Global Developmental Delay and Mental Retardation or Intellectual Disability: Conceptualization, Evaluation, and Etiology

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KEYWORDS

• Global developmental delay • Mental retardation
• Intellectual disability • Evaluation • Etiology

CONCEPTUALIZATION

Neurodevelopmental disabilities are a common problem collectively in child health that challenge primary and specialty medical practitioners at varying levels, including (1) early recognition, (2) accurate diagnosis, (3) appropriate evaluation, (4) determination of etiology, (5) securing needed interventions, (6) just resource allocation, and (7) predicting eventual outcomes.[1–4] Neurodevelopmental disabilities are a group of chronic clinically distinct disorders that all share a documented disturbance, quantitative, qualitative, or both, in developmental progress in one or more developmental domains compared with established norms.[5] These domains, although not mutually independent or exclusive, include (1) motor (gross or fine), (2) speech and language, (3) cognition, (4) personal-social, and (5) activities of daily living. Neurodevelopmental disabilities are divided into various subtypes essentially functioning as ''terms of convenience'' that quickly capture a group of children who share

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impairments and mandate a common approach to diagnostic evaluation, possible medical requirements, therapeutic needs, required interventions, and individual or family challenges to participation and integration.[6]

Ideally, neurodevelopmental disabilities are diagnosed over time rather than at a single point of clinical encounter. This diagnosis occurs against a backdrop of a highly individualized developmental trajectory that may not be smooth or consistent over time. Indeed, what is ''normal'' may have wide variation, and establishing a clear boundary line may be difficult in a particular individual case.[7]

''Global developmental delay'' refers to a disturbance in an individual child across one or more developmental domains.[8] Such a child has limitations or delay in the widespread acquisition of skills that is directly observable and measurable in the context of the natural progression of children. The use of this term reflects difficulties in agreeing on the objective measurement of intelligence and cognition in a consistent, reliable, and valid fashion in the young child (ie, less than 5 years of age). The most recent consensus definition considers global developmental delay as a disturbance across a variety of developmental domains that is defined operationally as a significant delay (meaning 2 or more standard deviations) lower than the mean on objective norm-referenced age-appropriate testing in two or more developmental domains. Typically, there is delay across all domains.

A multidimensional approach has been used to define ''mental retardation'' in the most recent consensus statement put forward in 2002.[9] According to that definition, mental retardation is conceptualized as ''a disability characterized by significant limitation both in intellectual functioning and in adaptive behavior as expressed in conceptual, social, and practical adaptive skills.'' Thus, the definition extends beyond the traditional concept of a general subaverage level of intellectual function as captured in the measurement of an ''intelligence quotient'' (IQ). Adaptive behavior was envisioned to include those skills that an individual must acquire to function within the context of the expectations of his or her everyday life. Within the framework of the International Classification of Functioning, Disability, and Health (ICF) model of health and disease, mental retardation is manifested by significant problems in (1) an individual's capacity to perform (ie, impairment), (2) the ability to perform (ie, activity limitations), and (3) the opportunity to function (ie, participation restrictions).[10] The disability that is mental retardation is lifelong and originates at an early age well before the age of 18 years.

This definition for mental retardation requires the awareness of certain contextual assumptions implicit in its definition. These include the following: (1) the limitations and functions are considered within the context of an individual's typical environment, (2) assessments used to yield a diagnosis of mental retardation are sensitive to and reflect varying linguistic and cultural diversity, (3) limitations that are necessary for diagnosis coexist with recognized strengths, (4) providing a profile of possible limitations envisions a spectrum of required supports for the individual, and (5) the quality of life for an individual with mental retardation can be improved by implementation of these envisioned supports.

More recently the term *intellectual disability* has emerged to replace that of *mental retardation*.[11] This change in terminology is reflected in the change in title of the American Association of Mental Retardation (AAMR) to the American Association on Intellectual and Developmental Disabilities (AAIDD). The term *intellectual disability* is thought to be synonymous with that of *mental retardation*, but its use is preferable because it reflects the recent change in our construct of disability and aligns better with the recent emerging emphasis on functional behaviors and contextual factors. A period during which both terms are used concurrently can be envisioned; however,

it can be foreseen that within the next few years, the term *intellectual disability* is likely to replace that of *mental retardation*.

As presently conceptualized, global developmental delay and mental retardation or intellectual disability represent predominantly clinically defined and recognized symptom complexes that are related but not necessarily synonymous.[12] Although the use of the term *delay* within global developmental delay suggests the possibility of maturational catch-up, the reality as revealed by recent longitudinal studies suggests otherwise.[13] Almost overwhelmingly, children meriting the diagnosis of global developmental delay in the preschool years, when reassessed later at school age, continue to meet diagnostic criteria for this particular entity. Indeed, many older children now diagnosed with mental retardation or intellectual disability were initially diagnosed on retrospective review with global developmental delay.[14] Thus, these entities share common features, and at their core, both represent defects or disorders in learning.[6] Thus, a common approach to their evaluation and understanding their etiology is used for the remainder of this particular article.

The diagnosis of global developmental delay and mental retardation or intellectual disability is often initially formulated based on clinical judgment rather than on formal standardized assessments.[6] Such judgment should be based on extensive direct experience with individuals who have these entities and should be validated by (1) direct observation, (2) reliance on reliable third-party informants, (3) input from an interdisciplinary team skilled in multidimensional assessments, and (4) the use of standardized tests of development and intelligence. Potential errors in measurement by these standardized tests have to be considered, and this is reflected in the concept of the standard error of measurement (SEM).[15] This refers to the observation that the score actually obtained on the application of a single test is not a precise one but is rather bounded by a zone of uncertainty or range of confidence. This implies that there should be some conceptual hesitation, or indeed reluctance, regarding applying these specific diagnostic constructs based on strict numeric cutoff points. This is especially so when the score obtained on a single test and its SEM span the actual cutoff point to be used. It is well recognized that the reliability and accuracy of a specific measure are increased by its repeated application over a longitudinal interval. This is especially noteworthy, given that any child's development is a dynamic process occurring over a trajectory that need not be consistently smooth or even.[7] A child's development and cognitive evolution frequently follows a path of rapid or abrupt acquisition of new skills followed by a period of practice and consolidation that may resemble a plateau to the external observer.

EVALUATION

The evaluation of the child who has a global developmental delay or mental retardation or intellectual disability is a time- and labor-intensive process. There are multiple objectives in this medical evaluation, and these include the following elements: (1) confirming and classifying the precise neurodevelopmental disability; (2) through history, physical examination, and selective laboratory testing, ascertaining a possible underlying etiology; (3) identifying and arranging for needed supports and rehabilitation service interventions; (4) counseling the family regarding the implications of the diagnosis from individual and familial perspectives, including a discussion of possible recurrence risks and possible outcomes; and (5) identifying possible intercurrent medical or behavioral conditions that may require specific medical or other interventions to optimize the realization of the child's full developmental and cognitive potential (ie, seizure disorders, attentional difficulties, sleep disturbances, spasticity, behavioral

disorders).[1,3,4,6] This detailed evaluation often requires input from several health professionals who provide complimentary expertise that ensures a complete and thorough evaluation. Frequently, it is these professionals, rather than the physician, who possess the skills and time available to apply standardized assessments that objectively document the child's developmental and cognitive deficits and serve to validate the physician's original clinical judgment. In addition to evaluation, these health professionals become partners in care provision and ideally assume responsibility for ensuring the implementation of goal-directed therapeutic interventions, on a short- and long-term basis, that optimize the child's potential and improve the overall quality of life for the child and family. In addition, more than one visit with the child and family is often necessary to ensure that one is not dealing with a progressive neurodegenerative process. A second visit also ensures the reliability of clinical, developmental, and cognitive assessments. In addition, a second visit is often an initial prerequisite to ascertaining the results of investigations requested and ensuring that appropriate service interventions have been implemented.

History

The evaluation of the child who has a global developmental delay or mental retardation or intellectual disability begins with a careful and detailed history. Of fundamental importance is the comprehensive family history that covers three generations and uses open-ended questions regarding the health and developmental status of family members. Oftentimes, specific neurologic disorders need to be suggested so that there is a full disclosure of important relevant conditions. The possibility of parental consanguinity needs to be probed for in addition to any previous familial neonatal or infantile deaths or maternal pregnancy losses. Ethnic heritage and geographic origin may also be clues to a possible underlying etiology and directed specific laboratory testing.

Much information needs to be obtained on the mother's pregnancy with the affected child. Adverse antenatal events, such as per vaginal bleeding, gestational diabetes, intercurrent infections, or medical conditions, should be asked about. Maternal prescription medication use or the use of tobacco, alcohol, or illicit drugs may have important implications on the developing fetus. The timing of labor, whether it was spontaneous or induced, its duration, mode of presentation, and the actual means of effecting delivery, need to be ascertained. Several specific questions need to be addressed regarding possible adverse events during the labor and delivery process, and these include detailing such items as meconium staining, abnormalities noted in fetal heart monitoring, and the indication for caesarean section if it occurred. Objective important parameters to be determined include the child's birth weight, activity, pulse, grimace, appearance, respiration (APGAR) scores (including those beyond 5 minutes if originally distressed); the duration of an infant's postnatal stay; and the occurrence of any relevant neurologic symptoms as a newborn. Answers to these questions may provide an important clue to timing the origin of a child's developmental difficulty to a prenatal or perinatal occurrence.

Subsequent to birth, the child's medical history, which includes possible hospital admissions, surgical procedures, chronic ongoing medical conditions, and current medication use, needs to be documented. Parental marital, custodial, and socioeconomic status, with the latter pertaining to employment and educational attainment, needs to be documented in addition to existing child care arrangements. Given the relevance of early psychosocial deprivation or disruption and its effect on child development, possible adverse early psychosocial situations, such as adoption, parental neglect, abuse, or removal of the child's care from a caregiver, have to be determined.

Current status with respect to the provision of rehabilitation services would be a helpful guide in determining what services still remain to be obtained.

Once this background is obtained, the child's developmental history can be placed into its proper individual, familial, and social context. The precise developmental domain and the age of the child for initial parental concern regarding developmental difficulties should be elicited. Developmental progress in each of the specific developmental domains should be established by asking questions regarding key motor and language milestones (**Table 1**). To assist in this solicitation, it may be necessary to ask the parents about a child's specific developmental status at a certain milestone age (ie, first or second birthday). Although not encouraged, it may be helpful to have the parents compare the child under evaluation with their other children regarding the pace of skill acquisition over time. One needs to determine specifically if there has been any loss of function or developmental skills. Current developmental performance in each domain needs to be ascertained in addition to performance with respect to key activities of daily living, such as toileting, dressing, feeding, and self-hygiene in the older child.

Given their high frequency, one should carefully probe for any possible coexisting autistic features, such as poor eye contact, emotional inappropriateness, the desire for repetitive play or sameness, and inappropriate social interactions with respect to emotional cues.[16] In addition, possible comorbid paroxysmal behaviors, disruptive sleep disturbances, significant behavioral concerns, and feeding difficulties should be sought for.

Table 1
Guide to early child development and functional milestones

Age	Motor	Language	Social/Play
2 months	Head up in prone	—	Smiles, fixes, and follows
3 months	Head/chest up in prone, grasps placed object	Coos	Laughs
4 months	Rolls, reaches	—	—
6 months	Sites with support, weight bears	Babbles, turns to sound	Mouthing objects
8 months	Sites without support, weight bears	Turns to name	—
10 months	Pincer grasp, starting to cruise, crawling	"Bye-bye" wave	Drinks from cup
12 months	Walks but falls easily	First words	Finger feeds, objects in and out of containers
15 months	Walks steadily, scribbling	Pointing, multiple single words	Spoon use, assists in dressing
18 months	Up/down stairs with assistance, climbs, throws ball	Two-word phrases, pointing to body parts	Builds towers, plays with others
24 months	Up/down stairs, one step at a time, kicks ball	Three-word phrases, pronoun	—

Data from Shevell MI. Office evaluation of the child with developmental delay. Semin Pediatr Neurol 2006;13:256–61.

Physical Examination

The second phase in the evaluation of the child who has a global developmental delay or mental retardation or intellectual disability is the physical examination. This examination consists of a formal component and a less formal observational component. The formal component consists of a general physical and neurologic examination. The general physical examination includes the measurement of height and weight and plotting their relevant percentiles. There should be a careful search for dysmorphic features, which need to be considered within the context of familial and ethnic variation. The child must be undressed completely, and the skin must be carefully examined for possible stigmata of a neurocutaneous disorder, such as a hypomelanotic macule or a café-au-lait spot. The abdomen should be palpated for possible enlargement of the liver or spleen, which can be suggestive of a storage disorder, and the spine should be examined carefully for any defects or overlying cutaneous abnormalities that may suggest a myelodysplasia.

An essential yet often overlooked element of the neurologic examination is the obtaining of the occipital frontal head circumference, which is then plotted to yield an age- and gender-appropriate percentile. Documented macrocephaly (head circumference greater than the 98th percentile) or microcephaly (head circumference less than the second percentile) then mandates obtaining and plotting the head circumference measurements of available parents and siblings and obtaining prior measurements for the affected child and then plotting the evolution of head circumference percentiles over time. The formal neurologic examination then consists of cranial nerves, which includes ascertaining if there are any visual field defects, pupillary abnormalities, funduscopic changes, nystagmus, facial paresis, excessive drooling, dysphasia, dysarthria, or head tilt. The motor component of the neurologic examination focuses on the detection of any asymmetries or possible lateralizing features with respect to muscle bulk, strength, tone, stretch reflexes, and plantar responses. Through observation, the quality of limb movements should be determined, and any dyskinesias, such as tremor, dysmetria, dystonia, athetosis, or chorea, should be documented. If ambulatory, the gait of the child should be observed and described in detail if abnormal. A good noninvasive assessment of possible proximal muscle weakness is to observe the child getting up from a supine position (ie, Gower sign) or squat or by going up or down adjacent stairs, and, in the upper limbs, by reaching above shoulder height. Tests of manual dexterity include throwing and kicking a ball, jumping in place, or hopping on one foot.

The neurodevelopmental assessment is the largest component of the physical examination in this particular clinical setting. Much of this assessment can take place by observation during the extended history-taking initial portion of the patient or family encounter. This observation can be facilitated by providing a child-friendly environment that has much in the way of the availability of age-appropriate playthings. Through observing the child's interaction with these playthings, the developmental level in various domains can be assessed in a detached and nonthreatening manner. In so doing, the child can be reassured and made comfortable in what may be an initially threatening environment for many children. It is helpful to maintain a reassuring physical proximity between the child and his or her caregiver. Indeed formal examination can frequently take place when the child is sitting on the caregiver's lap. Even for the preverbal child, it is reassuring and comforting to explain in advance the sequence of what is going to be done as it unfolds and to defer to the end of the examination any direct physical manipulation of a body part.

The observational neurodevelopmental examination is frequently complimented by a more formal developmental assessment. This involves the ascertainment of

language skills by identifying pictures, body parts, colors, shapes and exploring possible story-telling capabilities and the grasp of more abstract concepts and analogies. Spontaneous speech and the response to direct questions provide the ability to assess a child's vocabulary content in addition to grammatic and semantic capabilities. Comprehension can be assessed by progressively increasing complex commands put forward by the examiner or by the caregiver. Cognitive skills are an extension of language testing and can be evaluated by the child's grasp of specific concepts (ie, small or big, short or long, open or close, over or under) by the response to direct questioning or commands and by exploring a child's grasp of analogies or the use of objects. Gross motor skills are usually best assessed by direct observation, gait analysis, the ascent and descent of stairs, and ball playing. Fine motor skills are best assessed through the use of blocks or, in the older child, by specific pen and paper tasks, such as a copying various shapes or drawing a figure. Capabilities with respect to activities of daily living are best determined by direct questioning of the caregiver.

Laboratory Investigation

The heterogeneous nature of global developmental delay and mental retardation or intellectual disability, together with the wide-ranging profile of underlying etiology and the extensive range of possible laboratory investigations to be undertaken, is a particular challenge for the individual practitioner. Fortunately, to guide the practitioner, recent guidelines have emerged from a variety of different professional sources. These sources include the American College of Medical Genetics,[17] the American Academy of Neurology/Child Neurology Society,[6] and the American Academy of Pediatrics.[18] These guidelines and consensus statements are based on expert opinion, together with a thorough review of the available published literature. All these guidelines emphasize a selective rational approach that is individualized to the particular context of the child and family under evaluation. No ''one size fits all'' algorithm has yet been formulated, nor can one be reasonably anticipated in the near to intermediate future.

If, after a detailed history and physical examination, a specific clinical diagnosis is suspected, laboratory investigations should selectively target this clinical suspicion.[6] Thus, if there is evidence for possible intrapartum asphyxia, neuroimaging should be undertaken; if a specific genetic syndrome, such as Prader Willi or Angelman syndrome, is suspected, a targeted fluorescent in situ hybridization (FISH) probe should be ordered; or if there is suspicion of fragile X syndrome, FMR1 triplet repeat testing should be requested.[17,18] The evidence strongly suggests that in the absence of a clinical diagnosis after history and physical examination, routine screening of all individuals with global developmental delay and mental retardation or intellectual disability with high-resolution banding karyotyping, FMR1 triplet repeat testing, and neuroimaging may yield an underlying etiology in approximately one sixth of cases.[6] Genetic testing with high-resolution banding karyotyping and FMR1 triplet repeat testing is indicated even in the absence of apparent dysmorphic features, although the etiologic yield is appreciably increased if dysmorphic features are recognized on examination.[6] The etiologic yield of neuroimaging is also enhanced by the presence of neurologic findings (ie, microcephaly, lateralizing asymmetries), with MRI preferable to CT when it is readily available.[6] Of particular note is that the yield on various laboratory investigations tends not to be affected by the degree of global developmental delay or mental retardation or intellectual disability, nor does it tend to be different between the genders.[6]

At present, unselected metabolic screening cannot be justified in the context of global developmental delay or mental retardation or intellectual disability based on recent reviews.[6,17–19] A yield of 1% or less has been found, with a higher yield reported in targeted screening of highly inbred populations.[20] This is especially so in the context of a geographic locale in which routine newborn metabolic screening is undertaken. Clinical clues have been recognized suggesting that metabolic screening may be warranted to detect an apparent inborn error of metabolism. These clinical clues include (1) a prior family history of a similarly affected child; (2) parental consanguinity; (3) documented developmental regression; (4) episodic decompensation; (5) suggested dysmorphology, which may include the involvement of non–ectodermal-derived organ systems; (6) failure of appropriate growth; and (7) various ophthalmologic and retinal abnormalities. Nonscreening as a newborn may also lower the threshold for metabolic screening, as does neuroimaging findings of basal ganglia involvement in the absence of any evident intrapartum asphyxia or unexplained white matter changes. Metabolic screening typically involves capillary blood gas, lactate, ammonia, liver function studies, serum amino and urine organic acids, serum carnitine levels, and very-long-chain fatty acids. In addition, the clinical availability of a complete set of FISH probes that target the subtelomeric regions of each chromosomes has yielded abnormalities even if routine karyotyping at a high-resolution level has been normal.[21,22] Microarray comparative genomic hybridization, which measures copy number changes in DNA sequences in small segments over the entire genome (ie, deletions, duplications), has also yielded positive results with prior normal karyotyping documented in the clinical context of global developmental delay or mental retardation or intellectual disability.[23–25] These technologies can be expected to have increasing clinical availability and application and may even supplant routine high-resolution karyotyping in the near future.

Routine molecular testing of various genes involved in neuronal and synaptic function is not yet available on a clinical basis. Clinical suspicion of a possible underlying etiology, such as Rett syndrome, or atypical features of a known syndrome may prompt targeted molecular testing, however.[18] These specialized and targeted studies are best undertaken in conjunction with the input of a clinical geneticist or neurogeneticist.

The high frequency of associated sensory impairments in the context of global developmental delay and mental retardation or intellectual disability mandates vision and hearing screening. Hearing screening requires auditory evoked response testing or formal audiometric assessment.[26] Vision screening usually requires the input of an ophthalmologist.[27] In addition to auditory evoked responses, electrophysiologic studies are indicated in certain particular situations.[6] Somatosensory evoked responses (four limbed) should be considered when there are lateralizing neurologic findings or the suggestion of an underlying myelodysplasia. Visual evoked response testing is indicated in the context of possible retinal or visual processing abnormalities. Electromyography or nerve conduction study is warranted when there is a clinical suspicion of peripheral neuromuscular involvement or neuroimaging evidence of central white matter involvement. Electroencephalography should be reserved for those situations in which there is a clinical suspicion of a paroxysmal disorder that may be epileptic or convulsive in nature.

ETIOLOGY

Etiology can be conceptualized as ''a specific diagnosis that can be translated into useful clinical information for the family, including providing information about

prognosis, recurrence risk, and preferred modes of available therapy."[28] This conceptualization is a pragmatic and practical one that is directly relevant to the questions posed by the concerned family regarding their child who has a global developmental delay or mental retardation or intellectual disability.[29] The high compliance of parents with requested, often invasive, investigations suggests considerable familial motivation to understand the reason behind their child's developmental disability. Finding out a reason often has important implications with regard to future family planning and rendering more reasonable familial expectations regarding their child's future developmental trajectory.

The literature is replete with several studies reporting wide variations in the etiologic yield for children who have a global developmental delay or mental retardation or intellectual disability.[19,30–34] These variations reflect differences in sample population characteristics, the method of classification, and diagnosis of neurodevelopmental disability in addition to the availability of genetic and imaging technology and its consistent application to the individual affected child. More recent retrospective and prospective studies have reported an etiologic yield usually around 50%. The top etiologic categories representing approximately three quarters of all etiologic diagnoses made include (in descending order of apparent frequency) (1) genetic syndrome or chromosomal anomalies, (2) intrapartum asphyxia, (3) cerebral dysgenesis, (4) early severe psychosocial deprivation (ie, attachment disorder, removal from the family home), and (5) antenatal toxin exposure (ie, alcohol or multidrug).

Studies have shown that roughly one third of etiologic diagnoses are made subsequent to history and examination alone.[30] In a further third, laboratory testing is used to confirm a diagnosis suspected on the basis of history and examination, and in the remaining third (roughly one sixth overall), etiologic diagnosis is made on the basis of laboratory testing alone, usually undertaken on a screening basis. Success in finding an underlying etiology may be enhanced by certain clinical and physical examination findings, such as the absence of coexisting autistic features, an abnormal prenatal or perinatal history, microcephaly, or an abnormal formal neurologic examination. In addition, neurologic findings and microcephaly enhance the yield on neuroimaging studies, whereas dysmorphology enhances the yield on cytogenetic and molecular genetic studies. In addition, it has been noted that the determination of an underlying etiology frequently has implications with respect to recurrence risk estimation and the modification of ongoing medical management and therapeutic imperatives for a particular child.

Roughly 10% of children who have a global developmental delay or mental retardation or intellectual disability have an underlying associated cytogenetic abnormality.[18,35] In roughly 40% of these children, their neurodevelopmental disability was thought to be originally nonsyndromic in that no dysmorphic features were apparent. An equal percentage has had three or more dysmorphic features on formal dysmorphologic examination. Indeed, one study demonstrated that the dysmorphologic examination was contributory to diagnosis in roughly four fifths of cases and essential in almost two thirds. Using comprehensive FISH techniques to detect submicroscopic telomeric rearrangements, which represent approximately half of all structural chromosomal abnormalities, has led to an etiologic diagnosis in approximately 7.5% of children who had routine cytogenetic studies previously.[21] Yields on such subtelomeric studies can be improved by using a five-item checklist that emphasizes the presence or absence of particular clinical features.[36] Similarly, recent studies on various microarray comparative genomic hybridization techniques have also yielded an additional approximately 7% detection rate in children with previously negative results, which have included detailed clinical assessment,

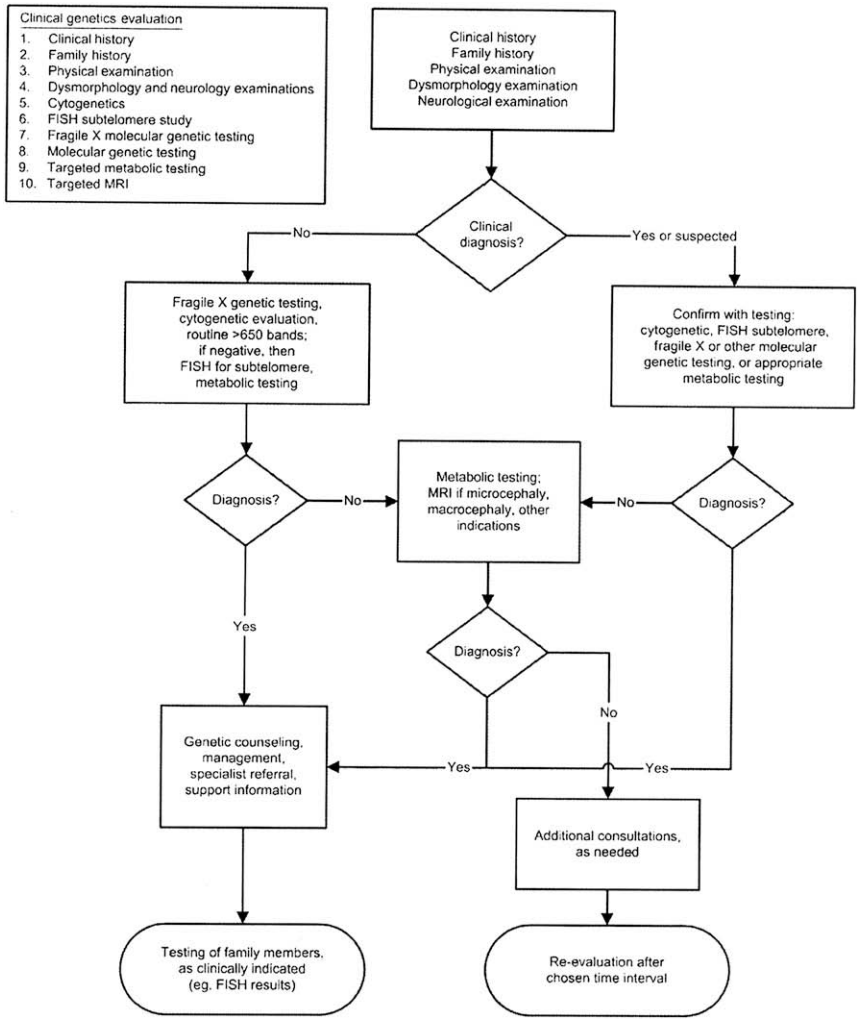

Fig. 1. Approach to the clinical genetics evaluation for developmental delay/mental retardation. (*From* Moeschler JB, Shevell MI, Committee on Genetics. Clinical genetic evaluation of the child with mental retardation or developmental delays. Pediatr 2006;117:2307; with permission.)

cytogenetic studies, and neuroimaging.[25] In the most recent study on this particular target population, this yield was apparent in children who are nonsyndromic and nondysmorphic in appearance.

Originally, reports on neuroimaging did not note any added value in terms of etiologic yield.[37] Advances in neuroimaging capability have clearly been paralleled by an added value in detecting acquired injury of various causes, unsuspected cerebral dysgenesis that may be subtle, or disturbances in white matter maturation, however.[38] Indeed, certain studies have noted that advanced neuroimaging techniques, such as MRI, are useful for detecting abnormalities in up to 50% of children who have a neurodevelopmental disability.[6] Proton magnetic resonance spectroscopy (MRS) provides the mechanism of measuring the biochemistry of the brain on a regional basis and is

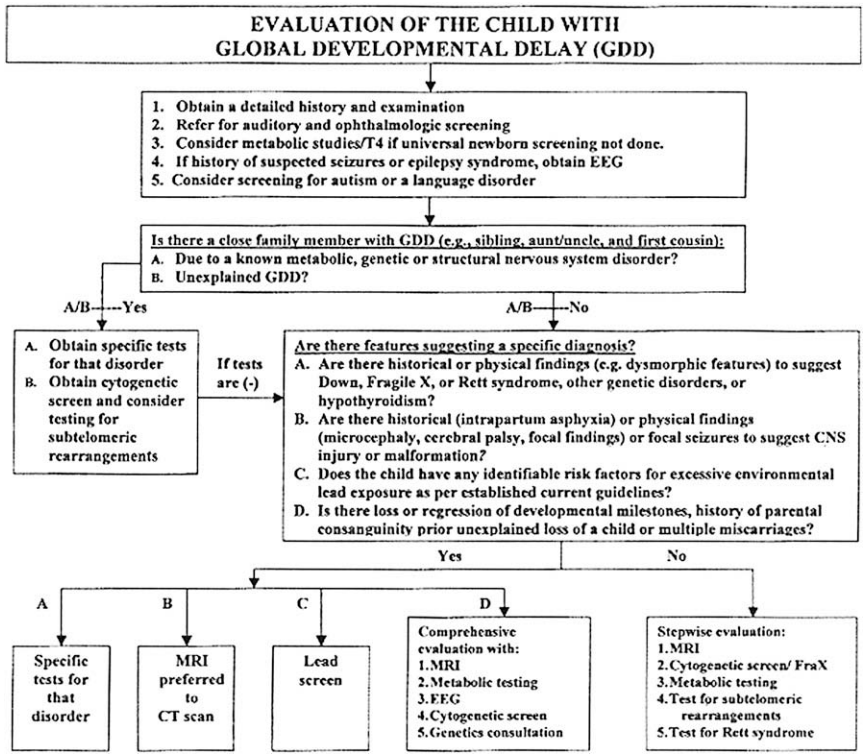

Fig. 2. Algorithm for the evaluation of the child who has a developmental delay. Audiologic and ophthalmologic screening is recommended in all children who have a global developmental delay. Metabolic studies usually consist of obtaining a urine organic acid screen, quantitative serum amino acids, serum lactate and ammonia levels, capillary or arterial blood gas, and thyroid function studies. CNS, central nervous system; EEG, electroencephalography; FraX, fragile X syndrome. (*From* Shevell MI, Ashwal S, Donley D, et al. Practice parameter: evaluation of the child who has a global developmental delay. Neurology 2003;60:376; with permission.)

useful in the diagnosis of certain genetic and metabolic conditions.[6] Advances in neuroimaging, specifically diffusion tensor imaging (DTI), which permits approximating the position and direction of major white matter tracts in the central nervous system, should refine our ability to detect more subtle abnormalities that underlie global developmental delay and mental retardation or intellectual disability at an etiologic level.[6]

SUMMARY

Global developmental delay and mental retardation or intellectual disability offer challenges to the practitioner at several different levels. Accurate recognition of these most common of subtypes of neurodevelopmental disabilities is a central precondition to their correct evaluation and management. Proper evaluation is a time- and labor-intensive process that emphasizes several different goals. This evaluation should not take place in professional isolation and often requires the input of a variety of additional medical and rehabilitation professionals. The question of why a particular child has a neurodevelopmental disability is an important one that should always be posed

at least once for each child, and every reasonable attempt needs to be made to answer this question using available investigations in a rational and selective way. Guidelines now exist to assist the practitioner in selecting the appropriate investigation path to be pursued, and these guidelines should be used to inform the selections of investigations made (**Figs. 1** and **2**).[8,18] These guidelines are simply suggestions to improve evaluation. They are not invariable constraints that ''hardwire'' the medical professional's response to the individual child who has a global developmental delay or mental retardation or intellectual disability. Although challenging and time consuming, the evaluation of these children offers many professional rewards and is a necessary first step in a family's adaptation to their child's chronic condition, for which a ''quick fix'' is almost never available.

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