific treatments include providing supplementation of

mitochondrial cofactors such as antioxidants, B vitamins, coenzyme Q10, and carnitine, but as yet there are no rigorous trials of these agents.

See Also

▶ Vaccinations and Autism

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Mixture Modeling

▶ Latent Variable Modeling

MLD

▶ Metachromatic Leukodystrophy

Moban

▶ Molindone

Mobile Work Crew Model

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Synonyms

Community work crew; Community-based work team; Enclave; Supported employment group; Work team

Definition

A mobile work crew model follows the practice of placing together several individuals to work in the community as a team or "crew." Typically, the individuals have a disability and are accompanied by a nondisabled support person or job coach. This type of work group falls under the category of supported employment. The mobile work crews may work at various locations but often specialize in a specific area such as janitorial services, lawn care, maintenance jobs, etc. These jobs are in the community but may not be integrated with employees outside the work crew and may not require competitive rates of production. The mobile work crews are often associated with an agency providing vocational or day services to people with autism. In some cases, individuals with autism may be able to learn needed vocational skills while on a mobile work crew to lead to a higher level of employment or competitive employment.

M

See Also

▶ Employment
▶ Employment in Adult Life
▶ Vocational Training

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Möbius Syndrome

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Synonyms

Moebius syndrome

Definition

This very rare congenital disorder (perhaps 1 in 100,000 births) is characterized by facial paralysis and a lack of ability to move the eyes from side to side. This is a result of failure of normal development of the sixth and seventh cranial nerves. Sometimes, other facial nerves are also affected – if the eighth nerve is affected, hear loss is present as well.

Abnormalities in other areas can include problems with the chest wall and extremities. Given the lack of facial expression, most individuals with the condition are assumed not to have normal intelligence, but this is not correct. The condition is named after the neurologist who described it in the last 1800s. Treatment is supportive in nature. The etiology of the syndrome remains unclear with some suggestion of genetic links as well as links to teratogenic drugs such as thalidomide.

A few studies, mostly case reports and at least one case series, have suggested a potential increased risk for autism. The significance of this association remains unclear.

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Modeling

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Synonyms

Example, demonstration; Representation

Definition

Modeling refers to an intervention procedure that provides an example or explicitly demonstrates a verbal or social behavior targeted for intervention. The demonstration serves as a standard for imitation or comparison by the learner by providing an example of the structure or content of a targeted language or social behavior. The modeled demonstration can be presented either verbally or visually through pictures or videos. The modeling procedure may take one of six forms: model-recast, model-prompt-imitation, aided modeling, interactive modeling, in vivo modeling, and video modeling.

– Model-recast is a method that provides a model of the structural or semantic properties of language for the child by recasting a child's utterance during discourse interaction. The recast/model supplies missing grammatical aspects or semantic relationships while maintaining the child's central meaning. For example, if the child omits the auxiliary verb and present progressive tense marker

when saying "doggie eat," the adult recast or model would maintain the meaning but provide the missing grammatical markers, as in "The doggie is eating."

– Model-prompt-imitation is an elicitation procedure that presents a target language or social behavior and elicits the targeted behavior from the child in a model-prompt-imitation format. For example, if the target language behavior is the appropriate response to question forms, the clinician or adult may model the expected response and prompt the child to imitate as in "What is your name?" followed by the model "My name is Jack," and then a prompt to imitate: Tell me: "My name is Jack."

– Aided modeling occurs during instruction in the use of an augmentative and alternative communication (AAC) device wherein the adult uses the AAC device as well as speech to demonstrate the expected communication output.

– Interactive modeling facilitates language development in a socially interactive format. The adult follows the child's lead and provides a verbal gloss of the actions and focused attention to objects by the child. For example, if a child looks at or picks up an object, the adult verbalizes or glosses the child's actions or attention focus by modeling the appropriate language, for example, "Ball," "This is a ball." If the child performs an action on the object, the adult would provide a language model or gloss of the action, such as "throw ball," "Jack is throwing the ball."

– In vivo modeling involves the real-life situational observation of typical persons performing a task.

– Video modeling involves a child viewing a video demonstration of a target behavior that serves as a model for imitation and comparison.

Modeling has been found to be an effective intervention technique for children and adolescents with autism, especially the use of model-prompt-imitation, aided modeling, in vivo modeling, and video modeling. Less is known

regarding the use of the model-recast method in teaching verbal skills to children with autism spectrum disorders.

See Also

► Augmentative and Assistive Technology
► Imitation
► Picture Exchange Communication System
► Prompt Hierarchy
► Video Instruction

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Modification

► Reasonable Accommodation

Modifications

► Modified Testing
► Special Needs

Modified Checklist for Autism in Toddlers (M-CHAT)

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Synonyms

CHAT; Checklist for Autism in Toddlers; M-CHAT

Abbreviations

AAP	American Academy of Pediatrics
ASD	Autism spectrum disorder
CESDD	Checklist for Early Signs of Developmental Disorders
ESAT	Early Screening of Autistic Traits quesionnaire
FUI	Follow-up interview
NPV	Negative predictive value
PEDS	Parents' Evaluation of Developmental Status
PPV	Positive predictive value
Se	Sensitivity
Sp	Specificity

Description

The Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, & Barton, 1999a) is a screening measure developed to identify young children with an elevated risk for autism spectrum disorder (ASD) through parent report. This instrument is one of the most commonly used screening instruments for ASD in toddlers worldwide.

The checklist was developed and validated for children between 16 and 30 months old. Parents are asked to answer 23 yes/no questions about the usual behavior of their child. Responses of parents indicating typical development are balanced. Children screen positive for ASD if they fail three or more items in total or if they fail two or more out of six critical items, derived from discriminant function analysis. These six critical items ask about the child's interest in other children, response to name being called, following a point of the parent, own pointing and showing to indicate interest, and imitation (Robins, Fein, Barton, & Green, 2001b).

In addition to the parent report, a follow-up interview (M-CHAT FUI; Robins, Fein, & Barton, 1999b) was designed to ascertain responses of parents for screen positive children. Parents are asked to clarify the items failed by their child in a structured format. To ensure presence or absence of specific behaviors, parents are asked to give some examples of these behaviors. In addition, detailed information about the frequency of the behaviors is elicited. Including this follow-up interview in the screening lowers the amount of false positive screens, without compromising the sensitivity of the instrument (see also the section on "Psychometric Data"). This interview can be conducted in person or over the phone (Robins & Dumont-Mathieu, 2006; Robins et al., 2001b).

Historical Background

The M-CHAT is an adaptation and extension of the Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen, & Gillberg, 1992; Baron-Cohen et al., 1996). The CHAT was originally designed to screen for autism, not ASD, in 18-month-olds. The child's general physician or health visitor completes the checklist, for example during the 18-month routine check-up. The CHAT consists of two parts: nine parent questions (part A) and five observation items that have to be administered by trained professionals (part B). For more details about this measure, see ▶ CHAT entry.

The M-CHAT modified the CHAT into an instrument completely reliant on parent report, because this may be more accurate than a brief observation by a professional (Robins & Dumont-Mathieu, 2006). The first nine items of the CHAT (part A) were included as such in the M-CHAT. In addition, 21 new items were formulated to compensate for the loss of the observation part (part B) of the CHAT, but also to broaden the signs of ASD included in the checklist. The authors of the

M-CHAT wanted to identify a greater range of children on the autism spectrum, not solely children with autism. Based on preliminary analyses of the first 600 children, eight items were dropped because they lacked discriminant power or because parents misunderstood their content. In addition, one item about social referencing was added, leading to the final 23 items in the checklist (Robins et al., 2001b).

Since the development of the M-CHAT, the instrument has been translated into more than 30 languages, including Arabic, French, Dutch, German, Spanish, Portuguese, Chinese, and Japanese. The checklist itself, the follow-up interview, and the different translations are available for free download for clinical, research, and educational purposes (see www.mchatscreen.com). For use with Chinese and Japanese children, some adaptations to the M-CHAT were made. For the Japanese version, the M-CHAT was translated and some illustrations were added to the items about declarative pointing, showing, gaze following, and social referencing, in order to encourage caregivers to notice negative symptoms (Inada, Koyama, Inokuchi, Kuroda, & Kamio, 2011). For Chinese children, Wong and colleagues (2004) combined the M-CHAT and CHAT into a new screening measure: the CHAT-23. This instrument incorporates a Chinese translation of the 23 items of the M-CHAT (part A) and the five observation items of the CHAT (part B). The authors suggest using part A as a Level 1 screening instrument for use in the general population, followed by administration of part B as a Level 2 screening instrument for screen positive children on part A. For more details on the CHAT-23, see the ▶ CHAT entry.

Psychometric Data

Discriminant Validity

Several studies have evaluated the psychometric properties of the M-CHAT as a screening instrument for ASD in toddlers. The original validation study included 1,122 children from a nonselected population and 171 high-risk children screened through early intervention service providers. All children were between 16 and 30 months old.

There were 39 children identified with ASD in this sample: three from the unselected sample and 36 from the high-risk group. None of the children in this study who were evaluated after screening positive had an entirely typical development. Robins and colleagues (2001b) estimated the psychometric properties of the M-CHAT through discriminant function analysis classification based on known diagnoses of ASD before follow-up of the entire sample. The sensitivity (Se) was estimated at .87, the specificity (Sp) at .99, the positive predictive value (PPV) at .80, and the negative predictive value (NPV) at .99. They used this approach because calculation of Se and Sp depends on follow-up of both positive and negative screen children to ascertain diagnosis in all children and follow-up was still pending. Dumont-Mathieu and Fein (2005) reported estimates on the Se and Sp of the M-CHAT based on the first 940 children of the original sample who were rescreened at age 4. This rescreen resulted in six possible missed cases. Se was estimated at .85 and Sp at .93.

A study by Kleinman and colleagues (2008) showed that the PPV of the M-CHAT depends on the inclusion of the follow-up interview and on the sample of children to which it is applied. These authors screened a completely new sample of children between 16 and 30 months old: 3,309 low-risk children from an unselected sample and 484 high-risk children from early intervention service providers. For the total sample, the PPV after a positive screen on the M-CHAT was only .36. However, if this positive screen was also confirmed by the follow-up interview, the PPV increased to .74. There were also some differences found in PPVs between the low- and high-risk groups. Without follow-up interview, the PPVs were .11 and .60 for, respectively, the low- and high-risk group. When positive screens were confirmed with the follow-up interview, the PPVs were .65 and .76 for, respectively, the low- and high-risk group.

Pandey and colleagues (2008) added 2,983 new children between 16 and 30 months old to the Kleinman and colleagues (2008) sample in order to compare the PPVs of younger (16–23 months old) versus older children (24–30 months old). In this study, all positive screen children were based on parent report and follow-up interview. In the

high-risk sample, the PPV was .79 for the younger children and .74 for the older children. In the low-risk sample, the PPV was .28 for the younger and .61 for the older children.

Although the M-CHAT has been translated in many different languages, the validation of these translations is still pending. Some findings on the Arabic, French, Portuguese, Spanish, Sinhala, and Japanese version have been published (Canal-Bedia et al., 2011; Eldin et al., 2008; Inada et al., 2011; Losapio & Pondé, 2008; Perera, Wijewardena, & Aluthwelage, 2009; Rogé, Chabrol, & Unsaldi, 2009), but these findings were mostly based on small high-risk samples. Two recent published studies form an exception. Inada and colleagues (2011) reported on the discriminant validity of the Japanese version of the M-CHAT in 1,187 low-risk children of 18 months old, of whom 20 were diagnosed with ASD at age 3. These authors suggest a different cutoff of two or more failed items in total, at which the Se was estimated at .75, the Sp at .89, the PPV at .11, and the NPV at .99. Canal-Bedia and colleagues (2011) reported on the validity of the Spanish translation of the M-CHAT in two large samples, but the study lacked data on possible missed cases. Therefore, the Se and Sp cannot be estimated (reported Se was 1). The PPVs they reported were .35 for a first sample of 2,480 children, including 63 high-risk children recruited from early intervention service providers, and .19 for a completely unselected sample of 2,055 children.

Item Analysis

In the initial validation study, all but two items discriminated well between children with and children without ASD. Only the item about enjoyment in being swung or bounced on the knee of the parent and the item asking parents if their child can walk cannot distinguish children with and without ASD (Robins et al., 2001b).

Ventola and colleagues (2007) compared the scores of 195 children who screened positive on the M-CHAT between 16 and 30 months of age and who were subsequently diagnosed with either an ASD, a global developmental delay, or a developmental language disorder. Even when overall language level was controlled for,

children with ASD could still be differentiated from children with other developmental disorders, based on their scores on four items: response to name, declarative pointing, imperative pointing, and following a point.

Reliability

Two studies reported on the internal consistency of the M-CHAT. Robins and colleagues (2001b) calculated a Cronbach's alpha of .85 for the entire checklist and .83 for the six critical items. These results were replicated by Kleinman and colleagues (2008). They reported alpha's of .85 and .84, respectively, for the entire checklist and the six critical items.

Inada and colleagues (2011) looked at the interrater reliability of the Japanese translation of the M-CHAT by comparing the scoring of mothers and fathers of a limited subsample of 24 children. The scoring results of these parent couples were highly correlated: Pearson's $r = .93$. In addition, they looked at the test-retest reliability by asking 22 mothers to fill out the M-CHAT again after on average 8 days. Again, scores on the M-CHAT were highly correlated: Pearson's $r = .99$.

Clinical Uses

The M-CHAT has been available for both research and clinical use since the late 1990s. With the recent recommendations of the American Academy of Pediatrics (AAP) to conduct population-wide screening for ASD at 18 months (AAP, 2006), the use of the M-CHAT as a Level I screening instrument for ASD has been recommended by some. However, validation of the M-CHAT is still ongoing and longitudinal follow-up will have to shed light on possible missed cases to enhance the accuracy of the estimates of sensitivity and specificity for the M-CHAT (see also Mawle & Griffiths, 2006; Robins & Dumont-Mathieu, 2006). Finally, validation of the different translations is still pending.

Based on the current findings, when using the M-CHAT in clinical practice as a Level 1 screening measure, one can expect many false positive

screens, especially when used in unselected samples and when the user does not incorporate the follow-up interview in the screening. Therefore, Kleinman and colleagues (2008) suggested a higher cutoff for failing when screening in the general population or to combine the use of the M-CHAT as a Level 1 screening instrument with a Level 2 screening instrument or more in-depth parent interview and behavior observation for borderline cases, before a full-scale autism evaluation is instituted.

Different studies used the M-CHAT as a Level 2 screening instrument. For example, Dereu and colleagues (2012) used the Checklist for Early Signs of Developmental Disorders (CESDD; Dereu et al., 2010) as a Level 1 screening instrument in an unselected sample of 7,092 infants and toddlers attending day-care centers, combined with the M-CHAT as a Level 2 screening instrument for positive screen children on the CESDD or for children at-risk for ASD because of a delayed language development. They compared the M-CHAT with the early screening of autistic traits questionnaire (ESAT) (Dietz, Swinkels, van Daalen, van Engeland, & Buitelaar, 2006; Swinkels et al., 2006) for a referred sample of 197 children between 16 and 30 months old based on the CESDD results and concluded that the discriminant power of these screening instruments for ASD were comparable, although some differences were found in the Se and the Sp of the different instruments. Glascoe, Macias, Wegner, and Robertshaw (2007) looked at combining a broadband developmental-behavioral screening test as a Level 1 screening instrument, the Parents' Evaluation of Developmental Status (PEDS), with the M-CHAT as a Level 2 screening instrument. These authors advised to base referrals on three or more discrete types of concerns on PEDS, to reduce overreferrals by 70%, while maintaining high levels of sensitivity (81%). However, Pinto-Martin and colleagues (2008) showed in their study that the PEDS missed the majority of children who screened positive for ASD on the M-CHAT. They concluded that this supports the use of an ASD-specific tool for all children in conjunction with regular standardized developmental screening.

See Also

▶ CHAT
▶ Screening Measures

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Modified Testing

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Synonyms

Accommodations; Accommodations in testing; Modifications

Definition

Modified testing refers to a number of accommodations and modifications that can be made to an instructional assessment to meet a student's individual needs. Common accommodations and modifications include:

- Use of computer or scribe for written response
- Use of augmentative communication device for oral response

- Extended testing time
- Individual or small group administration
- Use of a reader
- Administration in quiet room or space

When testing modifications are determined to be necessary by the Planning and Placement Team, the modifications and accommodations should be identified specifically on the Individual Education Plan (IEP).

See Also

▶ Assistive Devices
▶ Test Bias

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Modifier Genes and Autism Susceptibility

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Synonyms

Epistasis; Modifier loci

Structure

Autism spectrum disorders (ASD) are considered to be among the most heritable of neuropsychiatric disorders, yet the genetic architecture of ASD is complex. Unlike monogenic disorders, which may be characterized by simple Mendelian patterns of autosomal dominant or recessive inheritance, the majority of the cases of idiopathic autism do not follow such a predictable pattern. For this reason, elucidating the genetic mechanisms of ASD presents a considerable challenge. Our current understanding of the genetic architecture of ASD is that it likely involves the complex interplay of both variants that are rare and common in the general population (discussed in more detail below), together with environmental and epigenetic factors, which are not well understood (Gupta & State, 2007; Hoffman & State, 2010).

In ASD, modifier genes likely contribute to the complex genetic architecture and to susceptibility. A modifier gene is a gene that influences, or *modifies*, the expression of a second gene. More specifically, a modifier gene does not simply mask the expression of another gene but rather alters the way it is expressed without necessarily preventing its expression. For example, in a monogenic disorder, a modifier gene can interact with the known causative gene so as to influence the severity of the disorder. Therefore, modifier genes contribute to variability in the expression of a particular phenotype such that their interaction with the causative gene can exacerbate or diminish the severity of a clinical presentation (Jorde, Carey, & Bamshad, 2010).

For example, in autism, there are many cases of pedigrees in which two siblings carry a genetic variant that is a known risk factor, yet only one child is affected, or one child has a more severe presentation than the sibling. Such findings, which are inconsistent with predictions based on Mendelian patterns of inheritance, are pervasive in the ASD genetics literature. The term *epistasis* describes the phenomenon of the interaction of modifier and disease-causing genes. Epistasis is likely to be a key factor in disorders characterized by complex genetics, which include not only neuropsychiatric disorders, such as autism, but

hypertension, diabetes, and asthma as well. The presence of multiple susceptibility loci has the effect of diminishing the power to identify a causative gene (Cordell, 2002).

Function

Our current conceptualization of the genetic architecture of ASD is particularly germane for understanding the potential role of modifier genes in ASD. For example, it is important to observe that the earliest studies of the genetics of ASD and other psychiatric disorders were based primarily on the common disease-common variant hypothesis, which posits that common alleles, which occur at a frequency of >5% in the general population, account for the majority of the genetic risk of these disorders (El-Fishawy & State, 2010). However, after decades of research, common variation alone was found to account for only a small percentage of the predicted heritability of ASD.

By contrast, the rare variant-common disease hypothesis has been gaining in momentum. Evidence for this hypothesis stems in part from findings of an increased risk of *de novo* variation in ASD in simplex families, as well as the lack of consistent findings from three large, unbiased genome-wide association studies (Anney et al., 2010; Wang et al., 2009; Weiss, Arking, Daly, & Chakravarti, 2009). In addition, rare variant approaches to candidate gene identification have been clearly pivotal in identifying genes of major effect and highlighting relevant molecular pathways in ASD (Hoffman & State, 2010).

Regardless of this conceptual shift, it is likely that both common and rare variant alleles contribute to susceptibility in ASD. Because common variants are associated with relatively modest effect sizes, it is likely that common variants may function as modifier genes in ASD. Rare alleles, such as those that are found to be causative in Mendelian syndromes, have large effect sizes. Therefore, with respect to epistasis, one could imagine that a rare allele could be causative, and its expression could be influenced by common alleles at different loci. However, there is emerging evidence that even some rare variants may carry modest effect sizes

and, therefore, may also perform a similar role as a modifier to another rare, causative gene in ASD susceptibility (State, 2010; State & Levitt, 2011).

Moreover, pleiotropy has emerged as a central theme in the genetic architecture of ASD such that the same genetic mutations can manifest in vastly different clinical phenotypes in different individuals. One explanation for this may be locus heterogeneity, or variation at multiple genetic loci, which together influence the expression of a known risk factor, and have the potential to result in a range of clinical presentations (State & Levitt, 2011). Moreover, it is possible that a combination of rare variants with modest effect sizes and/or common variants at different loci serves as modifying genes in ASD. Therefore, modifier genes likely play a key role in autism and contribute to the varying relationship between genetic mutation and clinical manifestation.

Pathophysiology

One of the challenges of identifying modifier genes and gene interactions that contribute to ASD susceptibility is the need for appreciable power in genome-wide studies intended to identify alleles associated with small effect sizes. An alternate approach taken in some studies is to identify *endophenotypes*, or heritable phenotypes with a presumed genetic etiology. These studies utilize quantitative trait loci (QTLs), which are definable traits that are associated with a particular disorder. The rationale for using QTLs in genetic studies is that it can be used to identify the genetic risk for a particular trait, as opposed to relying on all of the diagnostic criteria for a disorder. Clinical diagnostic categories may be associated with multiple alleles, which complicates the assessment of heritable genetic risk (Abrahams & Geschwind, 2008).

Further, the presence of subclinical symptoms in family members of an affected individual argues for the relevance of QTL-based approaches (Abrahams & Geschwind, 2008) and suggests that there may be common variants with modest effect sizes that influence phenotype in family members as well. For example, studies have shown that siblings and parents of boys with ASD have quantifiable differences

in social responses compared to the general population, suggesting that they share some but not all of the risk alleles that contribute to ASD (Constantino et al., 2006; Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009).

Multiple QTLs may be defined for ASD, given the range of behaviors associated with this group of disorders. One QTL which was utilized in a study to identify common variants associated with ASD was "age at first word," in order to identify impairments in language development (Alarcon et al., 2008). The rationale for the use of this QTL in part is that many unaffected siblings of children diagnosed with ASD experience speech and language delay. This study identified a QTL on 7q34-7q36, which falls in *contactin-associated protein-like 2* (Alarcon et al., 2008), a gene that has been strongly implicated in ASD by multiple rare variant studies as well. Therefore, QTLs represent a potentially informative approach to identify susceptibility genes with smaller effect sizes in highly heterogeneous disorders with complex genetic architecture. Moreover, our current conceptualization of the genetic architecture of ASD is that it involves the complex interplay of rare variation, both at the level of the sequence of DNA and the structure of chromosomes, which may function in a causative or modifying manner, depending on the effect size of a particular variant, and common alleles, which have a modifying role, together with environmental factors. At this time, larger genome-wide association studies are needed to obtain the power to identify modifier genes with relatively modest effect sizes.

See Also

▶ Common Disease-Rare Variant Hypothesis
▶ Pleiotropy

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Modifier Loci

▶ Modifier Genes and Autism Susceptibility

Moebius Syndrome

▶ Möbius Syndrome

Molindone

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Synonyms

Moban

Definition

Molindone is a traditional antipsychotic medication developed for the treatment of schizophrenia. It is more potent than chlorpromazine, but less potent than antipsychotic medications such as haloperidol (▶ Antipsychotics: Drugs, ▶ Haloperidol). Molindone has somewhat unique feature in that it is not associated with weight gain, and, indeed, patients treated with molindone may even lose weight. Molindone has been studied in children but has not been studied in children or adults with autism.

See Also

▶ Haloperidol

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Monotone

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Synonyms

Flat prosody; Monotonic voice

Definition

Monotone speech refers to a flat prosodic pattern in which the voice varies little in pitch or rhythm. This style of speaking can come across as dry and lacking in affective qualities. Many individuals with autism spectrum disorder use this style of speech, which can make them stand out as "different" in conversational situations and can be an obstacle to forming social relationships.

See Also

▶ Intonation
▶ Prosody
▶ Singsong

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Monotonic Voice

▶ Monotone

Monozygotic (MZ) Twins

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Synonyms

Identical twins

Definition

Twins are two individuals who are the result of the same pregnancy. Monozygotic twins each carry the identical genetic information or deoxyribonucleic acids (DNA).

Monozygotic twins form as follows. When a sperm from the father fuses with an egg from the mother, they form a single cell called a zygote, the earliest stage of an embryo. Further cell divisions occur during embryonic development. At an early point in this development, the embryo can be split into two separate embryos, the cells of each having originated from the initial zygote. Each of these embryos goes on to develop into a separate and complete individual. Since each originated from the same initial cell, each individual is identical in his or her genetic composition. Barring very rare genetic occurrences, since monozygotic twins share the same genetic material, their physical appearance will be identical, and they will be of the same sex.

In contrast, in the case of dizygotic twins, two separate eggs are released at one time. Each of these is then fertilized by a separate sperm and forms a distinct zygote and embryo. Since each sperm and egg carry distinct genetic material, each of the two embryos will, thus, carry distinct genetic material. On average, dizygotic twins' genetic material is only about 50% identical, as compared to 100% for monozygotic twins. Since each dizygotic twin carries distinct genetic material, his or her physical appearance will be distinct. Dizygotic twins may be of the same sex. However, they might also be of different sexes.

The occurrence of monozygotic twins is rare and more rare, in general, than the occurrence of dizygotic twins. Monozygotic twinning occurs at a rate of approximately 4 in every 1,000 live births worldwide. Monozygotic twins comprise approximately one third of all twins. Two thirds are dizygotic twins. Studies indicate that the rate of monozygotic twinning in the absence of fertility treatments is fairly uniform across different populations around the world. This is in contrast to the uneven ethnic worldwide distribution of dizygotic twinning in the absence of fertility treatments. The rate of both monozygotic and dizygotic twins has increased worldwide since the 1970s. The majority of the increase has resulted from the increase in dizygotic twins born as a result of fertility treatments.

Twin pregnancies of either type increase pregnancy risk and especially the risk of preterm delivery and low birth weight. Approximately 51% of twins are born preterm compared to 9.4% in singletons.

See Also

▶ DNA
▶ Genetics
▶ Twin Studies in Autism

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Mood Disorders

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Synonyms

Clinical depression; Major depression; Unipolar depression

Short Description or Definition

Autism spectrum disorders (ASDs) are a heterogeneous group of neurodevelopmental disorders characterized by impairments in three symptom domains: social interaction, communication, and behavior. The DSM-IV-TR (2000) includes autistic disorder (AD), Asperger's syndrome (AS), and pervasive developmental disorder-not otherwise specified (PDD-NOS). Recent studies in Europe and the United States indicate a prevalence of ASD ranging from 2 to 9 per 1,000 individuals. Males, compared to females, are circa four times more frequently affected (Rinehart, Bradshaw, Brereton, & Tonge, 2002; Williams, Wheeler, Silove, & Hazell, 2010). Based on the presence or absence of intellectual disability (ID), individuals with AD can be divided in two subgroups: low-functioning autism (LFA, i.e., IQ below 70) and high-functioning autism (HFA, i.e., IQ above 70). AS and high-functioning autism can be distinguished by clinical presentation, focusing on the absence of a delayed language development in AS (Rinehart et al., 2002).

Recent studies show that more than 70% of all children diagnosed with ASD have at least one and 41% have at least two comorbid psychiatric disorders (Simonoff et al., 2008). In adults with ASD, comorbid psychiatric disorders are common as well. The most common coexisting psychiatric conditions in children and in adults with ASD are intellectual disability, attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, and mood disorders (Geurts, Deprey, & Ozonoff, 2010). This section will focus on the epidemiology, natural history, prognostic factors, outcomes, clinical expression, pathophysiology, evaluation, differential diagnosis, and treatment of mood disorders in patients with ASD.

Categorization

The term "mood disorder" describes a group of axis I disorders according to the DSM-IV-TR characterized by mood disturbance. This group can be divided into bipolar disorders and depressive disorders. Bipolar disorder is a complex disorder in which the core feature is pathological disturbance in mood ranging from extreme elation or mania to severe depression usually accompanied by disturbances in thinking and behavior, which may include psychotic symptoms. It is an episodic, chronic illness, usually with full or almost full recovery between episodes. The diagnosis requires that a person has suffered one or more episodes of (hypo)mania in their life with or without episodes of depression at other times. Depressive disorders include the major depressive disorder, depressive disorder-not otherwise specified, and dysthymia. Major depressive disorder (also called major depression, unipolar depression, or clinical depression) is the most common depressive disorder. The diagnosis depressive disorder-not otherwise specified

contains any depressive disorder that does not meet criteria for a specific mood disorder. Dysthymia is a condition characterized by a chronic low mood (DSM-IV-TR, 2000).

Epidemiology

The prevalence rates for depression in the general population are for preschool children (<5 y) 1%, for children (6–12 y) 2%, for adolescents (12–18y) 5–8% and for adults 10–15%. Depressive symptoms are the most common psychiatric concern in patients with ASD and are more likely to occur in adolescence and adulthood. Patients with ASD show a higher risk for developing depressive symptoms compared to the general population (Sterling, Dawson & Estes, 2007). Reported prevalence rates of mood disorders in ASD vary due to differences in study populations, duration of follow-up and variation in methods (Stewart, Barnard & Pearson, 2006; Geurts, Deprey & Ozonoff, 2010). In addition, autistic symptomatology tends to mask cardinal features of depression and presentation of depressive symptoms might be atypical in patients with ASD, causing a bias in the prevalence rates (Simonoff et al., 2008; Lainhart & Folstein, 1994). In study of adults (age 16–60 years) with ASD the lifetime prevalence rate of depression was 53% and in a younger study population this prevalence ranged from 4–38% (Hovander et al., 2009). Leyfer et al., (2006) showed that around 10–15% of children and adolescents (mean age 9) with ASD, ever had depressive symptoms, 10% met criteria for a major depressive disorder and about 2 % met criteria for a depression NOS.

In patients with Asperger Syndrom (AS) the prevalence of comorbid depression is reported most frequently with a prevalence of around 30% (Matson & Nebel-Schwalm, 2007). Though the study by Kim et al., (2000) showed an equal prevalence of depression in children with AS and HFA. A possible explanation for this finding might be that because of their higher cognitive abilities, individuals with AS or high-functioning autism are more aware of their problems and internalise these depressive thoughts more frequent than individuals with low-functioning autism (Cederlund, Hagberg & Gillberg, 2010; Sterling, Dawson & Estes, 2007). For children with LFA, no studies to date have been able to systematically determine the prevalence of depression (Magnuson & Constantino, 2011). Little is known about the prevalence of Dysthymia in persons with ASD. Dysthymia is less common compared to depressive disorders (Simonoff et al., 2008).

Natural History, Prognostic Factors, and Outcomes

Mood disorders are episodic disorders with either a marked change in the context of type of symptoms and variability in intensity of symptoms over time (Leyfer et al., 2006; Matson & Nebel-Schwalm, 2007). Due to difficulties in diagnosing a coexisting depression in these patients (see also the sections "Clinical Expression and Pathophysiology" and "Evaluation and Differential Diagnosis"), symptoms are often severe and/or prolonged at time of diagnosis (Skokauskas & Gallagher, 2010). Clinical evidence suggests that the outcome of autism might be affected by the presence of coexisting psychiatric disorders in ASD (Ghaziuddin, Ghaziuddin, & Greden, 2002). Especially, depression can have a negative impact on long-term outcome. Effects on a patient and a patient's family can be wide ranging. Patients with ASD can show a regression of behavioral skills, social withdrawal, and aggressive and oppositional behavior. These changes can interfere with a person's placement in the community and his or her social relationships. In addition, cases can be complicated by the development of catatonia which can result in extremely slow movements and a regression of self-care skills. Depression may also put an autistic patient at risk for suicide, especially when symptoms are severe. There are few reports on suicidal behavior among patients with autism spectrum disorders (ASDs). Causes of underreporting may be the low rate of suicidal behavior among children and preadolescents and the underdiagnosing of ASDs in the adult psychiatric setting. Data concerning duration of depressive symptoms in ASD are not available yet.

Clinical Expression and Pathophysiology

Symptoms of ASD and depression show a considerable overlap, which makes it harder to diagnose depressive disorders. Signs of ASD like abnormal speech patterns and social withdrawal might be confused with symptoms of depression such as psychomotor retardation or fatigue. Depressive patients with ASD show a difference in symptom presentation compared to patients without ASD, since expression of depressive symptoms is colored by ASD behavior. Many of these patients are not able to express their feelings, because of difficulties in expressing and communicating emotion due to poor integration between different modalities of nonverbal expressions and insufficient language skills to verbalize changes in feelings and mood (Perry, Marston, Hinder, Munden, & Roy, 2001; Stewart, Barnard, Pearson, Hasan, & O'Brien, 2006; Skokauskas & Gallagher, 2010). Patients with HFA are more capable in showing their feelings compared to patients with LFA, although even for them it remains difficult to express sadness. As in depressed persons without ASD, in depressed patients with ASD one of the main features is a depressed mood. However, in patients with ASD, its presence is more often reported by a patient's close relative than by self-report (Stewart et al., 2006). This is also the case with behavioral changes, appetite, and sleep disturbance. The majority of patients with ASD and comorbid depression show a decrease in self-care and increased social withdrawal. In youth with ASD, preoccupation with themes of death has also been noted during depressive periods (Ghaziuddin, Alessi, & Greden, 1995, Perry et al., 2001). When severity of depressive symptoms increases, self-esteem becomes more negative in individuals with Asperger's syndrome.

With the onset of depression in patients with ASD, both decrease and intensification of autistic symptoms have been reported. Specific depressive symptoms for individuals with ASD, especially in those with HFA, might be the loss of interest in subject of previous preoccupation and a decline in rigid behavior (Ghaziuddin et al., 2002; Stewart et al., 2006). However, these changes in behavior might be often interpreted as an improvement by their close relatives; in fact, these changes could be a sign of the presence of a depression. Presented symptoms are not always mood-related. The new onset of a depression, for example, is usually associated with a new onset or exacerbation of maladaptive behavior consisting of an increase in aggressive behavior, agitation, irritability, automutilation, compulsive behavior, hypoactivity, or a decline in daily skills (Geurts et al., 2010, Ghaziuddin et al., 2002, Stewart et al., 2006). Especially self-injury and aggression are often reported. Thus, in all individuals diagnosed with ASD, it is important to investigate whether or not behavior is related to the natural history of ASD, or has changed due to a comorbid disorder. Every ASD patient, especially those with LFA, should be screened for depression if there is a recent history of aggressive outbursts, in the setting of irritability, appetite, and sleep disturbance. In patients diagnosed with LFA, the most frequent signs of depression are a change in level of functioning; a regression in skills such as incontinence, severe appetite, sleep, and weight disturbance; and the presence of aggression. More unusual features are catatonia and other psychotic behaviors (Ghaziuddin et al., 2002). Patients with autistic disorders had more severe symptoms of depression and social withdrawal compared to patients with PDD-NOS (Pearson et al., 2006).

The exact pathophysiology of depression in patients with ASD remains unclear. Depression is known to be caused by genetic and environmental factors. Autistic children suffering from a depression are more likely to have a family history of mood disorders (Gillberg & Billstedt, 2000). Autism and depression seem to cluster in some families, suggesting that in a subgroup of patients, common genetic factors seem to be responsible. However, there is also evidence for an independent genetic origin of these factors (Hallett, Ronald, & Happe, 2009). The excess of depression in these families does not seem to be related to the stress caused by raising a child with ASD.

Life events play an important role in the onset of depressive symptoms. Problems with the

regulation of emotion have an impact on mood in autistic patients (Hill, Berthoz, & Frith, 2004). Stressful situations can be overwhelming for patients with ASD, and even to mild life events, they can respond intense. Children with ASD who develop a major depression experienced more negative life events such as family illness, parental divorce, and bereavement (Ghaziuddin et al., 1995). Data on this correlation in adults have not been described yet. Autistic patients might respond with depressive symptoms to negative events because of a genetic predisposition to depression (Ghaziuddin et al., 2002). It is not clear if patients with HFA respond more severely to negative life events compared to patients with LFA.

Social relationships in patients with ASD seem to be related to the development of depression as well. Interpersonal conflict with family members has been strongly associated with depressive symptoms in children with autism spectrum disorders. In addition, autistic children with more friendships of poorer quality were found to have the highest levels of depression (Lopata et al., 2010).

Factors affecting the occurrence of depression might be age, level of intelligence, social functioning, and the presence of other psychiatric or other medical disorders. Most cases of depression in patients with ASD have been described in adolescents and adults (Ghaziuddin et al., 2002; Matson & Nebel-Schwalm, 2007; Sterling, Dawson, Estes, & Greenson, 2007). This could be due to problems of assessment of psychiatric conditions in children with ASD. However, clinical experience suggests that the rate of depression in autistic patients rises with age (Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998). An explanation for this increase with age could be the more pronounced developmental gap between these patients and their same-aged peers and the lack in adaptive skills of executive planning abilities to take necessary steps toward independent living (Sterling et al., 2007). Patients with AS and HFA are, because of their better intelligence, more aware of their social handicap and difference from other people than patients with LFA. On the other hand, these patients are more in need for social

contact but may not have the social skills to successfully participate in social relations. Awareness of one's own role in failed social situations contributes to a lower self-esteem and discouragement. Therefore, patients with AS and HFA seem to be at risk for developing depressive symptoms (Cederlund, Hagber, & Gillberg, 2010). In addition, depressed autistic patients were found to have a higher intellectual ability and less impaired social functioning and adaptive skills compared to nondepressed autistic patients (Ghaziuddin et al. (1998)). It is not clear, however, whether a lack of insight in one's own level of impairment in children with LFA confers a protection from depressive states. Though, in severe autistic patients with a lower IQ, fewer depressive symptoms were reported (Magnuson & Constantino, 2011). Better adaptive skills are associated with increased rates of depression as well.

Evaluation and Differential Diagnosis

As previously described, a coexisting depressive disorder in children and adults with ASD can be difficult to diagnose due to impairments in cognitive functions and an overlap in symptoms between different psychiatric conditions. For patients, these impairments make it difficult to describe experiences and mental state. Symptoms are often reported by a patient's close relative instead of by the patient him-/herself. Therefore, it is important to involve a patient's parents and teachers in the diagnostic process. Kanne, Abbacchi, and Constantino (2009) found that when using the Achenbach System of Empirically Based Assessment, a higher percentage of parents reported their children as having depressive symptoms than their teachers did. Using the Youth Self-Report form, Hurtig et al. (2009) found strong agreement among adolescent patients with AS, their parents, and their teachers, indicating awareness of such difficulties.

Diagnosis is based on clinical expression of depressive symptoms reported by a patient, its close relatives, and clinicians. Due to a lack of a "gold standard" diagnostic tool, many different diagnostic instruments have been used for assessment of a depressive disorder in autistic patients.

Traditional measures of diagnosis have, in general, not been tested for validity and reliability in ASD populations. DSM-IV-TR diagnostic criteria used to identify psychiatric disorders in developmentally disabled patients may identify only the "tip of the iceberg" (Leyfer et al., 2006). In *children and adolescents* the Diagnostic Interview for Children and Adolescents, DICA IV, the Child Behavior Checklist CBCL, the Leiter-R-Questionnaires, the Kiddie Schedule for Affective Disorders and Schizophrenia K-SADS-PL, and the Children Depression Inventory CDI (based on the Hamilton Rating Scale for Depression) have been often used. One study used a modification of the Kiddie Schedule for Affective Disorders and Schizophrenia in children and adolescents with autism for the assessment of comorbid psychiatric disorders. They developed additional screening questions and new coding options and found and reported a sensitivity of 100% and a specificity of 93.7% for major depression in their sample (Leyfer et al., 2006). Reiss and Valenti-Hein (1990) developed the Reiss scales for the screening of comorbid psychiatric disorders in children and adolescents with intellectual disability (ID). Results from their study population suggest that these instruments are particularly well suited for screening and for helping in the analysis of the relationships between certain behavior problems and psychopathology in patients with ID (Reiss & Valenti-Hein, 1990). In general, observations of behavior and activities are important in the assessment of depression because of their limited verbal abilities and their tendency to express thoughts and feelings through play.

In *adults*, the Beck Depression Inventory (BDI) and the Hamilton Rating Scale for Depression (HRSD) are two of the most widely used scales to assess the severity of depressive symptoms (Stewart et al., 2006). The Beck Depression Inventory, a multiple choice self-report questionnaire containing 21 items relating to symptoms of depression, was found to be an adequate screening instrument for depression in adolescent and adult males with AS (Cederlund et al., 2010). However, even if questions of the BDI and the HRSD have been adapted, some questions may remain difficult for patients with ASD and their relatives. For example, these diagnostic instruments ask patients to rate their mood and if they have feelings of guilt or worthlessness. Therefore, some autistic patients may not express these feelings during a depressive episode because these feelings are not in their repertoire (Leyfer et al., 2006; Stewart et al., 2006).

During the lifespan, different problems related to ASD can appear resulting in differences in a person's behavior. To determine whether a person's behavior is due to an underlying autism spectrum disorder or due to a comorbid psychiatric condition, a clinician can asses a patient's developmental history, focusing on the consistency of symptoms over time and pervasivity in different situations. Thus, it will be easier to determine whether a comorbid disorder was already present and if symptoms of comorbidity or ASD are changing (Geurts et al., 2010). As mentioned before, if a change in symptoms of an autistic patient occurs, it is important to screen him or her for comorbid disorders.

The differential diagnosis of depressive disorders in patients with ASD is comprehensive because of an atypical presentation of symptoms. There are several distinct categories of disorders including depressive disorders, bipolar disorders, anxiety disorders, and disruptive disorders. Depressive disorders include a (major) depressive episode, depression NOS, and dysthymia. Determined by the presence of manic or hypomanic symptoms, a patient can be diagnosed with a coexisting bipolar I disorder and bipolar II disorder, respectively. When a change of or increase in symptoms is reported in an autistic patient, one should be aware that these symptoms can still exist due to an autism spectrum disorder. An increase in obsessive compulsive behavior can point towards the onset of a depression but be a sign of an obsessive compulsive disorder as well. Anxiety is often present in depressed patients with ASD, but coexisting anxiety disorders should be excluded. In children, a depressive disorder is characterized by agitation and externalizing behavior problems. Therefore, differential diagnostic disruptive disorders have to be considered. Adjustment disorders and schizophrenia are a part of the differential diagnosis of depression in autistic patients as well.

Treatment

There is a lack of studies that directly assess the effects of residential programs, treatment programs, and education programs on depressive symptoms in patients with ASD. However, there are interventions that can reduce mood and related behavioral problems in patients with ASD. Some high-functioning depressive patients with good verbal skills may benefit from psychodynamic psychotherapy. In these cases, a highly structured and directive approach is required. Structured psychotherapy combined with appropriate behavioral and educational interventions are recommended by some studies. In more able and older patients, cognitive behavioral therapy might help them to cope with anger and other depressive symptoms. This therapy is seldom successful without integration and recurrence in treatment.

The main treatment for depression in patients diagnosed with ASD is pharmacological including selective serotonin reuptake inhibitors (SSRIs), mood stabilizers, antipsychotics, and hypnotics. SSRIs seem to be the most effective drugs in depressive autistic patients (Stewart et al., 2006). These agents are being increasingly used in ASD to control depression and aggression (Ghaziuddin et al., 2002). Serotonin is linked to the mediation of psychological processes such as mood, social interaction, sleep, obsessive-compulsive behaviors, and aggression. Increased levels of whole blood and platelet serotonin have been reported in people diagnosed with ASD, and therefore, SSRIs are associated with an improvement of ASD symptoms (Williams et al., 2010). Moreover, treatment in autistic patients with depressive symptoms is in some study populations including children, adolescents, and adults associated with a decrease in low mood, sleep disturbances, and aggressive and self-injurious behavior and an increased capacity for self-care as well (Hollander, Phillips, & Yeh, 2003; Perry et al., 2001; Stewart et al., 2006). In autistic nondepressed children, low doses of SSRIs (venlafaxine) improved repetitive behaviors, hyperactivity, and communication and language functions (Hollander, Kaplan, Cartwright, & Reichman, 2000). However, a Cochrane review found no evidence for the effectiveness of SSRIs as a treatment for children with ASD (Williams et al., 2010). This review focused on the treatment of ASD using SSRIs and did not specifically focus on a coexisting depression.

The Hamilton Rating Scale for Depression (HRSD) is developed to evaluate or report depressive symptoms in nonautistic patients. Since depressive symptoms in patients with ASD show a considerable overlap with these ASD symptoms, but other important signs like increased aggressive behavior are missed, this HRSD is not very sensitive and easy to use in an autistic population. A study by Buchsbaum et al. (2001) reported no significant improvement of depressive symptoms seen in autistic adults treated with SSRIs in depression. However, using the HRSD, some small positive effects of fluoxetine and fluvoxamine on aggressive behavior and anxiety, respectively, in this study population of adults with ASD have been described.

At this time, SSRIs cannot be recommended as a treatment for autistic children in general. Decisions about the use of these agents in depressed patients with ASD should be made on a case by case basis (Williams et al., 2010). Reported side effects of different SSRIs are headaches, sedation, aggressiveness, agitation, and lip dyskinesia by using citalopram. Fluoxetine can cause weight gain and increase agitation, and venlafaxine can cause aggression, nausea, and behavioral activation. Mood stabilizers such as valproate and levetiracetam can improve symptoms related to affective instability and aggression in autistic patients. The atypical antipsychotic agent risperidone can improve disruptive behavior in patients with ASD. Tremor, weight gain, and increased appetite are reported adverse effects (Hollander et al., 2003).

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Mood Stabilizers

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Definition

Mood stabilizer is a term used to describe a group of medications that are used in the treatment of bipolar disorder. Currently, mood stabilizers including lithium, valproic acid, and its derivatives, carbamazepine and several antipsychotic medications, are now approved for the treatment of bipolar disorder.

See Also

▶ Lithium

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More Than Words

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Definition

More Than Words is a parent-based social-pragmatic intervention program for children with autism spectrum disorders (ASD). It includes education and social support for parents and early language intervention for children with ASD under the age of 5. The program is led by a Hanen-certified speech-language pathologist (SLP) and aims to help parents learn more about communication and, in turn, support their children in increasing their language and communication skills.

Historical Background

The Hanen Centre is a Canadian charitable organization that was founded in 1975 by Ayala Hanen Manolson to increase knowledge and training of adults to help children become more effective communicators. *More Than Words* was adapted from another Hanen program, *It Takes Two to Talk*, to help meet the needs of parents and their children on the autism spectrum. The parent guidebook was written by Fern Sussman, a speech-language pathologist, and was published in 1999 by the Hanen Centre in Toronto, Ontario (The Hanen Centre, 2007).

Rationale or Underlying Theory

The goal of this program is to "empower parents to become the primary facilitator of their child's communication and language development thereby maximizing the child's opportunities to develop communication skills in everyday situations" (The Hanen Centre, 2007). *More Than Words* reflects a family-centered model of intervention. This program believes that since the parent or caregiver is the most important and constant element in the child's life, they have an invaluable opportunity to provide consistent interventions in a natural setting to assist their children in experiencing meaningful interactions.

A social-pragmatic theory of language acquisition is the theoretical foundation for *More Than Words*, asserting that the development of communication occurs in the context of the interaction between the child and the important adults in his or her life. Strategies taught in the program are intended to help parents become more responsive to their children's communication attempts in order to facilitate their language skills. Parents also learn ways to manipulate the environment to increase joint attention and the motivation to communicate.

Goals and Objectives

The *More Than Words* program outlines three main objectives for parents in helping to support their children's communication skills: parent education, early language intervention, and social support for parents (The Hanen Centre, 2007). As part of the parent education component, parents develop a better understanding of their child's strengths and challenges by learning about their child's learning style and sensory preferences. They also learn about basic concepts relating to language and communication and what stage of communication their child is in. This helps them to set goals and recognize communication attempts.

The second objective of *More Than Words* is for parents to carry out early communication and language intervention. The Hanen-certified speech-language pathologist (SLP) works collaboratively with parents to develop goals and implement responsive strategies that can be applied to interactions with their child across a variety of contexts. This is a flexible process and is intended to become a consistent, yet natural part of the day-to-day exchanges between the parent and child. As part of this intervention, parents video-record interactions and strategy implementation with their child. The SLP then reviews the video with the parents and provides feedback to help increase their awareness of their interactions along with the communicative behaviors demonstrated by their child. The SLP facilitates the parents' metacognitive thinking in the video review to encourage their consistent use of the new strategies.

The third objective is to provide social support for parents, who are at greater risk for fatigue, frustration, depression, and anxiety than parents without a child with developmental disabilities. Support within this context is valuable because it comes from a professional who understands the unique strengths and challenges of their child, as well as from other parents in the group who can empathize and share experiences.

Treatment Participants

More Than Words was designed for parents and their children under the age of 5 with ASD. It can be used with children who are verbal or nonverbal.

Treatment Procedures

The program is led by a Hanen-certified SLP and is offered to groups of up to eight families at one time. There are three major components of this program. First, there is a preprogram assessment and baseline video recording of an interaction between the parent and child. Next, parents participate in seven sessions of group training, totaling a minimum of 17.5 h. These sessions are led by the SLP and include discussion, PowerPoint presentations, and video clips that aim to help parents learn about early communication and

language, how to manipulate the environment to help their child communicate, identify their child's stage of communication, and how to set realistic communication goals. The parents' interactions with their children are video recorded, and three of these recordings are reviewed with the SLP. As part of the video feedback sessions, the parent observes and then describes the strategies they implemented with their child. The SLP probes parent understanding of what was observed and how what a parent did either facilitated or failed to facilitate communication change. The SLP provides coaching to the parents, based on the strategies taught during the parent education sessions. The program is supported by a guidebook, DVD, and PowerPoint slides with video clips.

Efficacy Information

This program seeks to target the communication challenges that are present in children with autism spectrum disorders. The guidebook provides illustrations and step-by-step examples, giving parents a readable and easy to understand resource with opportunities to practice what they learn in the context of everyday activities. Intervention strategies used in this approach, including modeling, reinforcement, and imitation, are commonly used best practices in early education and speech-language therapy and are directly related to the individual child's communication goals. The video-recorded interactions between the child and parent are periodically reviewed by the certified SLP, ensuring that the strategies are implemented in an effective and consistent manner.

Two studies have examined the effectiveness of More Than Words for families and children with ASD. The first examined the facilitation of parental understanding of ASD and the social communication of their children following implementation of the More Than Words program (McConachie, Val Randle, Hammal, & Le Couteur, 2005). Results indicated that parents increased their use of facilitative strategies and children with ASD increased their vocabulary

size. A second study found similar results for three families of children 2.8–3.2 years of age with parents increasing their use of responsive strategies and children increasing their vocabulary (Girolametto, Sussman, & Weitzman, 2007).

Outcome Measurement

A number of studies provide empirical evidence demonstrating positive outcomes of a social-interactionist intervention for children with ASD (Chapman, Leonard, & Mervis, 1986; Duchan, 1989; Mirenda & Dollennan, 1986). There is also a recent body of literature that supports this type of intervention being successfully carried out by parents (Aldred, Green, & Adams, 2004; Mahoney & Perales, 2003). Two published studies specifically examine the efficacy of *More Than Words*. The first was a controlled trial measuring the effectiveness of parent training on the use of facilitative interaction strategies to enhance the communication skills and behaviors of their children (McConache et al., 2005). This quasi-experimental study included 26 children and parents in an experimental group and 25 children and parents in a control group. Parents in the experimental group participated in the *More Than Words* training program. The results showed a measureable effect on both the parents' and their children's communication skills. The parents of children diagnosed with ASD showed an increase in responsiveness. The children whose parents attended *More Than Words* had significantly greater vocabulary size than those in the control group, as measured by parental report on the *MacArthur-Bates Communicative Development Inventory (CDI)* (McConachie et al.). The CDI is a frequently used measure of word and gesture comprehension and word and sentence production that is used to assess outcomes following the *More Than Words* program.

Another study examined the social interaction of three preschool children with ASD following their mothers' participation in *More Than Words* (Girolametto et al., 2007). This was a multiple case study design that aimed to extend the

previous study by using microanalytic coding procedures on the recordings of parent–child interactions. The results found that mothers increased their use of spontaneous interaction strategies and their children demonstrated increased vocabulary development and social interaction (Girolametto et al.).

Qualifications of Treatment Providers

The *More Than Words* program is led by a certified speech-language pathologist who has completed a specialized training by the Hanen Centre. First, the SLP needs to be trained in the *It Takes Two to Talk* program. Then, they can complete the 3-day, intensive, small-group training on *More Than Words*, led by a Hanen instructor.

See Also

▶ Hanen Approach
▶ Language Acquisition

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Moro Reflex

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Synonyms

Startle reflex

Definition

The Moro reflex, also known as the startle reflex, was initially described by the Austrian

pediatrician Ernst Moro (1874–1951). It represents one of the infantile reflexes, and it may be observed since birth in all newborns up to 5 months of age. The reflex is triggered when (1) a baby's head falls backward or quickly changes position and/or (2) the baby is startled by an unexpected loud noise. The reflex causes the baby initially to extend the neck and spread out widely the arms and legs (abduction) and then pull the arms back in a clasping motion (adduction). These movements are sometimes associated with cry. The Moro reflex, as well as other infantile reflexes (e.g., the grasping reflex), is considered a residual behavior from when nonhuman primates clung to their mothers swinging through the trees (Thies & Travers, 2001).

The absence, persistence, and/or exacerbation of the Moro reflex in childhood and adulthood is generally associated with profound disorders of the motor system (e.g., cerebral palsy). The assessment of the Moro reflex is carried out by pediatricians to evaluate the integration of the central nervous system in early infancy.

As early primitive reflexes, such as the Moro reflex, are gradually extinguished at around 5 months of age, research in this area in the ASD population is very limited. A retrospective study by Teitelbaum and colleagues (2004) suggested that infants later diagnosed with ASD show abnormal movement patterns that can be interpreted as primitive reflexes "gone astray"; that is, some reflexes are not extinguished at the appropriate age in development, whereas others fail to appear when they should. More empirical research is needed to specifically investigate the development of the Moro reflex in the ASD population.

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Mortality

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Definition

The term "autism" is used in this entry to describe all autism spectrum disorders, which include the various types of pervasive developmental disorders according to DSM-IV (American Psychiatric Association [APA], 2000-TR) and ICD-10 (World Health Organization [WHO], 1992).

The life expectancy of people with autism is of interest to parents, health professionals, and service providers concerned with these peoples' lifetime needs. Mortality information that includes the causes of death is important as it can help parents and professionals focus on reducing associated risks and ultimately the rate of mortality among people with autism.

Historical Background

Occasional deaths have been reported in all general follow-up studies of individuals with autism (Ballaban-Gil, Rapin, Tuchamn, & Shinnar, 1996; Billstedt, Gillberg, & Gillberg, 2005; Fombonne, Talan, Bouchard, & Lucas, 1989; Howlin, Goode, Hutton, & Rutter, 2004; Kobayashi, Mutara, & Yoshinaga, 1992; Larsen & Mouridsen, 1997). Causes of death include traffic accidents (Fombonne et al., 1989; Larsen & Mouridsen, 1997); unrecognized volvulus in a woman in a long-term psychiatric institution (Larsen & Mouridsen); status epilepticus (Howlin et al., 2004); and cases of drowning, pneumonia, and complications arising from long-term psychotropic medication (Ballaban-Gil et al., 1996).

However, systematic studies dealing with mortality and causes of death in autism are rare. There are difficulties in obtaining an adequate

sample size to calculate specific risks, in studying samples over a suitable time span, and in establishing the cause(s) of death.

Current Knowledge

Standardized mortality ratio (SMR) is frequently used to measure excessive mortality. The SMR is the quotient of the observed to the expected numbers of deaths, and an SMR of 1 indicates that the observed number of deaths is no different from what would be predicted for the general population: An SMR value greater than 1 indicates that the observed mortality exceeds expectations in the group under study.

Only three systematic follow-up studies specifically dealing with mortality and causes of death in individuals with autism have been published so far. Shavelle, Straus, and Pickett (2001) and Pickett, Paculdo, Shavelle, and Strauss (2006) reported mortality and causes of death in 13,111 people with autism who were receiving services from the California Department of Developmental Services between 1983 and 2002. The overall SMR was 2.4, indicating a mortality rate more than twice as high as for the general population. The increase in mortality was larger in females than in males. Mortality was associated with mental retardation with an SMR of 3.1 for participants with moderate, severe, or profound retardation, whereas the SMR was 1.4 for individuals with no or only mild mental retardation. Epilepsy was strongly associated with death risk. SMR was 36.9 in participants with epilepsy and moderate, severe, or profound mental retardation against 22.6 in those with no or mild mental retardation. Suffocation (SMR = 51.4 and 5.7, respectively) and drowning (SMR = 13.7 and 3.9, respectively) were also noted to be frequent specific causes of death and, like epilepsy, associated with the level of cognitive impairment. Similar results were obtained in a Danish study (Isager, Mouridsen, & Rich, 1999; Mouridsen, Brønnum-Hansen, Rich, & Isager, 2008) in which an overall SMR of 1.9 was reported in a nationwide cohort of 341

individuals with autism (average age 43 years) observed between 1960 and 2007. Again, the SMR was particularly high in females. Epilepsy (SMR = 35.0) and infectious diseases were among the most common causes of death. Epilepsy was notably marked in deceased females; five of the eight deceased females had epilepsy. Different kinds of infectious diseases (meningitis, pneumonia, appendicitis) were associated with death in seven individuals. In a Swedish community-based study of 120 individuals with autism, mean age 33.2 years, Gillberg, Billstedt, Sundh, and Gillberg (2010) found an overall SMR of 5.6. They also noted that the mortality rate was particularly high in females. Associated medical diseases (including epilepsy with cognitive impairment) and accidents accounted for most of the observed causes of deaths.

Prevention efforts to decrease mortality in people with autism need to address the conditions that are the immediate causes of death (i.e., infectious diseases, epilepsy, and accidents). However, the behavioral characteristics that define autism often make care difficult and can lead to exacerbations in the state of somatic illness or diagnostic delay, eventually leading to death-causing illness (Larsen & Mouridsen, 1997; Mouridsen et al., 2008). Assessing pain and discomfort in a cognitively impaired, nonverbal patient is difficult, and of paramount importance is the involvement of the parent(s) or other care providers, if available. The best pain assessment by proxy is that provided by caregivers or family members who know the patient well. Only they can identify changes from a patient's base line behavior that may signify pain and discomfort. Patients may be uncooperative or combative if they do not understand the need for help. It is important to realize that many people with autism react badly to any change in their environment, and therefore, a visit to a general practice or a hospital can be very alarming for them, in particular, if an unplanned acute hospital admission is necessary (Scarpinato et al., 2010; Souders, DePaul, Freeman, & Levy, 2002). In some patients, conventional peri- and postoperative management is impossible and alternative

strategies are needed (Dell et al., 2008; van der Walt & Moran, 2001). Likewise, venipunctures, intravenous insertions, and initiation or change of medical treatment can be difficult to carry through. It is also noteworthy that Williams, Dalrymple, and Neal (2000) found that 62% of parents reported difficulty giving medication to their children with autism.

An association between autism and epilepsy has been consistently reported, and the literature presents a wide range of co-occurrence estimates from 5% to 46% (Spence & Schneider, 2009). These authors also report that more severe intellectual disability is associated with greater rates of epilepsy. Considering the high prevalence of epilepsy in autism, it is therefore important to suspect the comorbidity of epilepsy in every individual presenting with autism. It follows that understanding the needs of this group is particularly important within any major epilepsy service. Since epilepsy is strongly associated with death risk, careful monitoring of anticonvulsant treatment is essential in those individuals with a concomitant occurrence of autism and epilepsy. However, the clinical identification of seizures may be difficult in some cases. The diagnosis of partial complex seizures, in particular, can be complicated by the presence of atypical body movements and behavioral patterns often seen in association with autism (Bauman, 2010). Obtaining a high-quality EEG can also be difficult, and effective communication usually has to be through a caregiver.

Since accidents are often avoidable, special attention should be paid to the safety of community surroundings. In the Mouridsen et al. (2008) study, two participants, who both lived in specialized institutions for autistic people, managed to swallow dangerous objects and choke on them during an unsupervised period. According to the standards of the caregivers, the two patients should never be left unsupervised.

As the rates of autism diagnoses increase (Rutter, 2005), it becomes more and more imperative for health care providers in any setting – family, institutions, and primary or acute care – to understand the unique challenges of people

with autism. The findings published so far underscore the importance of maintaining sufficient competence levels in the fields of internal medicine and neurology within the autism care system to recognize and properly manage somatic as well as neurological diseases. As there is little information about the best practice for providing care to people with autism in institutional or hospital settings, it is important to develop nursing standards that address care for people with autism.

Future Directions

To conclude, mortality is increased in people with autism, and individuals with diminished cognitive functioning or epilepsy are at particularly high risk of a reduction in life expectancy. However, increased understanding of the most common causes of death can help parents and other caregivers focus on reducing risk and, ultimately, the rate of mortality among people with autism.

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Motivation

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Definition

An important body of research relates to interventions that improve motivation in children with autism. This literature has been particularly relevant, as individuals with autism often appear unmotivated to engage in social and learning interactions. It has been hypothesized that a lack of motivation to engage in social and learning interactions may be caused by external variables (see below). Therefore, environmental manipulations should be effective in changing the response-reinforcer relationships that led to the development of these motivational deficits. Along those lines, a number of studies have focused on identifying specific variables that effectively improve motivation in children with autism. To start, child-driven approaches, such as providing the child with the choice of stimulus materials, activities, and conversational topics, have been shown to improve responding and attention (Koegel, Dyer, & Koegel, 1987). This has also been referred to in the literature as "following the child's lead," and its effectiveness has been well documented in regard to improving a range of behaviors such as communication, academics (Koegel, Singh, & Koegel, 2010), and socialization (Koegel et al., 1987). Such approaches have been compared and contrasted with previous empirically based approaches that focus on an adult-driven curriculum without any

input or consideration of the child with autism's changing reinforcer hierarchy and have been shown to be more effective.

Another variable that improves motivation to respond is the interspersal of new (acquisition) tasks that the child has not yet mastered with previously mastered (maintenance) tasks (Dunlap, 1984; Koegel & Koegel, 1986). Rather than repeatedly presenting new target tasks that are likely to be difficult, interspersing maintenance tasks with acquisition tasks results in increased correct responding in addition to improved overall responsiveness. Similarly, when tasks are varied frequently, rather than being taught in a drill-like context, motivation improves (Dunlap & Koegel, 1980). Another body of research relates to the manipulation of consequences for child responses. As opposed to using a strict shaping paradigm that only rewards responses that are as good or better than the previous response, child motivation can be improved by rewarding child's attempts to respond correctly that are free of disruptive or repetitive behaviors (Koegel & Egel, 1979; Koegel, O'Dell, & Dunlap, 1988). Related to this, providing direct and natural rewards, which are inherently linked to the child's response, results in improved motivation in terms of more rapid acquisition of the target behaviors (Koegel & Williams, 1980; Williams, Koegel, & Egel, 1981). That is, rather than providing an arbitrary unrelated reward (e.g., food item or token) contingent upon a correct response, the child is provided with rewards that are directly related to their behaviors. For example, a food may be given to a child learning first words contingent upon labeling the food item so that it is directly related to the child's response. The aforementioned procedures can be used in combination with one another and have been documented to improve motivation as measured by decreased levels of disruptive behavior; improved performance in academic, language, and social domains; and improved child affect (Koegel et al., 1987; Koegel & Koegel, 2006). Another variable that has been shown to affect child motivation for some (but not all) children is clinician affect. For example, research suggests that some children respond more

favorably when the clinician shows specific types of affect while providing reinforcers, such as either strong positive affect or low affect depending on the child. As a whole, these studies suggest that motivation appears to be measurable and treatable. At this point, the most effective programs use a combination of motivational procedures, applied simultaneously, to produce large changes in the behavior of children with autism. This body of literature has led researchers to conceptualize the construct of motivation as "pivotal" such that positive changes in a number of untreated symptoms/behaviors occur when a child with autism is motivated to respond (Koegel & Koegel, 2006). Thus, the literature on pivotal response treatment (PRT) uses motivational procedures as a core underlying principle of the intervention, and motivational components have effectively been incorporated into interventions for improving articulation (Koegel, Camarata, Koegel, Ben-Tall, & Smith, 1998), first words (Koegel et al., 1987), academic engagement (Koegel et al., 2010), and social conversation (Koegel et al., 1987) in children with autism. Additionally, studies have shown that collateral improvements in disruptive behavior occur when such motivational variables are employed without needing to target the disruptive behavior directly. While the general concept of motivation can be conceptualized by feelings of an individual, such as the desire or incentive to engage in activities, motivation also can be defined by observable and measureable behaviors. Specifically, motivation has been measured by task engagement, responsiveness, decreases in response latency, initiations, and affect, as well as an absence of avoidance behavior (Koegel, Koegel, & McNerney, 2001). During the intervention sessions when motivational procedures are incorporated into the teaching, the children show an increase in the number of responses and decrease in response latency, initiate new related behaviors, and demonstrate positive affect. Task engagement and responsiveness can be monitored by the number or rate of responses the child emits. Latency can be measured by assessing the amount of time that passes before the child begins to engage in a learning task or activity. Initiations are important in that if the children are motivated to engage in the tasks, they are

likely to spontaneously engage in the task, sustain participation, and initiate future activities. This also relates to generalization, as motivated children may spontaneously demonstrate the targeted responses across settings, behaviors, and people. Changes in affect can also be seen in motivated children. Affect is often rated by Likert scales in general categories of positive, neutral, and negative affect and has been defined as interest (e.g., child is alert and involved in the activity), happiness (e.g., the child smiles, laughs, and seems to be enjoying self), and enthusiasm (Baker, Koegel, & Koegel, 1998; Koegel & Egel, 1979; Koegel, Vernon, & Koegel, 2009). In addition to child affect, motivation can be measured by lowered levels of disruptive behaviors (Dunlap & Koegel, 1980; Koegel, Koegel, & Surratt, 1992). Multiple measures showing improved latency, affect, happiness, enthusiasm, and levels of disruptive behavior have been used to measure motivation with high degrees of reliability (Dunlap & Koegel, 1980).

Historical Background

The interest in the construct of motivation, as it relates to autism spectrum disorder (ASD), came about as a result of the apparent lethargy and disinterest individuals with autism may demonstrate in regard to social conversation, learning, and other activities (Lovaas, 1977). This led researchers to hypothesize theories for this lack of motivation. A possible theoretical explanation is related to the concept of "learned helplessness." Specifically, it has been hypothesized that during exposure to an uncontrollable outcome, a lack of contingency between the behavior and the outcome is learned (Seligman & Altenor, 1980). Simply put, if an individual receives noncontingent rewards or punishers, the individual will not initiate behaviors and will appear lethargic and inactive. Early animal studies that postulated the learned helplessness theory were carefully controlled and showed the effect of uncontrollable events causing a disruption in behavior. Specifically, the once responsive animals became unresponsive and lethargic. Subsequently, studies replicated this phenomenon using human subjects in controlled settings. They showed that if individuals' responses were not reinforced, they too simply stopped responding (Gatchel, Paulus, & Maples, 1975). Learned helplessness has also been hypothesized to occur in other human conditions, such as stress and depression (Miller & Seligman, 1975; Price, Tryon, & Raps, 1978). Some studies have also shown that physiological changes, such as norepinephrine depletion, weight loss, and ulcers occur at a higher rate when consequences are noncontingent and outcomes are uncontrollable (Abramson, Seligman, & Teasdale, 1978; Seligman & Weiss, 1980). Data also suggest that this theory may be highly relevant for autism as well (Koegel & Egel, 1979; Koegel & Koegel, 2006).

The theory of motivation is an important concept in regard to intervention for autism, as it supports the notion that some, or all, of the disability may relate to environmental variables. That is, the state of an apparent lack of motivation is hypothesized to occur when the individual's responses are uncontrollable, or "learned helplessness." In regard to children with autism, reduced social responding that begins very early in life due to central nervous system dysfunction may result in the children experiencing high degrees of noncontingent consequences. This may create a situation wherein the child learns that responding and reinforcement are independent. This weakening of the response-reinforcer relationship may cause a decrease in social responding and lower levels of motivation in children with autism.

Current Knowledge

The lack of responsiveness and long response latencies demonstrated by children with autism as well as an apparent lack of motivation and curiosity have been discussed since the 1960s when principles of applied behavior analysis were beginning to show promise with children with autism. Within the broad framework of environmentally manipulated behaviors, researchers discussed the role of reinforcers in this apparent lack of motivation. They proposed that the potency or availability of reinforcers may not be

adequate when a child with autism engages in difficult tasks (Koegel & Egel, 1979), thereby creating a lack of motivation. Koegel and Egel (1979) were the first authors to present the possibility of learned helplessness and the importance of motivation to address the problem. Following that publication, a number of studies addressed individual areas of intervention that appeared to directly improve motivation. In 1987, Koegel, O'Dell, and Koegel published work using an intervention package, containing a large number of motivational variables (discussed above), was especially effective.

Future Directions

Although the literature describes specific procedures for improving motivation, there continues to be a need for future research relating to the measurement of motivation, the refinement of existing procedures that improve motivation, and additional intervention procedures for improving motivation.

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M

Motivation Assessment Scale

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Synonyms

MAS

Description

The Motivation Assessment Scale (MAS) is a rating scale that assesses functions of problem behavior in individuals with developmental disabilities through informant responses. It includes 16 questions and is comprised of four subscales that each represents a possible function of the behavior: attention, escape, sensory, and tangible. Each question has six response options (0 = never, 1 = almost never, 2 = seldom, 3 = half the time, 4 = usually, 5 = almost always, and 6 = always). Scores are calculated by summing the item ratings within a particular subscale/function and calculating the mean rating for that subscale. High scores for one or more of the subscales suggest that those functions may be maintaining the individual's problem behavior (Durand & Crimmins, 1988), although the authors of the instrument do not specify what constitutes a high score. An example item on the MAS is "*Does this behavior occur when you are talking to other persons in the room?*" (Durand & Crimmins, p. 102). The MAS is considered an indirect assessment method because it is removed in time and place from the behaviors being measured (Floyd, Phaneuf, & Wilczynski, 2005).

Historical Background

The MAS was originally developed to assess the functions of self-injurious behavior, in particular (Durand & Crimmins, 1988), within a framework of applied behavior analysis. It was designed to be a more efficient alternative to direct functional behavior analysis methods (Durand & Crimmins, 1988). Based on previous literature identifying common functions of self-injurious behavior (i.e., social attention, tangible consequences, escape from unpleasant situations, and sensory consequences), Durand and Crimmins (1988) created four subscales, each representing a specific function, that comprise the MAS. The items were generated following interviews with teachers, clinicians, and parents of children with developmental disabilities.

Psychometric Data

In their original study based on 50 children with developmental disabilities who exhibited frequent self-injurious behavior, Durand and Crimmins (1988) reported interrater reliability coefficients ranging from .66 to .92 for the individual items and .80 to .95 for the raw mean subscale scores. Test-retest reliability, over a 30-day period, was calculated and the coefficients ranged from .89 to .98 for the individual items and .92 to .98 for the mean subscale raw scores. The authors also found that teachers' ratings on the MAS were highly predictive of student's behavior in an analogue experimental condition (Durand & Crimmins).

However, the psychometric properties of the MAS have since been questioned by other researchers (e.g., Paclawskyj, Matson, Rush, Smalls, & Vollmer, 2001), as subsequent studies examining the validity and reliability of the measure have produced inconsistent results. It has also been argued that research on the MAS and other indirect functional assessment measures has not carefully examined validity evidence based on scale content and informant response processes, evidence of user satisfaction with the measure, or the treatment utility of the scale (Floyd et al., 2005).

Some factor analytic research has provided support for the intended four-factor structure of the MAS (i.e., sensory, escape, attention, and tangible), although the factor structure was somewhat different for a sample with lower frequency problem behaviors (Singh et al., 1993). Other researchers have not found support for the

four-factor model, specifically the sensory function subscale (Kearney, Cook, Chapman, & Bensaheb, 2006). Joosten and Bundy (2008) also failed to find support for the construct validity of the MAS in the form of a four-factor structure or as a unidimensional measure of motivating factors for stereotyped behavior. In addition, Duker and Sigafoos (1998) results did not fully support the factor structure of the MAS, and their results suggest that the type of problem behavior may be differentially related to reliability and factor structure.

Research examining the internal consistency of the MAS has also produced inconsistent results. Cronbach's alpha coefficients for the subscales ranged from .68 to .86 in a study by Spreat and Connelly (1996) and .68 to .87 in a study by Duker and Sigafoos (1998). However, Shogren and Rojhan (2003) reported values ranging from .80 to .96.

Subsequent research on the interrater reliability of the rating scale has produced lower values than those reported in the original Durand and Crimmins (1988) study. Shogren and Rojhan (2003) found interrater reliability coefficients for the four subscales ranging from .35 to .73, and Streat and Connelly (1996) reported values ranging from .31 to .57. Another study found that interrater agreement depended upon the type of problem behavior (Duker & Sigafoos, 1998). For example, raters were less likely to agree on the functions of destructive behaviors (e.g., aggressive behavior) as compared to maladaptive (e.g., self-injurious behavior) and disruptive (e.g., screaming) behaviors (Duker & Sigafoos).

Research examining other types of reliability evidence for the MAS has also failed to provide clear evidence that the instrument is psychometrically sound. For example, Shogren and Rojhan (2003) reported test-retest reliability coefficients ranging from .71 to .89 for the four subscales, which are lower values than those reported originally by Durand and Crimmins (1988). Streat and Connelly (1996) also found evidence of poor reliability in the difference scores between subscales, which are used to make clinical decisions regarding the function of the problematic target behavior.

Clinical Uses

The MAS has been used clinically to identify possible factors that are maintaining an individual's problem behavior. The indentified function can then be used to develop an intervention program to reduce the problem behavior and to select reinforcers for appropriate behavior. Some have argued that the MAS should be used in conjunction with direct observation methods because of its psychometric limitations (e.g., Duker & Sigafoos, 1998; Shogren & Rojhan, 2003; Spreat & Connelly, 1996).

See Also

▶ Applied Behavior Analysis
▶ Behavioral Assessment
▶ Functional Analysis
▶ Functional Behavior Assessment

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Motor Control

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Synonyms

Cerebellum; Motor cortex

Definition

Motor control refers to the coordination of information exchanged between the neocortex in the brain and the muscular and somatosensory systems to bring about controlled, or voluntary, movements. Controlled movements are planned, organized, and initiated in the prefrontal, premotor, and primary motor cortices. Instructions for the movement are then sent through the spinal cord to the appropriate muscles to execute the movement. The somatosensory system provides feedback about the movement, and the basal ganglia, brain stem, and cerebellum fine-tune the movement by adjusting force and correcting for movement errors.

See Also

▶ Cerebellum
▶ Motor Cortex

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Motor Cortex

▶ Motor Control
▶ Precentral Gyrus

Motor Development Assessment

▶ Psychomotor Development Index

Motor Planning

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Definition

Motor planning can be broadly defined as the capacity to plan the necessary steps to achieve purposeful movements. It is often considered under the larger concept of praxis, which comprises the conceptualization, organization, and execution of an action sequence. Although the terms "motor planning" and "praxis" are sometimes used interchangeably, motor planning may be more accurately thought of as one element of praxis, distinct from both the idea behind the movement and its actual implementation. In addition to being dependent in part on neural motor systems, motor planning may be affected by the multimodal integration of sensory processes involved in proprioception, vestibular functioning, and vision, and by capabilities for preemptively formulating a mental sequence of actions.

The clinical assessment of motor planning typically occurs as part of a broader evaluation of

motor functioning. Few clinical tests specifically measure motor planning; however, a number of standardized instruments can provide relevant information. These include batteries that assess a range of motor abilities, such as fine and gross motor skills, limb and verbal praxis, and sensorimotor functioning. In addition, the assessment of adaptive skills and motor performance during everyday activities can provide some indication of motor planning ability. A thorough developmental history is also usually conducted for children with motor planning or praxis difficulties, including the documentation of major motor milestones and early motor behaviors.

Disorders related to motor planning and praxis include apraxia and dyspraxia. Apraxia is typically thought of as an acquired neurological condition in which skilled movement is impaired in the presence of intact basic sensorimotor and attentional functioning. The term "dyspraxia" is often used to describe similar symptoms that are present early in development and have a less concrete etiology. Deficits in praxis in autism spectrum disorder (ASD) generally fall under the category of dyspraxia or developmental dyspraxia. Disorders of praxis can affect multiple modalities, including fine motor functioning, gross motor functioning, oculomotor control, orofacial movement, and speech production.

Historical Background

General impairments in motor functioning have been documented in individuals with ASD since both Kanner's and Asperger's initial descriptions of the conditions. Since then, basic motor deficits have been consistently found in ASD, with many individuals displaying abnormalities in gait, postural control, coordination, balance, tone, and/or strength. Furthermore, there is evidence that aspects of motor dysfunction are often identifiable early in development, present throughout the lifespan, and pervasive across levels of cognitive functioning.

The study of praxis has been an area of increasing interest within the larger domain of motor functioning in ASD. One focus of earlier work related to praxis was the assessment of clumsiness, or motor incoordination, as a possible symptom to differentiate subtypes within the autism spectrum. Historically, clumsiness was often considered a particular characteristic of Asperger syndrome, whereas individuals with classic autism were thought to have preserved motor function. Most evidence now suggests that motor clumsiness does not discriminate among subtypes; individuals with both Asperger syndrome and autism show similar degrees of impairment. Although clumsiness and dyspraxia are sometimes used synonymously, it is important to recognize that clumsiness is a clinical description that does not address the specific nature of an underlying motor impairment. Current research has taken a more systematic and componential approach to studying dyspraxia, with the goal of identifying the precise roots of the movement disturbances seen in individuals with ASD.

Current Knowledge

Dyspraxia in ASD

The growing body of literature focused on dyspraxia in ASD has, on the whole, confirmed that both children and adults with ASD display deficits on overall measures of praxis. In fact, difficulties with skilled limb movements have become one of the more reliable motor findings in the field. Impairments have been found in the ability to produce actions in response to command, imitate actions, and carry out actions involving tools. Moreover, these impairments are seen in transitive movements, or those involving objects, as well as intransitive movements, which do not include objects and are often more symbolic. Although basic motor skills are associated with praxis ability, individuals with ASD consistently appear to display deficits in praxis beyond what can be accounted for by general motor dysfunction. This suggests that praxis is a specific area of weakness for individuals with ASD within the larger motor domain. In addition, although correlations between praxis and both age and cognitive ability have been reported, the available data largely indicate that symptoms of dyspraxia in ASD remain even after controlling

for these factors. Of particular interest, praxis impairment has been shown to predict the severity of autistic symptoms, whereas correlations between basic motor skill and ASD symptomatology have not been found.

Motor Planning in ASD

Research has also sought to examine the motor planning component of praxis more directly. One approach has utilized paradigms in which potential impairments at the planning or preparation stage of a goal-directed motor act can be assessed separately from impairments at the execution stage. An example is a task in which participants are required to generate hand movements toward alternating targets. The planning stage is defined as the time between the appearance of the target and the point at which the hand begins to move; the execution stage is defined as the time in which the hand is in motion. Research employing these types of tasks has found that the planning stage of movement is generally atypical in individuals with ASD, while the execution stage is similar to typically developing controls.

Motor planning abilities in individuals with ASD have also been investigated using a reach, grasp, and place paradigm, in which participants are instructed to reach for an object, pick it up, and place it in a specified location or orientation. In one study in which children were required to reach, grasp, and place a rod in a certain position, typically developing children consistently chose initial movements that allowed for a comfortable end state. In contrast, children with ASD were more likely to favor an easier initial grip, even when this forced an uncomfortable final hand posture. In a similar study, children were asked to pick up an object and place it in either a small or large container. Typically developing children took longer during both the reach/grasp and place stages on the trials with the smaller compared to the larger target container. This suggests global planning of actions, such that when the final step of a motor act requires more precision, the execution of earlier steps is also affected. In contrast, for children with ASD, only the place stage was longer, signifying that although they were affected by the increased precision required at

the end, they were less likely to plan for this in their initial actions.

Overall, the performance of individuals with ASD on reach, grasp, and place tasks indicates that they are less likely than typically developing individuals to plan goal-directed actions holistically. Instead, they seem to execute the necessary steps for a motor act independently, such that knowledge of the end goal does not influence the initial movements in an action sequence. However, there is some evidence to suggest that the motor planning behavior of children with ASD may not differ from their peers when tasks have fewer higher order cognitive demands. For example, on a more constrained grip selection paradigm in which children reached for and grasped a handle and turned it in a specified direction, differences in performance were not found between age-matched groups.

Related research has found that some individuals with ASD may have difficulty with coordinating the stages of a reach-to-grasp movement, failing to temporally couple the velocity of the reach stage with the timing of their hand opening during the grasp stage. One study found that lower functioning children with ASD did not seem to synchronize the timing of their reach and grasp based on target location and size in the same way as controls. Instead, they performed the movement in two distinct stages, completing the reaching movement first, and then opening their hand to grip the object. However, high-functioning children with ASD performed similarly to typically developing children, with the timing of the reach and handgrip movements well synchronized.

A final area of research on motor planning in ASD has explored how the advanced presentation of information about a target affects goal-oriented movements. One hypothesis is that goal-directed actions are planned in a predictable sequence, where the appropriate hand is chosen first, followed by the direction of the movement, then by the amount of movement necessary to achieve the target. This model has been tested through the use of a precue technique, in which prior information about hand, direction, and/or movement extent is given to the participant. Results indicate that young adults with and without ASD display a similar,

predictable pattern on this task, suggesting that they can effectively use advanced information to plan movements. Individuals in both groups tend to derive the most benefit from information pertaining to which hand to use, followed by information about direction, and finally by information about the amount of movement. Nevertheless, the reaction times of individuals with ASD were slower and more variable than those of their peers.

Clinical Significance

Motor deficits are not a diagnostic characteristic of ASD, yet the importance of studying how various aspects of motor dysfunction may contribute to the condition has been increasingly recognized. Without a doubt, impairments in planning purposeful movement can have deleterious effects on many aspects of daily functioning, including basic tasks like feeding and dressing. In addition, the impact of difficulties with motor planning on social and communicative functioning is a topic of growing interest. Some theories posit that the motor system plays a foundational role in certain interpersonal skills. The ability to effectively plan and produce movements within an appropriate time frame may be crucial for reciprocal social interaction. In addition, praxis ability has been empirically associated with imitation. Difficulties with imitation have been widely documented in ASD across ages and functioning levels: individuals with ASD have been shown to imitate less than their peers, display poorer approximations of imitated movements, and consistently make specific types of errors during imitation tasks. Furthermore, abnormalities have been found for the imitation of nonmeaningful movements, as well as movements with more social or symbolic significance, suggesting that a fundamental problem with skilled motor functioning may be involved in imitation impairments in ASD.

Future Directions

The extant research has established motor planning as an area worthy of further investigation in ASD. An important direction for future research will be to build on existing work exploring components of motor acts to identify the specific aspects of goal-directed movement that are affected in ASD, both globally and at different points in development. There is also a need for further research on how functioning in other domains may impact the components of movement. Although basic motor functioning, general intellectual ability, attentional skills, motor learning, and sensory abilities have all been implicated in the organization of movement, the relationship between these various skill domains and motor planning in individuals with ASD is still not well understood.

Recent work has specifically highlighted the need to distinguish between motor planning and higher order planning, the latter of which is thought to rely on executive functioning skills. Motor planning is distinctly dependent on the ability to implement learned movements, whereas executive planning requires abstraction and mental sequencing of goal-oriented decisions. Both motor and executive planning are often necessary to effectively prepare and execute actions, making it difficult to pin down the precise nature of movement planning difficulties in ASD. One viewpoint has been that individuals with ASD perform poorly on motor planning tasks because of executive functioning impairments, and that they would demonstrate intact performance on tasks that do not require executive skills. However, at least one study has shown that individuals with ASD perform poorly across a range of motor planning tasks regardless of the level of executive demand, suggesting that motor planning may be impaired even in situations that do not require higher order abilities.

Another direction for future research is continued exploration of the neurobiological underpinnings of motor planning and related functions in ASD. Although research in ASD has implicated abnormalities in a number of regions important in motor functioning, less work has specifically addressed functional atypicalities during motor tasks. The neurobiology of the motor system in typically developing individuals is well understood. Thus, studying the neural bases of motor dysfunction in ASD may offer a more

straightforward avenue for identifying structural and connectivity abnormalities in this disorder, potentially leading to a better understanding of the neural bases of other affected domains. In addition, functional neuroimaging studies can provide further information on how individuals with ASD approach motor planning tasks, helping to answer questions about the degree to which executive and other skills play a role in motor planning in this condition.

Finally, further research is needed to better understand if and how motor planning difficulties might influence the pathogenesis of core symptoms in ASD, including social and communication impairments. The answers to these questions will benefit from more research on the developmental timeframe of motor planning in ASD, and how this interfaces with other aspects of development.

See Also

▶ Apraxia
▶ Developmental Apraxia
▶ Developmental Dyspraxia
▶ Dyspraxia
▶ Executive Function (EF)
▶ Imitation
▶ Praxis

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Movement Assessment Battery for Children

▶ Movement Assessment Battery for Children: 2nd Edition (MABC-2)

Movement Assessment Battery for Children: 2nd Edition (MABC-2)

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Synonyms

MABC; MABC-2; Movement assessment battery for children

Abbreviations

AB	Age bands
ADHD	Attention deficit/hyperactivity disorder
AS	Asperger's Syndrome (AS)
ASD	Autism Spectrum Disorder
BOTMP	Bruininks-Oseretsky Test of Motor Proficiency
DCD	Developmental Coordination Disorder
PDD	Pervasive Developmental Disorders
PDMS-2	Peabody Developmental Motor Scales – 2nd Edition
TOMI	Test of Motor Impairment
TOMI-H	Test of Motor Impairment-Henderson Revision
UK	United Kingdom

Description

The *Movement Assessment Battery for Children – Second Edition* (MABC-2) (Henderson, Sugden, & Barnett, 2007) is a revision of the *Movement Assessment Battery for Children* (MABC) (Henderson & Sugden, 1992) and is one of the most widely used assessment tools by occupational therapists, physiotherapists, psychologists, and educational professionals (Barnett & Henderson, 1998; Brown & Lalor, 2009; Wiart & Darrah, 2001). The purpose of the MABC-2 is the identification and description of impairments in children's motor function. It is composed of two parts: the Performance Test and the Checklist (see Table 1).

The MABC-2 Performance Test involves children completing a series of fine and gross motor tasks on which they are scored and rated. The Performance Test is designed for use with children aged 3–17 years in one of three age bands (AB) (AB1, 3:0–6:11 years; AB2, 7:0–10:11 years; and AB3, 11:0–16:11 years) and evaluates motor skills under three categories: (1) Manual Dexterity, (2) Aiming and Catching, and (3) Balance.

The MABC-2 Checklist requires an adult who knows the children being assessed well to rate their motor competence on a 30-item scale. Since the MABC-2 is a revision of an existing instrument, it is important for professionals who use the motor skill battery to be familiar with its age range, scoring format, standardization sample, reliability, validity, and clinical utility. Details of the purpose, age range, administration, response

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 1   Movement Assessment Battery for Children – Second Edition (▶ MABC-2; Henderson et al., 2007) summary of Performance Test and Checklist data

Test section	MABC-2 Performance Test	MABC-2 Checklist
Purpose	The identification and screening of children with delay or impairment of their motor development, provision of appropriate intervention planning, clinical exploration, program evaluation, and as a research tool with children who are believed to be at risk of motor difficulties	The efficient and economical assessment of the movement competence of children and to identify children who are likely to have difficulty with their movement. The MABC-2 Checklist takes assessment into the everyday situations in which the child has to function, including the extent to which a child's attitudes and feelings about motor tasks are situation specific or more generalized. Therapists can also obtain parents' or teachers' views on a child's movement in everyday settings
Test age range	3:0–16:11 years across three age bands (AB) *AB1* 3:0–6:11 years *AB2* 7:0–10:11 years *AB3* 11:0–16:11 years	5:0–12:11 years
Who can administer?	Individuals who are certified by a professional organization recognized by Pearson Assessment or who have a graduate and/or postgraduate qualification relevant to their profession. This qualification code would include psychologists, speech therapists, physiotherapists, occupational therapists, mental health professionals, health practitioners, and education professionals. No additional specialized training is required; however, familiarity with test items is required. It is envisaged in the future that specialized training modules will be set up to allow a wider range of professionals' access to the MABC-2	Available to psychologists, classroom teachers, special education teachers, physical education specialists, pediatricians, occupational therapists, speech therapists, and physiotherapists. A child's parent or primary caregiver may also contribute to the completion of MABC-2 Checklist if requested by a professional
Time to administer	Individual administration usually takes approximately 20–40 min depending on the age of the children; however, 50 min is suggested for setup, testing, and completion of the record form	The MABC-2 Checklist can be completed with a group or individual and takes the respondent approximately 10 min to complete
Time to score	10–15 min	10 min
Materials/ equipment required	Stopwatch, clipboard, pencil, correct age band record form, test manual, and test kit containing full set of testing materials and manipulatives	Checklist and pencil
Method of administration	Physical demonstration of all items is required to ensure each child assessed fully understands the verbal instructions for each task. Verbal instructions are not scripted, allowing for the assessor to alter their language according to the age of the child and the child's level of comprehension. Important features of the physical demonstration are emphasized verbally to the child. The child is provided a practice phase (that is not scored/rated) and a formal trial (which is scored/rated)	A basic list of specific motor behaviors is outlined for the adult rater to observe and rate the child's performance and competency. A total score is obtained by summing the ratings, and this is then mapped onto a "Traffic Light" scoring system (outlined below under the "Scores Provided" heading)

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 1   (continued)

Test section	MABC-2 Performance Test	MABC-2 Checklist
Response format	The child's performance on a task can be recorded in 1 of 4 ways	In Sections A and B, the rater has four alternative responses for the child's task competence
	1 The child's best result for an individual task *	0 – Very Well 2 – Almost
	2 An "F" is recorded for a failed attempt	1 – Just OK 3 – Not Close
	3 An "R" is recorded for refusal to attempt or complete a task	The summed score of Sections A and B represents the total motor score and interpreted with the "Traffic Light" system outlined below. Section C allows for either a Yes or No response to factors that may affect a child's movement and is not meant to be summed. Rather, these factors should be reviewed by the assessor to determine how much the child is prevented from demonstrating their true capability due to the influence of the observed factors
	4 An "I" is recorded if it is inappropriate for a child to attempt a task	
	* If a child completes a task successfully according to the item parameters, the item is scored according to criteria and then converted to a scaled score reported as 1–5, where 5 indicates a poor performance. Some items are scored based on number of correct repetitions, length of time, or accuracy of responses	
Scale construction/ test structure	Eight tasks are administered across three specific components: (a) Manual Dexterity, (b) Aiming and Catching, and (c) Balance. Adding all eight scores yields a total motor impairment score (maximum 40). Overall scores that are below the 15th percentile are deemed *at risk*; those below the 5th percentile indicate a *definite movement impairment*	The Checklist comprises three sections
		Section A: 15 items regarding movement in a static or predictable environment
		Section B: 15 items regarding movement in a dynamic or unpredictable environment
		Section C: 13 items regarding nonmotor factors that may affect movement
Standardization sample	The norms of the MABC-2 are derived from a stratified sample of 1,172 children (48.3% male, 51.7% female) in the United Kingdom (UK), who were assessed between November 2005 and July 2006. This sample closely approximated the UK 2001 Census data. The test sample included 12 UK geographic regions, 16 age levels (e.g., ages 3–16 years), 4 ethnic groups (e.g., White, 90.2%; Black, 2.6%; Asian, 3.9%; and Other, 3.2%), and 5 levels of parental education	656 Children of the 1,172 sample fell into the age range of the MABC-2 Checklist. Of the 656, teachers for 395 children (50.9% male, 49.1% female) completed the MABC-2 Checklist. The test sample included 12 UK geographic regions, 8 age levels (e.g., ages 5–12 years), four ethnic groups (e.g., White, 90.4%; Black, 2.6%; Asian, 3.5%; and Other, 3.5%), and five levels of parental education. This sample closely approximated the UK 2001 Census data
Scores provided	Standard scores and percentile ranks are provided. Additional score interpretation according to a "Traffic Light" system is provided. This system is the same for both the MABC-2 Performance Test and Checklist, allowing for direct comparison if required. Any child whose score falls at or below the 5th percentile is regarded as having *a significant movement difficulty* (red zone), between the 6th and 15th percentile *at risk* (amber zone), and above the 16th percentile as unlikely to have a movement difficulty (green zone)	A percentile cute score is provided. The "Traffic Light" system shows whether a child is in the "green zone" which is within the age-expected normal range, in the "amber zone" indicating a need for monitoring due to minor delay or movement problem, or in the red zone where it is highly likely that child has a serious movement problem

format, scale construction, standardization, and scores provided of the MABC-2's Performance Test and Checklist are reported in Table 1.

The MABC (Henderson & Sugden, 1992) was normed with children from Canada, the United States, and the United Kingdom and has subsequently been translated into several European languages (including Swedish, Danish, Dutch, Italian, and Finnish) (Livesey, Coleman, & Piek, 2007) and Chinese (Chow & Henderson, 2003). Predominantly used throughout the United Kingdom, Canada, Australia, several European countries (e.g., the Netherlands, Belgium, Italy, Finland, Denmark, Sweden, and Greece), and Asia to assess pediatric motor impairments, it has been shown to correlate positively with other pediatric motor assessments used worldwide (Smits-Engelsman, Henderson, & Michels, 1998; Missiuna, Rivard, & Bartlett, 2006) and is well recognized as one of the most extensively utilized motor impairment assessments in the world (Chow & Henderson, 2003; Chow et al., 2006; Croce, Horvat, & McCarthy, 2001; Tan, Parker, & Larkin, 2001; Wiart & Darrah, 2001). The MABC norms have been evaluated in studies completed in other cultural contexts including Sweden (Rosblad & Gard, 1998), Japan (Miyahara et al., 1998), the Netherlands (Smits-Engelsman et al., 1998), Hong Kong (Chow, Henderson, & Barnett, 2001; Chow, Hsu, Henderson, & Yu 2006), Taiwan (Chow et al.), Israel (Engel-Yeger, Rosenblum, & Josman, 2010), United States (Van Waelvelde, Peersman, Lenoir, Engelsman, & Henderson, 2008), Greece (Ellinoudis, Kourtessis, & Kiparissis, 2008), and Singapore (Wright, Sugden, Ng, & Tan, 1994). Generalizability across European cultures has shown to be satisfactory; however, those studies conducted in Hong Kong, Taiwan, Singapore, and Japan suggested some cultural differences existed and that the MABC norms for those countries may need some adjustment (Livesey et al., 2007).

In addition to the worldwide recognition that the MABC has, the instrument has been utilized in many international studies covering a broad range of diagnostic categories such as developmental coordination disorder (DCD), learning disabilities, and autism spectrum disorder (ASD). Additionally, the MABC has been noted to identify more children with motor impairments more successfully (e.g., greater sensitivity and specificity) than that of the "gold standard" *Bruininks-Oseretsky Test of Motor Proficiency* (BOTMP) (Dewey & Wilson, 2001), while Crawford, Wilson, and Dewey (2001) have found that the MABC appears to be more sensitive and is able to better identify children with additional problems associated with learning or attention.

The authors have revised the MABC to generate the MABC-2, a "reliable, easily administered and valid measure of competence in three broad and carefully selected areas of motor performance" (Henderson et al., 2007, p. 117). The three broad motor skill categories that are assessed are (1) Manual Dexterity, (2) Aiming and Catching, and (3) Balance. Changes undertaken to produce the second edition involved revising existing items and introducing some new items. These changes are outlined in two sections below: *test content changes* and *test structure changes* (see Tables 2, 3, and 4 for details).

The MABC-2 *test content changes* are described under three areas: (1) *materials*, (2) *tasks*, and (3) *instructions*:

1. *Materials:* Brightly colored plastic pieces have been introduced to replace pieces originally made of wood. This change was undertaken to standardize the pieces and eliminate any room for variation between kits as well as taking into account health and safety regulations regarding item pieces when used with children in various settings.

2. *Tasks:* The test has maintained the original structure of the test by retaining eight test items across each age band organized into the three motor skill categories of Manual Dexterity, Aiming and Catching, and Balance. However, individual items have been altered as well as new individual items being introduced. The task changes across the age bands are outlined in Tables 2, 3, and 4.

3. *Instructions:* In previous research articles, the test instructions of the MABC have been called into question. Although no standardized verbal instructions are included in the second edition, clarification of the administration,

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 2 Changes made for age band 1 (3–6 years)

Motor skill task	MABC[a] task age band 1	MABC-2[b] task age band 1
Manual Dexterity 1	Post coins	Post coins
Manual Dexterity 2	Threading beads	Threading beads
Manual Dexterity 3	Bicycle trail	Drawing trail 1 (shape of visual trail has changed)
Aiming and Catching 1	Catching beanbag	Catching beanbag
Aiming and Catching 2	Rolling ball between goal posts	Throwing beanbag onto mat (new item)
Balance 1	One-leg balance	One-leg balance
Balance 2	Walking heels raised	Walking heels raised
Balance 3	Jumping over cord	Jumping on mats (new item)

(Henderson et al., 2007, p. 118)
[a]MABC Movement Assessment Battery for Children
[b]MABC-2 Movement Assessment Battery for Children – Second Edition

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 3 Changes made for age band 2 (7–10 years)

Motor skill task	MABC[a] task age bands 2/3	MABC-2[b] task age band 2
Manual Dexterity 1	Placing pegs/shifting pegs by rows	Placing pegs (new starting position and layout)
Manual Dexterity 2	Threading lace/threading nuts on bolt	Threading lace (lacing board is longer)
Manual Dexterity 3	Flower visual trail/flower visual trail	Drawing trail 2 (shape of visual trail has changed)
Aiming and Catching 1	Two-hand catch/one-hand bounce and catch	Catching with two hands
Aiming and Catching 2	Throwing beanbag/throwing beanbag into box	Throwing beanbag onto mat (mat with target now used instead of box)
Balance 1	Stork balance/one-board balance	One-board balance
Balance 2	Heel-to-toe walking/ball balance	Walking heel-to-toe forward
Balance 3	Jumping in squares/hopping in squares	Hopping on mats (mats used for this task)

(Henderson et al., 2007, p. 118)
[a]MABC Movement Assessment Battery for Children
[b]MABC-2 Movement Assessment Battery for Children – Second Edition

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 4 Changes made for age band 3 (11–16 years)

Motor skill task	MABC[a] task age band 3	MABC-2[b] task age band 3
Manual Dexterity 1	Turning pegs	Turning pegs
Manual Dexterity 2	Cutting out elephant visual trail with scissors	Triangle with nuts and bolts (new item)
Manual Dexterity 3	Flower visual trail	Drawing task 3 (shape of visual trail has changed)
Aiming and Catching 1	One-hand catch	Catching with one hand
Aiming and Catching 2	Throwing ball at wall-mounted target	Throwing ball at wall-mounted target
Balance 1	Two-board balance	Two-board balance
Balance 2	Walking backward	Walking toe-to-heel backward
Balance 3	Jumping and clapping	Zigzag hopping (new item)

(Henderson et al., 2007, p. 118)
[a]MABC Movement Assessment Battery for Children
[b]MABC-2 Movement Assessment Battery for Children – Second Edition

scoring of the test, and aspects of tasks to emphasize during demonstration have been provided to minimize the potential for ambiguity. The MABC-2 authors state that this provides flexibility in the mode of presentation and allows the assessor to ensure the examinee understands individual tasks.

The MABC-2 *test structure changes* are described under two areas: (1) *age extension* and (2) *reduction of age bands*:

1. *Age Extension:* The MABC-2 has been extended to encompass the assessment of children aged 3 years 0 months–16 years 11 months. The MABC-2 authors believed that a gap existed for the appropriate motor performance assessment for children aged 3 years. In order to assess children of this age, items were slightly adjusted to ensure the attention of a typical 3-year-old could be maintained as well as being fun, easily understood, and requiring minimal verbal communication. Similarly, as the MABC has been utilized and widely recognized for its use with assessment of children with DCD, two sources of requests for suitable motor performance assessments for children aged between 11 and 16 years have been identified. The first is due to the increase in the recognition of DCD as a clinical diagnosis and the importance of early assessment, identification, and intervention service provision to assist with coordination difficulties encountered so as to maximize children's developmental and motor skills. Current intervention for DCD occurs predominantly in during the primary school years due to the effectiveness of early intervention. However, the MABC-2 authors have noted that an increasing proportion of adolescents have not been identified earlier with coordination difficulties or have failed to benefit from intervention.

   The second source identified was due to ongoing worldwide research into children who have been born "at risk" of damage to their nervous system (e.g., born prematurely). This group of children exhibit cognitive skills within normal limits and do not meet the diagnostic criteria for cerebral palsy, but do experience severe difficulties with their motor performance which in turn affects their academic progression. Therefore, with the development and revision of the MABC, the MABC-2 can provide improved motor performance measurement instrument for younger and older children. This in turn will enable therapists and researchers to develop new intervention techniques, allow for more accurate and sound intervention, and provide a greater understanding of motor performance problems and their consequences over time.

2. *Reduction of Age Bands:* Previously the MABC had 4 ABs; however, pilot work by the test authors provided evidence that existing items could be revised and/or adapted across the extended age bands. Thus, AB1 and the previous AB4 had an age range of 4 years, and so AB2 and AB3 were collapsed in to one age band. Additionally, and perhaps more importantly, the test authors were aware of problems associated with children changing between age bands in the MABC during the course of an intervention program. Although correlations between similar items across the age bands were high, the authors recognized that they were not perfect. Hence, the final age bands for the MABC-2 are AB1: 3–7 years, AB2: 7–11 years, and AB3: 11–17 years.

The Qualitative Observations section remains a part of the MABC-2 test and allows the testing clinician to supplement the formal test results gathered from administering the Performance Test to a child. A chapter of the manual provides some assistance regarding the process of observation and how to utilize the Qualitative Observations section of the test in conjunction with the formal scores as well as taking into account both motor and nonmotor factors that can affect movement and a child's motor performance.

Historical Background

The MABC-2 is a composite of two complementary assessments: the Performance Test and the Checklist. The performance-based portion of the

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 5 Evolution of the versions of the *Movement Assessment Battery for Children – Second Edition* (MABC-2)

| 1. *Test of Motor Impairment* (TOMI) (Stott et al., 1972) |
| 2. *Test of Motor Impairment - Henderson Revision* (TOMI-H) (Stott et al., 1984) |
| 3. *Movement Assessment Battery for Children* (MABC) (Henderson & Sugden, 1992) |
| 4. *Movement Assessment Battery for Children-2* (MABC-2) (Henderson et al., 2007) |

MABC-2 was developed from the *Test of Motor Impairment* (TOMI) (Stott, Moyes, & Henderson, 1972). Development of the TOMI began in 1966 with a primary focus of identifying impaired or nonstandard motor skill performance. Since the TOMI provided little overall motor ability information about the children who were assessed with it, the TOMI was revised in 1984 (see Table 5). This revision, known as the *Test of Motor Impairment-Henderson Revision* (TOMI-H) (Stott, Moyes, & Henderson, 1984), decreased the number of items that a child was required to complete, added a behavioral checklist, and included room for recording qualitative observations related to children's motor skill performance.

In 1992, the Henderson and Sugden *Movement Assessment Battery for Children* (MABC) was published and retained the same items as the TOMI-H (see Table 5). However, the MABC was developed as a means of identifying children aged between 4 and 12 years considered being at risk of a motor impairment, and thus, normative data was added, and the scoring criteria and item descriptions were revised. The MABC consisted of 32 tasks that increased in difficulty across four age bands (AB): 4–6 years, 7–8 years, 9–10 years, and 11–12 years. Simultaneously, Keogh (1968), and subsequently Sugden (1972), developed a teacher checklist which served as preliminary to further evaluative assessments of a child's motor performance and to alert "teachers to the existence of children with movement difficulties" (Henderson et al., 2007, p. 113). Further development has led to it becoming the MABC Checklist (Henderson & Sugden, 1992; Reynard, 1975; Sugden, 1972).

Psychometric Data

Types of reliability data often reported for scales, tests, and measures include internal consistency, test-retest/time sampling reliability/temporal stability, interrater/interscorer reliability, intrarater/intrascorer reliability, alternate form reliability, and split-half reliability (American Educational Research Association [AERA], American Psychological Association [APA], & National Council on Measurement in Education [NCME], 1999; Anastasi & Urbina, 1997). Types of validity often reported for tests include face validity, content validity, criterion-related validity, and construct validity (AERA et al., 1999). Two subtypes of criterion-related validity frequently included are concurrent validity and predictive validity, while subtypes of construct validity often reported include factor analysis validity, discriminant validity, convergent validity, divergent validity, diagnostic validity, and rating scale validity (Fawcett, 2007). Details of the reliability and validity of the MABC-2 are reported in its manual.

The MABC-2 is a major revision of the well-known and frequently used MABC (Barnett & Henderson, 1998; Henderson et al., 2007). The test authors assume that the reliability data and validity information reported for the MABC are generalizable to the MABC-2. "Confidence in the MABC-2 score interpretation can be derived not only from the UK standardisation study but also from the extensive validation data reported in this and earlier manuals" (Henderson et al., p. 132). The MABC and MABC-2 may assess the same motor skill constructs in a similar format, but since the MABC-2 has added four new items, revised some of the retained items, reduced number of age ABs (the MABC had 4 ABs, while the MABC-2 has 3), and increased age range that it covers (the MABC-2 now covers ages 3–17 years), it is essentially a new, discrete test that needs to have its own specific measurement properties evaluated singly. This appears to be an inaccurate assumption made by the MABC-2 authors.

The MABC-2 test manual reports some preliminary reliability data for its Performance Test

based on the results of several studies completed by other investigators that involved experimental versions of the MABC-2 AB1 and AB3 tasks (see Table 6). Visser and Jongmans (2004) investigated the test-retest results for the MABC-2 AB1 with a group of 55 3-year-old children from the Netherlands. Chow, Chan, Chan, and Lau (2002), in another study involving a sample of 31 adolescents, evaluated the interrater and test-retest reliability of a translated version of the MABC-2 AB3 tasks into Chinese. Smits-Engelsman et al. (2008) reported about the interrater reliability of the MABC-2. In another inquiry involving 64 young adults, Faber and Nijhuis van der Sanden (2004) examined the intrarater and interrater reliability of a total score calculated for the MABC-2 AB3 tasks originally used by Chow et al. (2002). Details of the translation process for the Chinese version of the MABC-2 AB3 tasks used in the Chow et al. (2002) study were not reported in the test manual. Similarly, it was not reported if the version of the MABC-2 AB1 tasks used in the Visser and Jongmans (2004) investigation was translated into another language since it was used in the Netherlands. The studies completed by Visser and Jongmans (2004) and Faber and Nijhuis van der Sanden (2004) are both unpublished manuscripts, thus have not been peer reviewed nor are they readily accessible for review. The Faber and Nijhuis van der Sanden study involved 64 young adults aged between 18 and 28 which were outside the age limits of the MABC-2 and the geographical location where the study was completed was not reported. With all of these studies, there are issues of cultural context, translation of the MABC-2 Performance Test items, and only evaluating one AB at a time.

Henderson et al. (2007) reported a test-retest study involving 20 3-year-old children. Pearson product moment correlations ranged from 0.86 to 0.91 for the three Manual Dexterity tasks, while the Aiming and Catching and Balance tasks were less reliable with coefficients of 0.48 and 0.68. The test authors suggested that the test-retest reliability problems lie with younger children, aged between 3 and 4 years. In another study completed by the test authors, the test-retest reliability of the whole test involving all three ABs was completed. Sixty children, 20 from each AB, were included. Using the standard scores for the three test sections (Manual Dexterity, Aiming and Catching, and Balance) as well as the total test score, the Pearson product moment correlations were 0.77, 0.84, 0.73, and 0.80, respectively (Henderson et al.). This indicates reasonable test-retest reliability results for the MABC-2. It would have been informative if the test authors had completed similar studies evaluating the intrarater reliability, interrater reliability, and internal consistency of the Manual Dexterity, Aiming and Catching, and Balance test sections as well as the total test score involving all three MABC-2 ABs. At this time, this fundamental information is lacking.

The test manual states that no reliability data has been collected on the MABC-2 Checklist; thus, none is reported. The test authors do report reliability data about the MABC Checklist, but this is redundant since the MABC-2 Checklist has been revised. Test-retest reliability and internal consistency reliability data needs to be reported about the MABC-2 Checklist.

When it comes to the validity of the MABC, the test authors include a large body of evidence in the MABC-2 test manual (Barnett & Henderson, 1998; Henderson et al., 2007). However, generalizations from the MABC's validity findings to the MABC-2's validity cannot be readily made for a number of reasons. First, the age range is different between the two test versions with the MABC-2 now including children as young as 3 years and adolescents as old as 16 years. The ABs have fundamentally changed between the two test versions. The MABC ABs 2 and 3 have been collapsed into the MABC-2 AB 2. Finally, a number of test items have been revised, and four new test items have been added to the MABC-2. Hence, the validity properties of the first test cannot be generalized to the newer revised version in the opinion of this author.

Limited preliminary content, face, criterion-related validity and evidence about the MABC-2 Performance Test are reported in its test manual. Content validity of the MABC-2 Performance Test was established by input of an expert panel.

Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 6 *Movement Assessment Battery for Children – Second Edition* (MABC-2; Henderson et al., 2007) summary of MABC-2 Performance Test and Checklist validity and reliability data

Test section	MABC-2 Performance Test	MABC-2 Checklist
Reliability data reported	Limited reliability data reported is reported in the manual that is specific to the MABC-2. A study completed by Visser and Jongmans (2004) that reports test-retest results for AB1 for a group of 55 3-year-old children from the Netherlands is included in the test manual. Pearson product moment correlations ranged from 0.49 to 0.70 The test authors reported a second test-retest study involving 20 3-year-old children. Pearson product moment correlations ranged from 0.86 to 0.91 for the three Manual Dexterity tasks, while the Aiming and Catching tasks were less reliable with coefficients of 0.48 and 0.68. The test authors suggest that the test-retest reliability problems lie with younger children, aged between 3 and 4 years In another study that involved a translated version of AB3 tasks into Chinese, interrater reliability and test-retest reliability were evaluated on a sample of 31 teenagers by Chow et al. (2002). Intraclass correlation (ICC) coefficients for interrater reliability ranged from 0.92 to 1.00, while test-retest coefficients ranged from 0.62 to 0.92 In another study involving 64 young adults, Faber and Nijhuis van der Sanden (2004) examined the intrarater and interrater reliability of a total score calculated for the AB3 tasks originally used by Chow et al. (2002). The ICC scores were 0.79 (intrarater) and 0.79 (interrater) In a final study completed on the test authors, the test-retest reliability of the whole test involving all three ABs was completed. Sixty children, 20 from each AB, were included. Using the standard scores for the three test sections (Manual Dexterity, Aiming and Catching, and Balance) as well as the total test score, the Pearson product moment correlations were 0.77, 0.84, 0.73, and 0.80, respectively	The test manual states that no reliability data has been collected on the MABC-2 Checklist; thus, none is reported. The test authors do report reliability data about the MABC Checklist, but this is redundant since the MABC-2 Checklist has been revised
Validity data reported	Extensive validity data about the MABC is reported in the manual, and limited preliminary validity evidence (content, face, criterion-related) about the MABC-2 is also reported. Content validity of the MABC-2 was established by input of an expert panel. According the test manual, the expert panel was unanimous that the MABC-2 contents/items were representative of the motor domain it was intended to evaluate The test manual reports that face validity has been established by feedback obtained from a wide range of professionals who have used the MABC including psychologists, therapists, educational professionals, and physicians. The face validity appears to be based on the MABC and not the MABC-2 The test manual reports subtest and total test standard score correlations as evidence of the	Two validity studies are reported in the test manual. The first study involves a group of 20 children with DCD ages 6–11 years (Barnett et al., 2007). The MABC Checklist was completed by the children's parents. Scatterplots of Section A and Section B of the Checklist suggested a weak relationship between the two section scores. The MABC-2 Checklist Traffic Light system was able to indicate that the children continued to have motor skill difficulties in 19 of the 20 children. The test authors claim that this is evidence of criterion-related validity, but this is not clearly demonstrated The second study involves 24 boys with Asperger's syndrome with a mean age of 13.3 years (Siaperas et al., 2007). The MABC Checklist was completed by the children's parents. The MABC-2 Checklist Traffic Light system was able to indicate

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Movement Assessment Battery for Children: 2nd Edition (MABC-2), Table 6   (continued)

Test section	MABC-2 Performance Test	MABC-2 Checklist
	MABC-2 subtests evaluating related, but different motor abilities. The Manual Dexterity subtest was correlated with the Aiming and Catching (0.26), Balance (0.36), and total test score (0.76). The Aiming and Catching subtest was correlated with the Balance (0.25) and the total test score (0.65). The Balance subtest was correlated with the total test score (0.73) Evidence of criterion-related validity of the MABC-2 was reported in three studies in the test manual. First, using a sample of 31 Cypriot children, Kavazi (2006) examined the relationship MABC-2 Manual Dexterity items and the children's performance on the Goodenough and Harris Draw-a-Man Test. Correlations with the Posting Coins and Drawing Trail items and the Draw-a-Man Test were 0.66 The preliminary results of a second study completed by the test authors involving a small sample of 20 children who were initially assessed with the MABC and were reassessed using the MABC-2. The MABC-2 was able to indicate that the children continued to have motor skill difficulties. The type of validity being evaluated here is not clearly reported. The third study reports the results of 25 boys diagnosed with Asperger's syndrome who were assessed by the MABC-2 (Siaperas et al., 2007). The MABC-2 total test scores indicated that the majority of the boys (21/25) have impaired motor skills. The test authors are purporting that this is evidence of the MABC's discriminative validity	that in 23 of the 24 boys with Asperger's syndrome experienced motor skill difficulties. Again, the test authors make the claim that this is evidence of criterion-related validity, but how this is actually demonstrated is not clear
Clinical utility	The MABC-2 appears to have reasonable to good clinical utility. The international recognition of the MABC and its use with identifying children with DCD as well as other motor impairments has seen it become one of the most commonly utilized motor assessments. In addition, the brevity of the test across a wide age range of children furthermore enhances the utility of the MABC-2 in various clinical, educational, and research contexts. In summary, the MABC-2 is an improvement over the MABC and is best used as a screening instrument	

According to the test manual, the expert panel was unanimous that the Performance Test contents/items were representative of the motor domain it was intended to evaluate. The content validity of the MABC-2 Performance Test appears reasonable (see Table 6). The test manual reports that face validity has been established by feedback obtained from a wide range of professionals who have used the MABC including psychologists, therapists, educational professionals, and physicians. However, the face validity appears to be based on the MABC and not the MABC-2 Performance Test. Similarly, face validity of an instrument does not have inherent psychometric, objective, or numeric data attached to it to ensure that an instrument is evaluating the skills, attributes, or constructs it

claims to assess. Face validity is mainly based on an overall subjective impression of a test (AERA et al., 1999).

The test manual reported section and total test standard score correlations as evidence of the three MABC-2 Performance Test sections evaluating related, but distinct motor skill abilities (see Table 6). The Manual Dexterity section was correlated with the Aiming and Catching section (0.26), Balance section (0.36), and MABC-2 total test score (0.76). The Aiming and Catching section was correlated with the Balance section (0.25) and the total test score (0.65). The Balance section was correlated with the total test score (0.73). This provides evidence that the three MABC-2 Performance Test sections are measuring related, but discrete skills and "the fact that each component correlates well with the Total Test Score is re-assuring" (Henderson et al., 2007, p. 142).

Evidence of criterion-related validity of the MABC-2 Performance Test was reported in the form of three studies in the test manual (see Table 6). First, enlisting a sample of 31 Cypriot children, Kavazi (2006) examined the relationship MABC-2 Manual Dexterity section items and the children's performance on the *Goodenough and Harris Draw-a-Man Test* (Goodenough & Harris, 1963). Correlations with the Posting Coins and Drawing Trail items and the Draw-a-Man Test were 0.66. Limitations of this study were a small sample size (31 children) and correlating the children's fine motor skill performance with their performance on an outdated person drawing test. Given the fact that the Kavazi study only involved the Manual Dexterity section items from one MABC-2 AB1, the concurrent validity results are not generalizable to the whole measure. The scope of the Kavazi (2006) study was very narrow.

The preliminary results of a second study completed by the test authors involved a small sample of 20 children who were initially assessed with the MABC and were reassessed using the MABC-2 Performance Test (Henderson et al., 2007). The MABC-2 was able to indicate that the children continued to have ongoing motor skill difficulties. The type of validity being evaluated here was not evident to the reader. It would

have been more prudent to compare the whole MABC-2 to a well-established motor skill tests such as the *Peabody Developmental Motor Scales – 2nd Edition* (PDMS-2) or the *Bruininks-Oseretsky Test of Motor Proficiency, 2nd Edition*. Spironello, Hay, Missiuna, Faught, and Cairney (2010) examined the construct validity and concurrent validity between the short form of the BOTMP and the MABC, while Van Waelvelde, Peersman, Lenoir, and Smits-Engelsman (2007a) investigated the convergent validity between the MABC and the PDMS-2.

The third study reported the results of 25 boys diagnosed with Asperger's syndrome who were assessed by the MABC-2 Performance Test (Siaperas, Holland, & Ring, 2007). The MABC-2 Performance Test total scores indicated that the majority of the boys (21/25) had impaired motor skills. The test authors purported that this is evidence of the MABC-2 Performance Test's discriminative validity. The study by Siaperas et al. (2007) did not include a matched control group for comparison purposes, therefore, claims that the MABC-2 exhibits discriminant validity cannot really be supported.

One major weakness with the validity evidence reported in the MABC-2 test manual is the lack of construct validity evidence. There is no evidence that clearly indicated the MABC-2 Performance Test items are actually evaluating the motor skill constructs they claim they are. Evidence of construct validity can include divergent/convergent validity, factor analysis validity, diagnostic validity, rating scale validity, and/ or discriminative validity. The completion of a confirmatory factor analysis, a component of classical test theory, would provide valuable evidence if the items from the Manual Dexterity, Aiming and Catching, and Balance sections load on three discrete factors and whether the eight items that make the whole MABC-2 load on one overall motor impairment factor. Hypotheses about the MABC-2 Performance Test factor structure need to be explored further (Anastasi & Urbina, 1997).

In regard to the MABC-2 Checklist, two validity studies are reported in the test manual (see Table 6). The first study involves a group of

20 children with DCD ages 6–11 years (Barnett, Sugden, & Henderson, 2007). The MABC Checklist was completed by the children's parents. Scatterplots of Section A and Section B of the Checklist suggested a weak relationship between the two section scores. The MABC-2 Checklist Traffic Light system was able to indicate that 19 of the 20 children continued to have motor skill difficulties. The test authors claim that this is evidence of criterion-related validity, but how this is demonstrated is not clear.

The second MABC-2 Checklist study involved 24 boys with Asperger's syndrome with a mean age of 13.3 years (Siaperas et al., 2007). The MABC-2 Checklist was completed by the children's parents. The MABC-2 Checklist Traffic Light system was able to indicate that 23 of the 24 boys with Asperger's syndrome experienced motor skill difficulties. Again, the test authors make the claim that this is evidence of criterion-related validity, but how this is actually is demonstrated is not clear. Similar to the MABC-2 Performance Test, the Checklist has limited content, concurrent, and construct validity evidence. Further validity evidence is needed since one is left asking the question: do the MABC-2 Checklist items load on the constructs they claim to measure?

Clinical Uses

The MABC, and now the MABC-2, is one of the most widely used pediatric motor impairment assessments (Getchell, Pabreja, Neeld, & Carrio, 2007; Livesey et al., 2007; Van Waelvelde, Peersman, Lenoir, & Smits-Engelsman, 2007b). It has been used to assess a variety of diagnostic groups including children with (1) attention deficit/hyperactivity disorder (ADHD) (Miyahara, Piek, & Barrett, 2006; Pitcher, Piek, & Hay, 2003), (2) autistic spectrum disorders (ASD) (Green et al., 2002; Smith, 2004), (3) special language impairments (Hill, Bishop, & Nimmo-Smith, 1998), (4) developmental coordination disorder (DCD) (Chow et al., 2006; Niemeijer, Schoemaker, & Smits-Engelsman, 2006; Rosblad & Gard, 1998),

and (5) cognitive impairments or learning difficulties (Henderson & Sugden, 1992; Jongmans, Smits-Engelsman, & Schoemaker, 2003). Other diagnostic studies where the MABC has been used include congenital hypothyroidism (Kooistra, Schellekens, Schoemaker, Vulsma, & van der Meere, 1998), childhood encephalitis (Rantala, Uhari, Saukkonen, & Sorri, 1991), epilepsy (Beckung, Uvebrandt, Hedstrom, & Rydenhag, 1994), neurofibromatosis 1 (North et al., 1994), and hemiplegia (Mercuri et al., 1999). Individuals diagnosed with ASD, Asperger's syndrome (AS), and other related pervasive developmental disorders (PDD) often present with motor skill difficulties (Dziuk et al., 2007; Fournier, Hass, Naik, Lodha, & Cauraugh, 2010; Fuentes, Mostofsky, & Bastian, 2009; Gidley Larson & Mostofsky, 2006; Green et al., 2009; Jasmin et al., 2009; Ozonoff et al., 2008; Pan, Tsai, & Chu, 2009; Provost, Heimerl, & Lopez, 2007; Staples & Reid, 2010). Hence, the MABC-2 is a useful and relevant measure to use when assessing children with ASD, AS, PDD, and other related diagnoses.

The MABC-2 Performance Test and Checklist items provide invaluable information for practitioners related to the identification of and intervention with children presenting with motor difficulties. It can be used in a range of settings including clinical, community-based, child care, early intervention, early childhood education, primary and secondary school settings, private practice, hospital, and rehabilitation. It can be used as either a quick screening instrument or as one component of a comprehensive diagnostic evaluation. The MABC-2 Performance Test and Checklist items can be used by a variety of health and education professionals (including occupational therapists, psychologists, early childhood education teachers, social workers, counselors, physiotherapists, speech-language pathologists, nurses, pediatricians, physicians, and early intervention specialists among others) to evaluate the motor skills of children and adolescents aged 3–17 years. It is recommended that other sources of information (e.g., medical records, clinical observations, interviews with parents and teachers) be accessed as well. The clinical purposes the MABC-2 could be used for are establishing the

baseline of a client's gross and fine motor skills (often done in the context of an initial assessment), assisting with the formulation of a client's intervention goals, monitoring a client's progress after receiving intervention/remedial services, or providing evidence to justify the need for a client to receive continued services. The MABC-2 Performance Test and Checklist can also be used for research purposes such as evaluating the effectiveness of educational, psychological, therapeutic, or medical services provided to pediatric clients.

In summary, the MABC-2 is highly recommended for use by practitioners. It can play an important role in the assessment of and intervention planning for children and adolescents presenting with ASD, AS, and PDD.

See Also

▶ Bruininks-Oseretsky Test of Motor Proficiency
▶ Gross Motor Skills
▶ Occupational Therapy (OT)
▶ Peabody Developmental Motor Scales (PDMS)
▶ Sensorimotor Development
▶ Standardized Tests

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M

Movie Talk

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Synonyms

Delayed echolalia; Echolalia; Parroting; Scripting

Definition

Repeating or reciting lines heard in TV shows, movies, songs, books, etc., is a common language pattern among children with ASD. "Movie talk"

refs to repetitive speech taken from such a source, as opposed to a child's using novel, spontaneous language. Also known as scripting, the behavior involves reciting phrases or "chunks" of previously heard language and is synonymous with delayed echolalia. Some researchers believe "movie talk" is a form of self-stimulation used to tune others out or to work through a stressful or anxiety-producing moment. Others believe it is a means to initiate communication with others, or as a way to talk about an area of special interest.

Behavioral analysis may be an effective way to analyze the function of scripting for some children. By analyzing the antecedents and consequences of scripting for children and adults with ASD, it may be possible to identify functional replacements for this behavior.

See Also

▶ Echolalia

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MSEL:AGS

▶ Mullen Scales of Early Learning

MTL

▶ Medial Temporal Lobe

μ

▶ Mu Rhythm

μ Rhythm

▶ Mu Rhythm

Mu Rhythm

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Synonyms

μ; μ rhythm; Arciform rhythm

Definition

Mu (μ) rhythm is a type of emitted brain wave that can be measured via electroencephalography (EEG). The mu rhythm frequency band is defined by activity falling between 8 and 13 Hz and recorded by scalp electrodes over the sensorimotor cortex during waking neural activity. The mu rhythm band is posited to reflect the conductance of synchronized activity in large groupings of pyramidal neurons in the brain's motor cortex (Pfurtscheller, Neuper, Andrew, & Edlinger, 1997) but has also been proposed to reflect activity of the mirror neuron system (Pineda, 2005). The gradual loss of intensity and desynchronicity of neural activity, referred to as attenuation, is suggestive of an increased load on those specific cells and indicative of significant activation (Pfurtscheller et al., 1997). Attenuation of the mu rhythm has been noted during both the execution and observation of actions falling within one's behavioral repertoire. Physical movement in the body itself does not account for mu wave attenuation during an individual's observation of other's actions. The first neurological evidence of mu rhythm attenuation came from the work of Gastaut and Bert (1954) during observations of activity and response characteristics of subjects during motor tasks. It was noted that desynchronization of mu rhythm activity

from centrally located scalp electrodes occurred not only during the active movements of the subjects, but also during subjects' passive observation of the same actions performed by others in the absence of any other overt motor activity. Because of the observed attenuation of the EEG mu rhythm during the execution and observation of actions, it has been proposed to reflect mirror neuron system activity (Pineda, 2005).

Given the noted impairments in imitation, empathy, and social understanding in ASD and given that the mirror neuron system has been proposed to subserve many of these social cognitive abilities, the mu rhythm has been examined among ASD populations as an assessment of the mirror neuron system. Oberman and colleagues first found that children with ASD showed reduced attenuation of the EEG mu rhythm in response to the observation of simple actions (Oberman et al., 2005), providing support for the theory that the mirror neuron system is disrupted in ASD. Bernier, Dawson, Webb, and Murias (2007) replicated this finding in adults and observed that attenuation of the EEG mu rhythm is correlated with imitative abilities. This finding provided further support that the EEG mu rhythm may reflect activity of an execution/observation matching system, such as the mirror neuron system and that this system may be related to imitation abilities. Although the existence of a human mirror neuron system is controversial and the literature contains conflicting findings regarding the presence of a disruption of the EEG mu rhythm in ASD, the EEG mu rhythm continues to be utilized in the investigation of action execution and observation among individuals with ASD.

See Also

▶ Electroencephalogram (EEG)
▶ Mirror Neuron System

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Mullen Scales of Early Learning

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Synonyms

MSEL:AGS; Mullen Scales of Early Learning, American Guidance Service Edition

Abbreviations

ELC   Early learning composite

Description

The Mullen Scales of Early Learning: American Guidance Service Edition is an individually administered, multidomain measure of early development designed for children from birth to 68 months of age. It was developed by Eileen M. Mullen, Ed.D., and published in 1995. The MSEL:AGS consists of five individual scales: four cognitive scales that cover the age range from birth through 68 months (visual reception, fine motor, receptive language, and expressive language) and one gross motor scale that is administered from birth to 33 months. The four cognitive scales can be combined to produce an Early Learning Composite (ELC) that is said to represent "g" or "general intelligence."

The MSEL:AGS was based on the author's information processing and neurodevelopmental theories that conceptualize intelligence "as a network of interrelated but functionally distinct cognitive skills" (Manual, p. 1). By assessing these individual areas of development independently, the examiner can identify specific areas of strength and weakness. From the author's perspective, this developmental profile can be used to aid in making diagnoses and also in developing strategies for individualized intervention plans (Manual, p. 33). Brief descriptions of each scale are included below.

The visual reception scale consists of 33 items. It assesses the child's processing of visually presented information and includes tasks that require visual discrimination, categorization, and visual memory skills. While the scale is not completely "nonverbal," it was designed to minimize the amount of language needed to understand instructions and give a response. Items range from visually fixating and tracking moving objects in early infancy to matching shapes, pictures, letters, and words and remembering visual forms for older children.

The fine motor scale consists of 30 items and (similar to visual reception) also requires minimal receptive and expressive language skills. Fine motor items measure visual-motor planning and control, motor imitation, unilateral and bilateral manipulation of objects, and writing readiness skills. Individual items range from reflexively holding objects and bringing fist to mouth to stacking blocks, cutting with scissors, and copying shapes and letters with a pencil.

The receptive language scale consists of 33 items. This area focuses on the child's ability to process linguistic input and assesses auditory comprehension and auditory memory skills. At the earliest age levels, the items assess the infant's orienting to sounds and responding to voices. As the item difficulty increases, the young child is asked to follow verbal directions and respond to questions about spatial, color, size, length, and number concepts. Most items can be answered by pointing to a picture or handing over an object, but some of the more advanced items require brief spoken responses, such as answering general knowledge questions.

The expressive language scale consists of 28 items and involves the production of sounds/words and the use of auditory memory. Items range from vocalizing early vowel and cooing sounds in infancy to defining vocabulary words, repeating sentences, and solving verbal analogies.

The gross motor scale consists of 35 items. The manual states that this scale measures "central motor control and mobility" (p. 2) in a variety of positions that range from being held in the caregiver's arms to the child being fully upright and independently walking, hopping, and running.

Time required for administration of the full MSEL:AGS varies by the child's chronological age and ability level. The manual estimates administration takes approximately 15 min for 1-year-olds, 30 min for 4-year-olds, and 60 min for 5-year-olds. Directions include information on positioning infants up to 8–10 months of age and supplemental drawings. Some items can be scored based on parent report and therefore do not have to be directly observed. This is particularly helpful in expressive language items where it is often difficult to elicit vocalizations or spoken responses from young children in an unfamiliar setting. It is also permissible to vary the order of administration of both the scales and individual items within each scale and to readminister some items after a child has "warmed up." For children born prematurely (at or before 36 weeks gestation), scores may be calculated based on the child's corrected age up to 2 years.

The components of a complete MSEL:AGS include the Mullen test kit, stimulus booklet, record forms, and two manuals. The test kit contains most of the objects needed for item administration. However, some of these items lack the durability needed for young children (e.g., picture cards), and others present a potential choking hazard (e.g., small beads). The examiner must also supply a number of items not contained in the test kit, such as paper, cereal, large ball, colored tape or white chalk line, 6-in.-high bench, and stairs. Consequently, some preparation time is needed before each administration to insure that all the necessary materials are available.

The stimulus booklet contains black and white line drawings, primarily for use on visual matching, prewriting, receptive language, and expressive vocabulary tasks. On the record form, items are arranged in increasing order of difficulty for each domain. Arrows denote starting points for different ages, but examiners may use their judgment about which starting point to choose (e.g., the examiner may begin at an earlier start point for children with developmental delays). Brief descriptions are included for each item, along with cues for positioning infants and a scoring column. The MSEL:AGS Item Administration Book provides instructions for giving items in all five scales. For each item, this manual includes a list of needed materials, the recommended position for the younger infants (e.g., supported sitting, standing), administration directions, and scoring criteria. The instructions are generally understandable, particularly for professionals with experience in infancy and early childhood. The MSEL:AGS Manual provides information about the test's theoretical background, scale descriptions, general administration, scoring procedures, standardization and psychometric data, and raw score conversion tables. There are also three case studies provided to illustrate the use and interpretation of the MSEL:AGS.

Scoring for each scale varies from 1 point for a correct response to 0 points for an incorrect response on some items – to items where multiple points can be earned for correctly completing component parts. Basal and ceiling rules are the same for each scale. A basal has been established for a scale when a child earns at least 1 point for each of three consecutive items beginning at a starting point. Testing continues until the child obtains scores of 0 points on three consecutive items. The sums of raw scores for each scale are used to compute derived scores that include T scores (mean = 50; SD = 10), percentile ranks, and age equivalents for each motor and cognitive scale and an Early Learning Composite (mean = 100; SD = 15) based on the four cognitive scales. Descriptive categories are also available (e.g., very high to very low).

Historical Background

The Mullen Scales of Early Learning: AGS Edition (1995) represents a revision of the original Mullen Scales (1992) and combines the Infant MSEL (1989) and the Preschool MSEL (1992) into a single test with norms that span the age range from birth through 68 months. The author, Eileen M. Mullen, Ed.D., developed the MSEL:AGS based on 30 years of clinical experience testing young children with developmental disabilities. She designed it to include multiple developmental domains based on the assumption that specific abilities mature at different rates in infants and young children. Viewed from this perspective, a test yielding only a global score would not provide information about patterns of cognitive strengths and weaknesses that can be used to plan interventions (Manual, p. 9). To arrive at the item sets for the current edition, item analyses were conducted using the Rasch one-parameter IRT model in order to obtain item difficulty estimates and indices of goodness of fit. A few items were dropped from the earlier versions, and the remaining items were sequenced by order of difficulty for the MSEL:AGS.

The structure of the individual scales was built on the author's theory of information processing where gross motor learning is considered to be the foundation for conceptual development in both visual and auditory modalities (Manual, p. 7). Tasks from each of the four cognitive scales were analyzed in terms of the component processes required to perform them. Individual items in each scale are purported to target intrasensory (auditory or visual) processing or intersensory (auditory-visual) processing. More specifically, the visual reception and fine motor scales are designed to assess visual intrasensory processing, while the receptive language and expressive language scales are designed to assess auditory intrasensory processing. In addition, approximately half of the items on the receptive language scale are reported to assess auditory-visual intersensory processing. However, when one carefully analyzes the individual items, it is difficult to categorize them into purely one type of sensory processing since problem solutions

often require multiple skills across multiple modalities. For example, solving the form-board task on the visual reception scale involves understanding the spoken directions (auditory), matching the shapes to their recesses (visual), using fine motor control to place the shapes into their respective holes (visual-motor), and so on.

The MSEL:AGS is the second most widely used measure of early development after the Bayley Scales of Infant and Toddler Development, Third Edition (2006) (Chawarska & Bearss, 2008, p. 55). Before the Bayley III (2006) was redesigned to include cognitive, language (receptive and expressive communication), and motor (fine and gross motor) scales to replace the previous more global mental and motor scales, the Mullen Scales was frequently chosen for research studies because investigators wanted to be able to assess individual developmental domains (Klin, Saulnier, Tsatsani, & Volkmar, 2005). In addition, the relatively long age span (birth to 68 months) was very helpful for longitudinal projects (e.g., studies of the development of baby siblings of children with autism spectrum disorders).

Psychometric Data

The Mullen Scales was standardized on a sample of 1,849 children ranging in age from 2 days to 69 months and grouped into 16 age groups ranging from 2-month age intervals from birth to 14 months to 5-month age intervals from 15 to 68 months. However, there were uneven numbers of children across the 16 age groups, varying from a low of 84 children at 11–12 months to a high of 156 children at 27–32 months. Standardization utilized 71 clinicians from a variety of disciplines and took place at more than 100 sites across the United States. It extended over an 8-year period and was conducted in two phases that covered different time periods and included different geographic regions. Phase 1 spanned June 1981 to February 1986 and included children from the Northeast. Phase 2 covered the period between December 1987 and April 1989 and included samples from the South,

West, and North, and South Central areas of the United States. The standardization sample is described as "geographically diverse," but it is not representative of the entire United States. For example, no children in the 1–14-month age range were recruited from the North/South Central region (Bradley-Johnson, 1997). For the total sample, there were 48.7% females and 51.3% males which were very close to the US population estimates in 1990. However, there was some variability among the 16 age groups, e.g., males were overrepresented at 5–6 months (59.8%) and underrepresented at 27–32 months (43.6%). Parental consent and information on demographic variables (age, sex, race/ethnicity, father's occupation, and urban/rural residence) were obtained for all children in the sample. Settings for testing included kindergarten, day care, nursery, and homes. All children in the sample were from homes where English was the primary language. It should also be noted that children with known physical or mental disabilities were excluded from the standardization sample.

Chapter 6 of the manual provides information about the reliability and validity of the MSEL: AGS. In terms of reliability, information is provided about internal consistency, test-retest reliability, and interscorer reliability. As a measure of internal consistency, the manual presents split-half reliability coefficients for the 16 age groups of the standardization sample (Manual, p. 56). Modified split-half internal consistency coefficients were calculated for the five scales and the Early Learning Composite. The median values ranged from .75 to .83 for the scales and .91 for the ELC. However, four coefficients that were significantly lower than this range were omitted from the estimation of the median split-half coefficients. The author explained these omissions as being due to a ceiling effect on visual reception for the two oldest age groups and floor and ceiling effects on receptive language for the youngest and oldest age groups. With these same four age groups omitted, the standard error of measurement had medians ranging from 4.1 to 5.0 T score points for the scales and 4.5 standard score points for the ELC.

Test-retest reliability was reported in the manual for two samples based on administration of the original Mullen Scales of Early Learning. The first sample included 50 children from 1 to 24 months of age and the second sample included 47 children ranging from 25 to 56 months. The retest interval ranged from 1 to 2 weeks, with a mean test-retest interval of 11 days. For the younger sample, test-retest reliability was high for gross motor (.96) and ranged from .82 to .85 for the cognitive scales. For the older sample (which did not include children from 57 to 68 months), the median stability coefficients ranged from .71 to .79. Interscorer reliability was reported to be high (.91 to .99), but the number of scorers was not reported, and the sample only went up to 44 months.

The manual provides information about construct, criterion-related, and concurrent validity. Support for construct validity is provided by showing an increase in mean raw scores with increasing chronological age across all five scales. Intercorrelations and squared correlations were calculated for the five Mullen Scales for 5 age groups and the total standardization sample. Scales correlated with each other at low to moderate levels. This was interpreted as indicating both unique and shared variances. Exploratory factor analyses were also conducted for the five scales by 5 age groups. Only one factor was reportedly extracted at each age level and this was interpreted as supporting the Mullen ELC as a measure of "g" or general cognitive ability. However, establishing construct validity for this measure is problematic because there is a lack of supportive data for the author's theory about intrasensory and intersensory processing leading to the identification of the child's learning style and its subsequent implications for remediation (Bradley-Johnson, 1997).

Evidence for concurrent validity is based on three types of studies: (1) studies analyzed by the publisher correlating the MSEL:AGS with other measures such as the Bayley Scales of Infant Development (1969), Preschool Language Assessment (1979), and Peabody Developmental Motor Scales (1983), (2) studies reported in the manuals for the original Infant and Preschool Mullen Scales, and (3) studies reported in the research literature which primarily focused on differences between low-birth-weight and normal-birth-weight children. The MSEL:AGS correlated moderately well with the measures mentioned above – with higher correlations obtained when the specific Mullen scale more closely matched what the other instrument was purported to measure. For example, the receptive language scale on the Mullen correlated more highly with Auditory Comprehension on the Preschool Language Assessment (1979) than with the Bayley Scales (1969) Mental Development Index (that includes both verbal and nonverbal items).

Clinical Uses

The MSEL:AGS was designed for use by early childhood professionals working in a variety of settings, such as early intervention programs, preschool and kindergarten special education, universities, research laboratories, hospitals, rehabilitation centers, and private practice. The author described three major uses: (1) eligibility determination for early intervention and special education, (2) diagnostic assessment of children with special needs, and (3) individualized program planning (Manual, p. 5–6).

Under the Individuals with Disabilities Education Act (IDEA), infants and young children must meet specific eligibility criteria in order to qualify for early intervention or special education services. The MSEL:AGS includes three of the five areas of functioning that must be assessed (i.e., physical (including gross and fine motor skills), cognition, and communication), but additional assessment with another measure is needed to cover personal-social and adaptive/self-help skills.

Because the MSEL:AGS includes five individual scales, it is useful in diagnostic assessments where clinicians are trying to determine whether children are progressing within the typical range of development or whether they are demonstrating significant delays in one or more areas of development. Determining a profile of strengths and

weaknesses is essential in diagnostic assessments of children suspected to have a wide variety of disabilities, such as specific speech-language impairments, motor impairments (e.g., cerebral palsy), autism spectrum disorders, and global developmental delays. Clinicians also use patterns of performance to formulate recommendations for skills to address in intervention. However, as noted in the validity discussion above, the modality-specific approach to individualized program planning proposed in the MSEL:AGS has not been substantiated.

In summary, the MSEL:AGS has been widely used in developmental assessments of infants and young children. Both clinicians and researchers have appreciated the multiple domain structure and relatively broad age range. Although it is regularly used for diagnostic evaluations and eligibility determination for services, children with physical and mental disabilities were excluded from the standardization sample. In addition, much of the data used for standardization was gathered in the 1980s, so the norms are outdated, and there are no current plans to renorm this measure.

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Mullen Scales of Early Learning, American Guidance Service Edition

▶ Mullen Scales of Early Learning

Multidisciplinary Evaluation

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Definition

Multidisciplinary evaluation refers to the process of gathering both formal and informal data from a variety of sources to determine whether a student is eligible for special education services and to provide information about his or her current levels of functioning. "Multidisciplinary" implies that evaluations will be conducted using a team approach in which a number of professionals (e.g., speech/language pathologists, occupational therapists, physical therapists, psychologists) gather assessment data about the student.

Historical Background

Prior to the enactment of Public Law 94-142, many students with disabilities were either not being served in public schools or were not receiving appropriate education services. Lack of adequate or appropriate assessments contributed to inaccurate labeling as well as education of

students with disabilities. With the support of family associations, the federal government began to develop practices for children with disabilities in the 1950s and 1960s. The Elementary and Secondary Education Act (PL 89-10) and the State Schools Act (PL 89-313), both enacted in 1965, provided states with funding to improve the quality of education for students with disabilities. In 1975, the Education for All Handicapped Children Act, now referred to as IDEA (Individuals with Disabilities Education Act), guaranteed all students with disabilities the right to a free, appropriate public education. Another provision of IDEA included the need for a multidisciplinary assessment of students suspected of having a disability. Using a multidisciplinary approach to assessment, involving a variety of professionals with expertise in each area of need, contributed to more accurate diagnosis of children and the provision of more appropriate special education services for students with disabilities.

Current Knowledge

Developmentally based assessments including information about a child's cognitive, communication, social emotional, and adaptive skills are integral to the diagnosis and decision-making process for those suspected of having an autism spectrum disorder (ASD). Current research supports the need for evaluation of students suspected of having an ASD to take place within a framework that incorporates the knowledge and expertise of various disciplines. In addition to psychological assessment and evaluation of the student's communication abilities, assessment data from other sources such as occupational therapy or physical therapy are also valuable. Outside of the school setting, pediatric, neurologic, and genetic assessment data are also important (Klin, Saulnier, Tsatsanis, & Volkmar, 2005).

Autism spectrum disorders are characterized by atypical development in multiple areas, including cognitive development, communication abilities, social interactions, and play skills. A comprehensive approach to assessment that addresses all areas of concern is therefore necessary. To assess these multiple areas of functioning, a multidisciplinary team of professionals with expertise in these various areas must be involved in the assessment process (Noland & Gabriels, 2004).

Future Directions

While a multidisciplinary approach to assessment is essential for children suspected of having an autism spectrum disorder, data from various professionals allows for multiple and, potentially, conflicting views of the child. In order to avoid this possibility, it is recommended that professionals operate in a transdisciplinary manner by which the team collaborates to present a single, coherent picture of the child's strengths and needs. By working together to present this single picture of the child, professionals are able to offer a more accurate view of the child and more fully address the impact of deficits in one area on other areas of functioning (Klin et al., 2005).

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Multidisciplinary Team

► Interdisciplinary Team

Multidisciplinary Training (TEACCH Component)

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Definition

Training of professionals in approaches to intervention in autism has been an integral part of the TEACCH program since its inception in 1972. Training includes a wide range of topics in diagnosis, assessment, treatment, and education and occurs at TEACCH center throughout North Carolina and in multiple sites throughout North Carolina, other states, and across the world. The training methodologies encompass lectures with audiovisual supports, activities designed for participant experiential learning, and hands-on experience with student trainers (i.e., children, adolescents, and adults with autism). The trainings are led by TEACCH directors (typically a Ph.D. licensed psychologist) and TEACCH staff therapists who have been working in the program for many years and have been trained in the various training models. Over the years, hundreds of professionals from across the world have been trained to be trainers, working as part of a TEACCH-led team.

Historical Background

When TEACCH was established as a statewide mandated program for serving individuals with autism and their families in 1972, there was virtually nothing known about service delivery, evidence-based practices, nor effective ways of preparing professionals to work with this population. There was little interest in autism as a field and more misunderstanding than accurate understanding of the condition. TEACCH grew out of a NIMH-funded project led by Eric Schopler and Robert Reichler which, on a small scale, documented effective ways of supporting children and their parents. With the legislation creating TEACCH at the University of North Carolina came the task of starting three diagnostic and treatment centers, training staff, and putting a model into practice. Simultaneously, 11 classrooms for students with autism were established, 10 of which were in public schools across North Carolina. Most, if not all, of these school districts had never educated a child with autism nor were prepared to recruit and train teachers. TEACCH took on this responsibility and organized a major training program for the new teachers as well as clinical staff at the three regional centers. The first trainings were lengthy, intensive, and complex and were based in a classroom setting with students with autism, a training team, and new teachers and assistant for 2 weeks. Over the course of the 2 weeks, along with lectures and group discussions, trainees observed the training staff, learned the principles and practices of TEACCH, and gradually assumed responsibility for running the classroom during the second week. Staff to trainee ratio was high, close to one to one. This first model became a template for later variations of the training approach, based on the collaboration of trainer and trainee, experiential learning, and individualization. A major development in the model occurred about a decade later when a team

of three TEACCH trainers led by Dr. Gary Mesibov, Director of TEACCH, adapted the earlier model with a less intense trainer to trainee ratio and shortening the process. The curriculum remained the same, but the training methods modified to effectively train more participants. Over the next three decades, there have been other modifications to the core structure of this training model and development of briefer basic training workshops that can reach larger audiences. The efficiency and accessibility of the trainings enable the program to be disseminated across the entire United States and dozens of countries across the world. Coordination of these training programs was led for much of this period by Dr. Roger Cox and implemented by TEACCH directors and staff across North Carolina.

Paralleling the professional service training models has been the center-based training of students at all levels of training and across many disciplines. The centerpiece of this training has been the Clinical Psychology Internship Program, started in 1974, and the Psychology Postdoctoral Training Program, started in the mid-1980s. The internship program is part of the UNC Department of Psychiatry's broad Psychology Internship Program, a program accredited by the American Psychological Association since 1962. Former TEACCH interns have gone onto prominence in the field of autism as leading researchers, clinicians, and program directors. Students receive intensive and comprehensive training in the diagnostic, assessment, and intervention methods used by TEACCH and regardless of their discipline or time commitment to their training experience receive exposure to the basic philosophy and practices of TEACCH, as well as to the field of autism as a whole.

A third area of training, also center-based, is placement of professionals from countries outside the United States who are interested in learning TEACCH methods and practices that can be applied to their home country. These international interns spend anywhere from a month to a year at a TEACCH center learning about all aspects of the program and most have returned to their countries and made significant contributions to services for individuals with autism, their families, and professionals.

Rationale or Underlying Theory

The rationale underlying TEACCH training is based on a key component of its mission statement:

> The University of North Carolina TEACCH Autism Program creates and cultivates the development of exemplary community-based services, training programs, and research to enhance the quality of life for individuals with Autism Spectrum Disorder and their families.

TEACCH, while a North Carolina state agency, established to meet the needs of families in the state through direct services is also a significant part of the University of North Carolina and its School of Medicine. The dissemination of its knowledge and experience through training within North Carolina and around the world has been a primary activity since its inception in 1972.

Goals and Objectives

The goals and objectives of the TEACCH multidisciplinary training model are as follows:
1. To disseminate current knowledge, principles, and practices of the comprehensive TEACCH approach to the understanding and treatment of autism.
2. To provide state of the science training through effective and relevant ways to professionals in the field of autism in North Carolina, other states, and internationally.
3. To provide preservice education and training to undergraduate, graduate, and postdoctoral students across disciplines, including, but not limited to, psychology, psychiatry, speech pathology, education, social work, occupational therapy, pediatrics, and family medicine.
4. To provide experiential learning programs to students and professionals on specific tools and strategies, developed by TEACCH, such as structured teaching and the use of visual supports, working with parents as co-therapists, Child Autism Rating Scale (CARS2), Psychoeducational Profile – Third Edition (PEP-3), and TEACCH Transitional Assessment Profile (TTAP).

Treatment Participants

Historically, there have been three types of multidisciplinary training at TEACCH, as described above: in-service training of professionals, preservice training of students, and international interns. These types of training continue today, and each type tends to attract a different group of participants. The in-service training can be further divided into a five-day, intensive training model, which includes hands-on learning with student trainers, and other, more didactic workshops, typically of shorter duration (2–3 days) and with written scenarios to provide an experiential component. Thus far, two studies have examined these training models to evaluate their relative efficacy (Grindstaff, 1998, 2000). In 1999, participants of the 5-day model were primarily special educators (55.4%), followed by speech language pathologists (10.9%), psychologists (8.9%), occupational therapists (5.0%), educational consultants (5.0%), parents (4.0%), teaching assistants (3.0%), school administrators (3.0%), and regular education teachers (1.0%). Participants in the comparison group were similar, with special educators in the majority (51.6%), followed by teaching assistants (16.1%), speech language pathologists (9.7%), regular education teachers (6.5%), parents (6.5%), school administrators (3.2%), psychologists (3.2%), and educational consultants (3.2%). An interesting shift has taken place in the last 12 years, such that, in the summer of 2011, the group of participants in the five-day training model included fewer classroom teachers and a greater number of consultants who provide support to students with autism in regular education settings. Typically, the five-day model has attracted participants from across the United States, as well as a variety of foreign countries. The workshops have tended to attract a more local audience, specific to the region of North Carolina where the workshop has been held.

Preservice training includes students of all levels of training and from a variety of disciplines. Most often, these have been graduate students in psychology, speech language pathology, occupational therapy, and special education. Medical residents and fellows from pediatrics and psychiatry have also been an important subset. The greatest amount of training time and effort has been expended to develop the Clinical Psychology Internship. The TEACCH Intern spends at least 50% of his or her 12-month internship involved at TEACCH in autism-specific diagnosis, assessment, consultation, ad intervention. Competition for this internship can be fierce, as applicants come from across the US and Canada; many of them will go on to take leadership positions in the field as researchers, clinicians, and program directors.

International interns have come from a variety of countries; many of them were first exposed to TEACCH principles during a five-day training held either here in the US or in their home country. Collaborations have been particularly rich with professionals from Japan, and more recently, from Sweden and Norway, leading to a greater percentage of international interns from those areas.

Treatment Procedures

The five-day training model is the most intense of the in-service training programs. Participants first attend lectures about the culture of autism and structured teaching to orient them for the week. Subsequently, they spend a small portion each day in lecture; the bulk of their learning takes place in small teams as they observe the TEACCH staff, develop activities for the student trainers, implement these activities with the student trainers, and reflect on their collective experiences. Throughout the week, the principles of structured teaching are applied to the curriculum areas most relevant to students with autism: informal assessment, communication, independence, leisure skills, social engagement, and behavior management. Teams work with a different student trainer each day, ensuring that they have broad exposure to the diversity of the autism spectrum. The five student trainers are, of course, unique individuals, who also vary by age, cognitive ability, and severity of autism symptoms. Most training participants report that the opportunity to teach in the model classroom and interact with our student trainers is the

most memorable component of this training experience.

Workshops vary considerably because they cover a wide range of topics. The Fundamentals Workshop introduces participants to the culture of autism and structured teaching, similar to the first 2 days of the five-day training model. Other workshops focus on the diagnosis of autism spectrum disorders, approaches to social skills instruction, and adapting curriculum for students in regular education, early intervention, and many others. New workshops are developed as the need arises. Most recently, workshops for parents have expanded to address their need for information about upcoming transitions: preparing for kindergarten, middle school, and adulthood. In all cases, an attempt is made to include a component of experiential learning – typically some type of written exercise or thought experiment that provides an opportunity for participants to apply what they are learning to their classroom, client, or child (in the case of parents). It is much less common to be able to provide the "live" interaction with student trainers that is so powerful during the five-day training.

Preservice training is often scheduled to coincide with the academic calendar. Residents or graduate students may observe for as little as 1 day; many future pediatricians, for example, spend a day observing a TEACCH diagnostic evaluation in order to increase their awareness of autism spectrum diagnoses and to facilitate appropriate referrals. Other trainees spend a month, a semester, or an academic year at their local TEACCH center. Their experiences are tailored to meet their training goals and departmental expectations. As previously mentioned, the TEACCH psychology intern spends a 12-month year in the most intense preservice training. He or she may choose to spend an additional, fellowship year with TEACCH to develop greater independence as a clinician, participate in training efforts, and pursue research interests.

Training for international interns is also individualized, based on the expertise and interest of the intern. Many of these professionals are quite experienced in their discipline and with people with autism; however, they are seeking additional training specific to TEACCH principles and procedures. Often, they hope to acquire enough skill to implement TEACCH methodology in their home country, as well as the ability to communicate TEACCH principles to their colleagues. An intern may be responsible for establishing a new program or modifying an existing one to better reflect TEACCH principles. To that end, interns typically maintain an ongoing relationship with their TEACCH center to receive consultation and, sometimes, additional training.

Efficacy Information

Informal program evaluation takes place during every form of TEACCH training. Participants at all levels of training (in-service, preservice, and international interns) complete rating scales, answer written questions, and are generally encouraged to provide feedback to TEACCH staff. These responses have been universally positive. It is not uncommon for participants to report that their TEACCH training experience has proven more valuable than any other training program in which they have participated. Sometimes, participants also offer constructive criticism. Suggestions are always taken seriously and have sometimes resulted in a helpful revision to the delivery of the training model.

As mentioned above, there have been two formal evaluations of TEACCH's in-service training efforts, designed to compare the relative efficacy of the five-day training model versus the two-day Fundamentals Workshops (Grindstaff, 1998, 2000). Outcomes were compared across the participants (1) knowledge of the training content, (2) attributions of controllability with regard to the extreme behavior of students with autism, (3) self-efficacy, (4) negative affect, and (5) use of structured teaching. Measures were completed at the very start of the respective training programs and again 6 weeks post-training. Results indicated that both training models were effective in increasing the participants' knowledge of the training content; however, neither model was associated with significant change in participants' attributions, self-efficacy, or affect. Participants in the five-day training model reported a significant increase in their use of

structured teaching strategies back in their home environments; workshop participants did not. Grindstaff (2000) concluded that either training model could effectively convey the principles and philosophy of structured teaching but that only the five-day model (with its hands-on component) achieved the more elusive goal of helping participants apply structured teaching strategies to their classroom, clinic, or other work setting. Results from a small pilot study (Grindstaff, 2000) indicated that the Structured Teaching Checklist could be used by a trained observer to evaluate the degree to which a classroom has successfully implemented the principles of structured teaching; this tool could prove useful as a more objective measure of training participants' use of structured teaching, as the initial studies relied solely on self-report.

Outcome Measurement

Since its inception, the Structured Teaching Checklist (STC; Grindstaff, 2000) has been adapted for use as a standardized measure of TEACCH treatment fidelity (Hume, Boyd, McBee, Coman, & Gutierrez, 2011). The TEACCH Fidelity Form has been demonstrated to have strong psychometric properties (e.g., inter-rater agreement, test-retest reliability, and internal consistency) and reliably discriminates between classrooms that adhere to the TEACCH model versus other treatment approaches (Hume et al., 2011). The TEACCH Fidelity Form is specific to preschool classrooms, but perhaps, it could be elaborated to include classrooms for students at other stages of development, including a version for self-contained classrooms and one for students who are included in regular education settings. Once these additional versions are added, the TEACCH Fidelity Form will make an ideal measure for the effectiveness of TEACCH training.

Qualifications of Treatment Providers

For preservice training programs, there is typically a Ph.D. level psychologist who serves as the administrator and clinical director. Other trainers are often Masters level TEACCH staff who have served with the TEACCH program for a number of years and have demonstrated mastery of the principles of TEACCH training, as well as an ability to communicate effectively. There is a multistep process for becoming a TEACCH trainer that applies to TEACCH staff, as well as interested professionals from other organizations. First, the potential trainer must attend the five-day training model as a participant. He or she then returns as a "shadow trainer" – which means that he or she is apprenticed to an experienced trainer for the five days, with a focus on working with a specific student trainer, instead of the training participants. Shadow training is often repeated two or three times, until the potential trainer feels comfortable with a variety of student trainers. In the final stage of preparation, the potential trainer returns as a "reverse shadow" – which means that he or she now takes the lead not only with the student trainer but also with the training participants, with support from an experienced TEACCH trainer "behind the scenes." The potential trainer may continue as a "reverse shadow" until he or she is comfortable communicating about TEACCH principles and strategies, while also improvising with a student trainer. There is no specific time requirement for the completion of these stages of training, but the commitment is considerable.

In-service trainees and international interns receive supervision from the staff of their assigned TEACCH center. This always includes the center director, a Ph.D. level psychologist, as well as the Masters level psychoeducational therapists, who come from a variety of disciplines. If there is a TEACCH staff member from the same discipline as the trainee, the two are often matched in a mentor-mentee relationship.

See Also

► Informal Assessment
► Structured Classrooms
► Structured Teaching
► Treatment Fidelity
► Visual Supports

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Multihandicapped

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Definition

Multihandicapped refers to a person that has more than one disabling condition. The disability may be in the category of autism, mental retardation, hearing impairment or deafness, visual impairment or blindness, emotional disturbance, speech and language impairment, orthopedic impairment, or health impairment. When referred to as multihandicapped, the person typically has disabilities that are severe enough to require intensive support to handle the functions of daily living. In education, the term "multiple disability" is used for students who have two or more disabilities that effect their ability to access education through traditional means. Children with multiple disabilities have a combination of affected areas such as speech and language, mobility, learning, intellectual functioning, sensory losses or dysfunctions, and behavior or social problems. Children are impacted in different ways, and the disabilities will vary in level of severity and how they manifest in everyday performance. Children with autism may be identified as having multiple disabilities if diagnosed with autism and intellectual disability. Educational support is often needed in the classroom, and some children will need support in all settings throughout their lives. Programming for these children will be based on the characteristics they display which will vary widely depending on the areas involved. Typically, the educational team includes a variety of professionals such as special education and regular education teachers, physical therapists, occupational therapists, speech and language pathologist, adaptive physical education teachers, nurses, paraprofessionals, psychologist, and possibly medical professionals.

Historical Background

The term "multi" means many or several and is used frequently in numerous contexts. The term handicap has a more involved history, some of which is not based on facts that can be substantiated. There is a story that is associated with the word "handicap" that leads people to believe it was first used when people with disabilities were allowed to beg in the streets with their "cap in hand." There have been several attempts to dispel this myth but it seems to live on. The word does have a connection to a competitive sport dating back to 1650s but was not used in conjunction with a person with a disability until the early 1900s. As the term "handicap" evolved, it now refers to a person with a disability. The term alone does not give information as to what type of disability a person may have. Once multi was added to handicap, it came to have the meaning we know today of more than one disabling condition which makes functioning in daily activities more difficult when compared to a person without the disabilities.

See Also

▶ Disability

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Multilocus Genetic Models

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Definition

A multilocus genetic model means that a given phenotypic outcome is influenced by multiple genes (an individual gene is referred to as a locus) – this can imply multiple disease variants acting simultaneously in each patient, or single mutations in each patient, but in different genes (unsure of this definition). Tuberous sclerosis, for example, can be caused by mutations in either TSC1 or TSC2 (EntrezGene, OMIM). Coronary artery disease, on the other hand, could be due to more than one gene working in concert (e.g., Saade et al., 2011).

Some ASD cases are attributable to specific chromosomal abnormalities, or to deletions/rearrangements known to induce autism (when these rearrangements confer other symptoms and phenotypes in addition to autism, they are known as "syndromic" autism). No one cause has been found that explains more than 1–2% of autism cases (gross chromosomal abnormalities). A recent review summarized that taken together, all gross chromosomal abnormalities, all syndromes associated with autism, disruptions to known autism loci (e.g., SHANK3), and rare variants in candidate genes account for only 12–17% of autism cases, meaning that the majority of autism cases remain unclear with regard to specific genetic etiology (Buxbaum, 2009). Another estimate put it at 5–15% (Pinto et al., 2010). Additionally, even syndromic causes that associate strongly with autism, such as fragile X syndrome, are not completely sufficient to induce autism; there exist fragile X patients who do not present with autism or ASD. Though some cases are largely influenced by highly deleterious single-gene mutations, even these are likely modulated by mutations in other genes. Similar ASD phenotypes need not necessarily involve the exact same genes in each case; it is possible that many autism cases can be caused by any one of a number of combinations of different genes in neurological pathways.

Historical Background

Modern understanding of genetic inheritance is widely accepted to have begun with Gregor Mendel and his experiments with trait inheritance in garden peas. What we call Mendelian inheritance is the simplest form of transmission of genetic information: one gene, two or more alleles, a relationship between the alleles (dominant, recessive, codominant, incompletely dominant, etc.). Sex-linked traits modify the situation somewhat; disruptive mutations on the X-chromosome that may be recessive in females, being offset by the healthy X-chromosome, can be deleterious in males, who have only one X-chromosome. Multilocus disease models, while always theoretically possible, became more discussed in the late 1970s and early 1980s, particularly in the context of autoimmune diseases (see Rotter & Landau, 1984). A consensus for autism as a primarily genetic disorder did not fully emerge until the late 1980s to mid-1990s (Bailey et al., 1995; Bolton et al., 1994; Smalley, Asarnow, & Spence, 1988; Szatmari, Jones, Zwaigenbaum, & MacLean, 1998), and fairly quickly, it became apparent that single-gene inheritance models did

not explain most autism cases (e.g., Jorde et al., 1991). An early multilocus model of family recurrence in autism determined that 3 interacting genes, in a range of 2–10, best accounted for their data. Another multilocus model was put forth by Risch et al. in 1999. They concluded that on the basis of evidence seen in 97 affected sibling pairs (ASPs; both siblings diagnosed with autism) and 51 discordant sibling pairs (DSPs; one sibling had autism and one was unaffected), as well as follow-up in 50 ASPs and 29 DSPs, one or a few mutated gene loci in a given sibling pair did not adequately explain the increase in shared DNA inheritance between the affected siblings relative to the discordant siblings. On the basis of the families they assessed, the authors determined that a model based on 15 or more interacting gene loci explained their data better than a model with 10 or fewer gene loci (Risch et al., 1999).

As autism genetic models were being debated, a broader debate was emerging in the genetic field about the etiology of complex (multigenic), relatively common diseases. The common disease-common variant theory held that for a disease to remain relatively common in the population, the mutations being inherited must not be damaging enough, on their own, to reduce reproductive success of those carrying them, and therefore more severe common disease phenotypes must be due to the interaction of many common variants, each of a small effect size (contributing a small amount to the disease phenotype, and not disruptive enough to reduce reproductive fitness on its own) but significant enough when inherited in combination to induce a disease state. In contrast, the common disease-rare variant theory held that multiple rare variants, each of larger effect (more disruptive), were sufficient to cause common diseases. These deleterious rare variants would in theory be more prone to reducing reproductive success, but if many of these rare mutations were being generated spontaneously (de novo) rather than inherited from parents, in a large enough number of genes, it could explain the baseline prevalence of even severely disruptive alleles.

As evidence accumulated that methodologies driven by the common disease-common variant assumption (exemplified by genome-wide association studies) could account for only a modest proportion of common complex disorders, the common disease-rare variant theory gained traction in research on these disorders. Autism in particular was poorly accounted for by genetic methods seeking to associate common variation with the disorder (e.g., Anney et al., 2010; Curran et al., 2011; Hirschhorn et al., 2010). A few implicated genes and regions were replicated in other studies (e.g., MET, CNTNAP2, and 5p14.1) (Alarcon et al., 2008; Arking et al., 2008; Campbell et al., 2006; Jackson et al., 2009; Sousa et al., 2009; Wang et al., 2009; Weiss, Arking, Daly, Chakravarti, & Gene Discovery Project of Johns Hopkins & the Autism Consortium, 2009); however, common variants overall likely account for a small proportion of autism heritability (Pinto et al., 2010). Rare copy number variants (Bucan et al., 2009; Pinto et al., 2010; Sanders et al., 2011) began to gain attention as several studies suggested a role in autism. With the emergence of dense genome-wide marker SNP genotyping as well as exome sequencing, and follow-ups on these studies, evidence accumulated for a multi-hit etiology (i.e., mutations in multiple genes in the same person) in at least some autism cases, for example, FOXP1 and CNTNAP2 (O'Roak et al., 2011), CNTNAP5 and DOCK4 (Pagnamenta et al., 2010), and DMD and TRPM3 (Pagnamenta et al., 2011). The emerging methods allow us to concretely demonstrate the multilocus model in patient data, beyond just discussing its theoretical fit to the existing data.

Current Knowledge

The current state of the field is that large-scale chromosome rearrangements, genetic syndromes, and the few known definitively autism-associated loci (e.g., SHANK3, 15.q11-13) are of large effect size, but account for a modest proportion of total autism cases, and likely in conjunction with other genes in a given case. The majority of cases are likewise caused by mutations in a variety of genes, the list of which researchers are constantly working to validate, corroborate, and expand. The challenge is no longer to demonstrate the validity of

the theoretical underpinnings of the multilocus model but to use more and more precise genetic tools to establish exactly what genes, and perhaps networks of genes (e.g., gene families or biological pathways), are involved in autism.

Future Directions

As the prices of whole-exome and whole-genome resequencing continue to drop, these technologies, combined with wider- and wider scale genotyping of SNP markers across the entire genome, it will be possibly to analyze patients with autism at a finer and finer scale, potentially uncovering new viable candidate genes and contributing mutations, and strengthening or weakening the cases for existing candidate genes as we examine larger numbers of people in greater detail than ever before. These thorough analyses of individuals and their families represent the emerging present and near future in autism research.

See Also

▶ Common Disease-Common Variant Hypothesis
▶ Common Disease-Rare Variant Hypothesis

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Multiple Complex (or Multiplex) Developmental Disorder

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Definition

The greatly missed Donald Cohen, Volkmar, and Paul (1986) thought we should try and specify subgroups within the so-called not otherwise specified areas within the broader category of pervasive developmental disorders. From cluster analyses of a big group of individuals with atypical development, within the area on the fringe of autistic disorders, two categories emerged: Asperger's disorder (that was added to DSM IV 1994) and the group so-called multiplex developmental disorders (later renamed multiple complex developmental disorder to avoid confusion with MDD – "major depressive" disorder).

In this entry, this "heuristic" category is described.

Historical Background

Along with defined categories from the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision (DSM-IV-TR) includes so-called Not Otherwise Specified (NOS) categories meant for lesser variants or borderline conditions to the clearly defined cases.

The NOS subcategory for pervasive developmental disorder (PDD-NOS) was introduced in DSM-III-R (1986). Cohen et al. (1986) were concerned that having only two categories for autism in DSM-III-R would be too few to provide a more fine-tuned description of subgroups within what is now commonly named the autistic spectrum. These subgroups had been identified by on-cluster analyses on large groups of children with "atypical" behavior (Prior et al. 1975; Dahl, Cohen, & Provence, 1986).

Cohen et al. suggested that two new categories should be introduced in DSM-IV. The first one would be Asperger's disorder (Asperger, 1944; Wing, 1981), referring to individuals with developmental problems in the areas of social reciprocity, communication, and rigid and restricted patterns of behavior. These individuals differed from the classical Kanner autism in that they developed language at typical stages (yet not the adequate pragmatics), and they had motor clumsiness and intellectual preoccupations more than motor stereotypies. This category was finally included in DSM-IV, but the criteria did not include many of the features Asperger actually described (Miller & Ozonoff, 1997).

Multiple Complex (or Multiplex) Developmental Disorder, Table 1 Criteria for multiple complex developmental disorder (Cohen et al. 1994 – van der Gaag, Caplan, van Engeland, Loman, & Buitelaar, 2005)

1. Impaired regulation of states of mind and anxieties
A. Unusual or peculiar fears and phobias or frequent idiosyncratic or bizarre anxiety reactions
B. Recurrent panic episodes or flooding with anxiety
C. Episodes of behavioral disorganization punctuated by markedly immature, primitive, or violent behavior
2. Impaired social behavior
A. Social disinterest, detachment, avoidance, or withdrawal
B. Markedly disturbed and/or ambivalent attachments
3. The presence of thought disorder
A. Irrationality, magical thinking, sudden intrusion on normal thought processes, bizarre ideas, neologisms, or repetitions of nonsense words
B. Perplexity and easy confusability
C. Overvalued ideas, including fantasies of omnipotence, paranoid preoccupations, overengagement with fantasy figures, and referential ideation

Note. A total of five (or more) items from (1), (2), and (3), with at least one item from (1), one item from (2), and one item from (3) (Buitelaar & van der Gaag, 1998)

The second proposal (Cohen et al., 1986, 1991) on multiple complex developmental disorders (MCDD) was not included in DSM-IV. It was a heuristic proposal aimed at promoting research on a category well known in clinical practice (Green & Jones, 1998) and clearly emerging as a distinct cluster in the analysis of the children with atypical developmental (Dahl et al., 1986). These children had previously been described under different diagnostic labels, including "borderline children (Bemporad et al., 1982; Pine, 1974; Vela et al., 1983), schizoid personality in childhood (Wolff, 2003), and schizotypal children (Nagy & Szatmari, 1986). Ironically, it had been included in DSM-III (American Psychiatric Association [APA], 1980) with the label "Childhood-Onset Pervasive Developmental Disorder" but, for reasons that are not clear, was not continued into DSM-III-R and thus not considered in DSM-IV.

All these labels recognized children who could be placed "in the borderlands of autism." They share with more classically autistic children a lack of social sensitivity and empathy, but yet differ importantly from autistic children. Where children with "classic Kanner autism" lack imagination, these atypical children tend to get carried away by a far too-vivid imagination that blurs their reality testing.

Current Knowledge

The defining criteria for MCDD include (1) consistently impaired social behavior and sensitivity, (2) impaired regulation of affective state, and (3) impaired cognitive processing "thinking disorder."

The discriminative potential of these criteria in categorizing these children reaches sensitivity and specificity levels comparable to those for autistic disorder (Buitelaar & van der Gaag, 1998) (Table 1). The face validity of the concept was demonstrated in a series of independent studies (Towbin, Dykens, Pearson, & Cohen, 1993; Van der Gaag et al., 1995). The predictive validity is high (Van der Gaag, 1993). There is longitudinal persistence of symptoms in the area of development of social reciprocity and thinking disorders. The extreme problems in the regulation of affective states are less prominent in adolescents and adults. There is a marked shift toward symptoms from the schizophrenia spectrum in adults, with up to 17% of the cases meeting criteria of schizophrenia after one or several psychotic episodes and over 60% meeting the criteria for schizoid or schizotypal personality disorder (Van Engeland & Van der Gaag, 1994). Other differences come from studies on the stress-regulation

characteristics in the MCDD group (Jansen, Gispen-de Wied, van der Gaag, & van Engeland, 2003; Kemner et al., 1999) that show marked differences in these areas between individuals with autistic disorder and individuals with MCDD who, on these dimensions, are more similar to adults within the schizophrenia spectrum. The third characteristic of MCDD children includes "disordered thinking," which is commonly thought to be specific to schizophrenia.

Future Directions

In DSM V, the search for specific subgroups will be dropped. But research should be pursued along the dimensions of impaired regulation of affective states and thought disorder in individuals with autism spectrum disorders. This research will be important for a well-suited guidance and treatment program and to explore the boundaries between autism spectrum and schizophrenia spectrum disorders as apparently at least a portion of high functioning individuals with autism spectrum disorders are at risk of having psychotic episodes in their adult life and for developing schizophrenia and/or addictive behavior.

See Also

▶ Asperger's Disorder
▶ Psychosis
▶ Schizophrenia

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Multiple Phenotypes Associated With Disruption of a Single Gene

▶ Pleiotropy

Multiple Regression

▶ Regression Analysis

Multiplex-Simplex Comparisons

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Definition

"Multiplex" refers to families in which multiple individuals are affected by a specific disease, while "simplex" refers to families in which only a single individual has a specific disease. This distinction is important when designing a study to identify risk factors for ASD, as multiplex families are thought to be more likely to have shared risk factors (i.e., inherited risk), while simplex families are more likely to show de novo genetic risks. Accordingly major collections of ASD samples for genetic analysis are often designed to enrich for specific types of families, such as the Autism Genetic Research Exchange (AGRE) with many multiplex families and the Simons Simplex Collection (SSC) with exclusively simplex families.

Categorizing families as being multiplex or simplex can be difficult. For example, the presence of only a single affected individual among siblings may not truly reflect the underlying genetic architecture of that family. For example, an unaffected sibling could simply not have inherited a transmitted risk factor that is still present in the parents (and might be transmitted to the next sibling to be born). Alternatively, it is common to observe individuals carrying known genetic risk variants for ASD without showing clinical evidence of autism. The objective of making the distinction is to determine whether shared or unique risk factors are most likely to account for disease. Since ASD is likely to be the combination of many genetic and environmental risk factors, it is probable that many individuals with ASD have a combination of both shared and unique risk factors. The distinction between multiplex and simplex families is therefore best considered as a continuous spectrum that enriches for shared or unique risk factors at each respective extreme.

The distinction between multiplex and simplex families also has bearing on the risk of a further child having ASD. This risk is considerably higher in families with a previous child with ASD, especially if more than one child is affected (Ozonoff et al., 2011).

See Also

▶ American Board of Genetic Counseling
▶ Common Disease-Common Variant Hypothesis
▶ Common Disease-Rare Variant Hypothesis
▶ DNA
▶ Genetics

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Multi-skilling

▶ Role Release

Music Therapy

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Definition

Music therapy uses musical activities such as singing, playing instruments, and music listening to promote interaction between the therapist and the client and to meet the client's therapeutic needs. American Music Therapy Association (2005) defined music therapy as "the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program."

There are many different approaches in music therapy. In a broad sense, music therapy methods can be divided into either active or receptive music therapy, depending on whether the client is actively involved in live music-making processes with the therapist or the client is involved in a preselected music listening using either a recorded music or a live performance. In active, especially the improvisational music therapy intervention, interactive use of live and spontaneous music-making process between the therapist and the client, the client is encouraged and facilitated. Therefore, musical-therapeutic context evolves through musical interaction between the therapist and the client here and now and moment by moment. In receptive music therapy intervention, music is selected or precomposed based on the preference and needs of the client to accomplish certain therapeutic outcomes for individuals with autism spectrum disorders (ASD). Research evidences have indicated that both active and receptive music therapy methods are found to be effective at facilitating and improving communication and social interaction skills and to modify certain behaviors of individuals with ASD (Accordino, Comer, & Heller, 2007; Gold, Wigram, & Elefant, 2006; Rossignol, 2009; Simpson & Keen, 2011; Whipple, 2004). In clinical practice, music therapists tend to use the method that serves their client's individual needs, sometimes resulting in eclectic approaches.

Historical Background

Music therapy as a profession was established some time after the World War I and II in the USA and then in the UK. There have been various approaches in music therapy, depending on the different philosophies and principles of the founder of each music therapy approach in different clinical settings respectively.

Early music therapy pioneers such as Juliette Alvin, Paul Nordoff, and Clive Robbins worked with children with special needs including autism from the 1950s. These early pioneers used live interactive music (improvisation) to engage the children with ASD and to address their difficulties in communication and social interaction (Alvin, 1978; Nordoff & Robbins, 1971). Now, there are many music therapists working within the improvisational model of music therapy worldwide, especially in the UK and Europe.

Following are four internationally known improvisational models of music therapy:

1. *Free improvisation therapy* founded and developed by Juliette Alvin
2. *Creative music therapy* founded and developed by Paul Nordoff and Clive Robbins
3. *Analytically oriented music therapy* founded and developed by Mary Priestley
4. *Interactive music therapy* founded and developed by Amelia Oldfield

All four approaches above have been mainly developed in the UK.

Another significant approach in music therapy has been *behavioral modification model of music therapy* that was chiefly developed in the USA

and is still the primary music therapy intervention in the USA. The influence of behavioral modification model of music therapy is also prevalent worldwide especially for children with special needs including autism.

In the most recent literature review, Simpson and Keen (2011) has identified composed songs and improvisation as the predominant music therapy techniques used for children with ASD. Research evidence indicated that behavioral music therapy and improvisational music therapy all work well with individuals with ASD (Boso et al., 2007; Gold et al., 2006; Kaplan & Steele, 2005; Simpson & Keen, 2011).

Rationale or Underlying Theory

Music is often described as a universal or emotive language. Music therapists have attributed this mainly due to its power to reach and affect human emotions. No matter how disabled a person can be, anyone can respond to music, and musical responses are innate ability deeply engrained in human nature (Alvin, 1978; Kim, Wigram, & Gold, 2009; Nordoff & Robbins, 1971; Robarts, 1996). Moreover, musical experiences are often intrinsically joyful and interesting. Music often inspires, motivates, and brings people together even when they are total strangers. Kim and her colleagues (2009) claim: "Music acts as an essentially emotional, relational and motivational medium when, in music therapy, it is purposefully created to engender 'interpersonal relatedness' by employing a well-measured systematic intervention."

Thaut (1987) found that children with autism engaged significantly more time with the music than age-matched typically developing children. He (1988) analyzed musical responsiveness of children with autism, and that of children without autism through music improvisation they played, and found no significant difference in musical responsiveness between them. These studies indicate intact musical responsiveness and musical aptitude in children with ASD. Clinical implication of these findings suggests significant therapeutic potential in music that can be used in helping individuals with ASD in everyday life.

Music can be an excellent medium for emotional communication and social interaction for individuals who cannot easily assimilate the conventional ways of human communication and interaction. Instead of verbal exchange, nonverbal aspects of music such as playing simple instruments, vocalizing, and listening to music can provide an alternative way of communicating and engaging the individuals with ASD and others without ASD.

Music can be utilized to teach new skills (Buday, 1995; Kern & Aldridge, 2006; Lim, 2010), to help children with ASD perceive and recognize specific emotions (Katagiri, 2009), and to modify children's behaviors (Brownell, 2002; Kern, Wolery, & Aldridge, 2007) in a certain direction that can be helpful and adaptable in everyday life. As children with ASD are reported to respond better to songs than spoken words, a music therapist might create original songs (Brownell, 2002; Katagiri, 2009; Kern & Aldridge, 2006), or lyrics with familiar melody (Kern et al., 2007) about a specific behavior, and use these songs with children with ASD with specific therapeutic goals in mind.

Goals and Objectives

Goals and objectives of music therapy intervention for individuals with ASD are usually established through music therapy assessment. Music therapists assess the individual's needs, especially the domains of emotional, communicative, behavioral, and social responses and cognitive skills for individuals with ASD.

Systematic review of music therapy literature has indicated primary goal areas in music therapy intervention: (1) to promote socialization, (2) to increase communication and language skills, and (3) to modify maladaptive behaviors (Accordino et al., 2007; Gold et al., 2006; Simpson & Keen, 2011; Whipple, 2004).

Once broad goals are set up, the therapist identifies specific objectives that are observable and measurable such as "when therapist sings a 'hello song' in the beginning of the session, child will look at the direction of therapist 30% of the time."

Objectives of music therapy will change in time as therapy progresses. As autism spectrum disorders are complex developmental disorders showing variety and individuality across all ages and abilities, therapeutic objectives for individuals with ASD varies a lot from person to person and stage of each therapy process.

In the improvisational music therapy, the main goal of the therapy with individuals with ASD is to establish, maintain, and develop interaction between the therapist and the client through active music-making processes, and to deal with developmental and therapeutic issues that are presented by the client during each stage of therapy process.

Treatment Participants

Music therapy has been used for preschool and school-age children, adolescents, and adults with wide range of different abilities and symptom severity. The most common participants are preschool and school-age children with ASD in music therapy.

Treatment Procedures

When referral is made to a music therapist, the music therapist assesses the individual's needs, plans either individual or group music therapy sessions based on the needs of the individual, and implements and evaluates music therapy sessions where appropriate. Following are the typical music therapy procedures:

1. Referral: Referral to music therapy can be made by the parents, doctors, speech therapists, teachers, social workers, etc.
2. Assessment: The music therapist assesses the individual's needs in terms of his/her strengths and weaknesses through musical responses using various musical activities.
3. Goal setting: Treatment goals and objectives are developed based on the findings of assessment. Therefore, assessment will lead to setting up appropriate treatment plan for individuals with ASD.

4. Treatment implementation: Music therapy sessions can be one-on-one or in a group, which consist of musical activities that are designed to meet the individual's needs and therapeutic goals.
5. Evaluation: Music therapy sessions are regularly evaluated by the music therapist and often within the interdisciplinary team.
6. Termination of music therapy: The duration of music therapy varies from person to person, depending on the needs of the individual. Short-term therapy typically consists of 10–12 sessions. Long-term therapy can be up to 2 or 3 years. For young children with ASD, music therapy sessions are typically more than 3 months.

Children with ASD typically have once, twice, or thrice weekly music therapy sessions for about 20–50 min, depending on attention span and needs of the child. Kaplan and Steele (2005) investigated 40 music therapy clients with ages ranging from 2 to 49 years with ASD in Cleveland, USA. They found individual music therapy as the most common session type, followed by partner, small group (3–5 subjects), large group (more than 6 subjects), etc.

Efficacy Information

In the last few decades there have been accumulating research evidences indicating the efficacy of music therapy for individuals with ASD, with some promising results in the domains of social, communicative, and behavioral skills (Boso et al., 2007; Brownell, 2002; Buday, 1995; Edgerton, 1994; Katagiri, 2009; Kern & Aldridge, 2006; Kim et al., 2008, 2009; Lim, 2010).

Recently, there have been some systematic or narrative reviews on effects of music therapy for individuals with ASD. It was found that majority of published articles in music therapy for individuals with ASD were case studies with anecdotal evidences, and there have been limited numbers of well-designed empirical investigations typically with small samples (Accordino et al., 2007; Gold et al., 2006; Rossignol, 2009; Simpson & Keen, 2011; Whipple, 2004).

In the recent Cochrane review of music therapy for autistic spectrum disorder, Gold and associates (2006) selected three small controlled studies examining the short-term effect of brief music therapy intervention based on highly structured behavioral modification techniques for children with ASD. In all three studies, music therapy was compared to a placebo condition and was found to be more effective either in improving maladaptive behaviors or skills in verbal and gestural communication. They have noted, however, limited clinical applicability of such positive results due to the specific structure of three studies (daily individual therapy for only 1 week using largely receptive music therapy techniques) that was rather far-fetched from the real-world therapy situation.

There are only a few controlled studies of improvisational music therapy for children with ASD. Improvisational music therapy has been reported to promote communication, social motivation, and social engagement, but Edgerton's study reported limited generalizability (Edgerton, 1994; Kim et al., 2008, 2009).

In Kaplan and Steele's investigation (2005) on 40 music therapy clients with ages ranging from 2 to 49 years with ASD, however, 100% of parents and caregivers of these clients reported that these individuals with ASD generalized skills and responses obtained in music therapy to other environments.

One recent systematic review on treatments for individuals with ASD has selected music therapy as one of promising treatments (Rossignol, 2009), and the National Autism Center (2009) has given music therapy the classification of "an emerging evidence-based practice."

To be conclusive, more research should be undertaken in order to verify the promising effects and efficacy of music therapy.

Outcome Measurement

There have been many reports on the effective use of music therapy for children with ASD by both the parents of the children and music therapists (Accordino et al., 2007; Alvin, 1978; Nordoff & Robbins, 1971; Robarts, 1996).

Most common outcome measurements in music therapy are based on music therapists' own observation, either direct or through video recordings, and substantial clinical documentation. For observational outcome measurements, specific target behaviors are defined prior to conducting outcome evaluation. Some music therapy researchers measured specific target behaviors through direct observation using event recordings (Brownell, 2002; Kern et al., 2007). Others used video recordings to evaluate behavioral outcomes for children with ASD (Buday, 1995; Kern & Aldridge, 2006; Kim et al., 2008, 2009).

Edgerton (1994) specifically developed the Checklist of Communicative Responses/Acts Score Sheet (CRASS) in order to measure the child's musical and nonmusical communicative behaviors in improvisational music therapy. The CRASS has predominantly musical categories (91 out of 107) and only 16 items of nonmusical categories, of which 69 items were communicative responses and 38 communicative acts. The CRASS is not, however, easily comparable with other measurements, nor applicable to any other therapy situations.

Kim and associates (2008) used standardized tools such as the Early Social Communication Scales (ESCS) and the Pervasive Developmental Disorder Behavior Inventory (PDDBI) as outcome measurements for improvisational music therapy with preschool children with autism. The ESCS is a structured toy play measurement for nonverbal social communication skills that is applicable to young children with ASD. The PDDBI is an informant-based rating scale designed to assess the responsiveness to intervention in children with ASD.

While it is important to use observational outcome measurements in music therapy, it is also pertinent to develop standardized outcome measurement in music therapy for individuals with ASD that is valid, reliable, and comparable to other standardized measurements.

Qualifications of Treatment Providers

Music therapy services are provided by registered music therapists who have completed an accredited

music therapy degree program by the music therapy association in each country respectively.

In the USA, Australia, Canada, and South Korea, music therapists typically hold either undergraduate or master's degree in music therapy. In the UK, music therapists typically hold a master's degree in music therapy and have state registration with Health Professions Council.

In the USA, there are large numbers of American Music Therapy Association–approved programs providing equivalency or certificate degrees in music therapy for people that have already obtained a degree in related fields. Individuals who have completed an approved music therapy degree program are qualified to take the national board certification examination and can earn the credential of MT-BC (Music Therapist-Board Certified) after passing the exam. South Korea has recently benchmarked the American system and has set up the national music therapy certification examination for music therapists.

See Also

American Music Therapy Association: www.musictherapy.org
Australian Music Therapy Association: www.austmta.org.au
British Society for Music Therapy/Association of Professional Music Therapists: www.apmt.org
Canadian Association for Music Therapy: www.musictherapy.ca
National Association of Korean Music Therapists: www.nakmt.or.kr
Nordoff-Robbins Center in the UK: www.nordoff-robbins.org.uk
World Federation of Music Therapy: http://wfmt.info/WFMT/Home.html

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Mutual Gaze

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Synonyms

Eye contact; Eye-to-eye gaze; Social gaze; Visual attention to eyes; Visual orienting to eyes

Definition

What Is It?

Mutual gaze occurs when two people make eye contact or look into each other's eyes. Mutual gaze is an important part of social communication and perception of others' emotion states and is the one of the foundational skills necessary in the development of joint attention (George & Conty, 2008; Morales, Mundy, Crowson, Neal, & Delgado, 2005; Saito et al., 2010; Senju & Johnson, 2009). Mutual gaze has been described as "the most powerful mode of establishing a communicative link between humans" (Farroni, Csibra, Simion, & Johnson, 2002).

When Does It Occur?

From birth, infants are innately motivated to gaze into their caregivers' eyes. In fact, the field of vision of newborns is approximately the distance required to make eye contact when held by an adult (Stern, Hofer, Haft, & Dore, 1985). Infants prefer to look at faces over other stimuli, especially faces that engage them in mutual gaze (Farroni et al., 2002). Eye-tracking studies have revealed that when looking at faces, even infants preferentially fixate on the eyes over other facial features (Mauer & Salapatek, 1976).

Mutual Gaze and ASD

One of the most prominent features of autism spectrum disorder (ASD) is an atypical pattern of eye contact and reduced levels of mutual gaze with social partners (Klienmann, Dziobek, Hatri, Steimke, & Heekeren,en 2010). Although reduced levels of gaze behavior at 6 months was not found to be predictive of autism diagnosis at 24 months (Young, Merin, Rogers, & Ozonoff, 2009), toddlers with autism do show abnormal gaze to the eye region and decreased shared affect (Chawarska, Volkmar, & Klin, 2010). Eye-tracking data for children with ASD have shown active avoidance of direct eye contact through increased gaze shifts away from the eye area (Klienmann et al., 2010). The DSM-IV-TR includes reduced eye contact as one of the symptoms of ASD: "*marked impairment in the use of multiple nonverbal behaviors (e.g. eye-to-eye gaze,...) to regulate social interaction and communication*" (American Psychiatric Association, 2000, p. 70).

There are currently four models that are used to explain the decreased levels of mutual gaze or eye contact in children with ASD:

1. *The affective hyperarousal model* which posits that gaze avoidance is an adaptive response for individuals with ASD who find focusing on the face and eyes of others to be strongly adversive

2. *The affective hypoarousal model* which posits that individuals with ASD experience hypoactivation of the amygdala, which interferes in the association of a positive social reward with making eye contact, resulting in reduced levels of eye contact

3. *The communicative intention detector model* that proposes that individuals with ASD engage in less eye contact because they do not understand the social salience of eye contact in understanding others' states

4. *The fast-track modulator model* which states that atypical eye contact in ASD could be caused either by an impairment in the subcortical face and eye contacting detecting route or in the network of cortical and subcortical structures specializing in the processing of social information (Senju et al., 2009)

See Also

▸ Eye Gaze

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Mutual Regulation

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Synonyms

Co-regulation; Emotion regulation; Emotional synchrony; Self-regulation

Definition

The construct of emotion regulation refers to "the extrinsic and intrinsic processes responsible for monitoring, evaluating and modifying emotional reactions" (Thompson, 1994). Important to this definition is the emphasis on both intrinsic and extrinsic processes, which may include both internal or self-driven processes and external or mother-driven support. This mother-driven support of the child's emerging emotional processes is co-regulation.

The development of emotion regulation is a process that occurs over the first years of life. Beginning in infancy, children learn to regulate emotions, attention, and behaviors through the external scaffold of mothers. The process gradually becomes an internal, self-driven process (Kopp, 1989). As children gain a greater ability to regulate these processes, they also show a greater ability to remain flexible while facing the ongoing social demands of their environment.

Mother-child interaction research has contributed to our knowledge of emotion co-regulation by emphasizing the dynamic and interpersonal nature of the construct. These studies have found that typical mothers and children are sensitive to each other's emotional states and that mothers regulate child emotional states by reading emotion signals and modulating child arousal (Field, 1994). In addition, work in this area has found that the quality of interpersonal regulation between mother and child predicts later social-emotional outcomes in the child, including self-control and social competence (Feldman, Greenbaum, & Yirmiya, 1999).

Several studies have begun to examine the development of emotion regulation in children with autism. Bieberich and Morgan (2004) employed parent report measures to examine emotion regulation outcomes. In another study, emotion regulation and temperament in children with autism spectrum disorder was measured by behavioral coding of maladaptive and adaptive regulation strategies during a mildly frustrating delay task. Results showed that children with autism employed less adaptive strategies and a greater range of strategies compared to typical controls (Konstantareas & Stewart, 2006). These findings are among the first empirical support for a specific disturbance in emotion self-regulation in children with autism.

A recent study explored the development of emotion co-regulation in young children with autism and their mothers within the context of an early social-communication intervention (Gulsrud et al., 2010). Results showed that children displayed significant distress in almost half of their interactions with their mothers, and these episodes of distress lasted on average 20% of the total length of the interaction. Children most frequently engaged in active strategies (tension release, avoidance, and distraction). Similarly, mothers most frequently engaged in active strategies (redirection of attention, prompting/helping, and physical strategies) during child negativity. These results suggest that both mothers and children are actively working together to regulate the child's emotions and that co-regulation is a viable construct for study in this population.

See Also

▶ Co-regulation
▶ Emotion Regulation
▶ Self-regulation
▶ Temperament

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Mutually Acceptable Written Agreement (MAWA)

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Definition

A "mutually acceptable written agreement" is a binding document that is the result of a mediation session. Mediation is a negotiation session, typically used as an informal alternative to the adversary system, facilitated by a neutral third party who tries to help the parties in the dispute to reach a mutually acceptable written agreement. The agreement can cover a wide range of issues including issues that would not be recognized in a court of law. There is some uncertainty as to whether a mutually acceptable written agreement is legally enforceable. Most states require that these agreements be reduced to writing and be signed by both parties, and many states require that the agreement be filed in court. Furthermore, there are often statutes that provide requirements for an agreement reached in a particular type of mediation setting. In the absence of legislation, one must look to common law contract principles as authority on whether the agreement is enforceable. These agreements may also be subject to agency law for the purpose of determining whether those entering into the agreement have the authority to do so.

See Also

▶ Consent
▶ Liability

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Myoclonic Spasms of Infancy

▶ Infantile Spasms/West Syndrome