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Mathematical Learning Disabilities in Special Populations: Phenotypic Variation and Cross-Disorder Comparisons

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Abstract

What is mathematical learning disability (MLD)? The reviews in this special issue adopt different approaches to defining the construct of MLD. Collectively, they demonstrate the current status of efforts to establish a consensus definition and the challenges faced in this endeavor. In this commentary, we reflect upon the proposed pathways to mathematical learning difficulties and disabilities presented across the reviews. Specifically we consider how each of the reviews contributes to identifying the MLD phenotype by specifying the range of assets and deficits in mathematics, identifying sources of individual variation, and characterizing the natural progression of MLD over the life course. We show how principled comparisons across disorders address issues about the cognitive and behavioral co-morbidities of MLD, and whether commonalities in brain dysmorphology are associated with common mathematics performance profiles. We project the status of MLD research ten years hence with respect to theoretical gains, advances in methodology, and principled intervention studies.

Keywords

mathematical learning disabilities; dyscalculia; math disabilities; cognitive phenotypes

DEFINING THE PHENOTYPE

What is mathematical learning disability (MLD)? The papers in this special issue adopt different approaches to defining the construct, and in so efforts to establish a consensus definition. The papers in this special issue contribute significantly to identifying the MLD phenotype in a variety of developmental disorders, by specifying the range of assets and deficits in math, considering whether individual variation represents error variance or principled phenotypic differences, and characterizing the natural course progression of MLD over the life course. An additional outcome of this special issue is that, collectively, the papers contribute to efforts to differentiate MLD from the broader construct of mathematical difficulties (MD) associated with a range of cognitive and socio-cultural influences. They also demonstrate some of the challenges that we face when classifying children as having mathematical learning disabilities.

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Assets and Deficits in Math

While deficits in math are central to MLD, it is also important to study those math skills that are intact. Variations in the patterns of assets and deficits demonstrate how dissociable skills in mathematics may be from one another, which facilitates identification of unique and related mathematical processes, thereby identifying the varied routes to MLD. The papers in this special issue contribute to a fuller delineation of assets and deficits (both absolutely, in terms of comparisons with typically developing children; and relatively, in terms of an individual's own profile) in each of a variety of conditions.

Children with 22q11.2 deletion syndrome (22q11DS) show considerable difficulties in mathematics that involve impairments in procedural calculation, math word problem solving, and understanding and representing numerical quantities despite preserved math fact retrieval [see De Smedt et al., 2009]. Children with spina bifida meningocele (SBM) demonstrate relative strengths in basic number knowledge, and weaknesses in single digit arithmetic, counting strategies, geometry, estimation, and word problem solving [see English et al., 2009]. Girls and women with Turner syndrome show age appropriate number comprehension and processing skills, including magnitude judgments and single digit arithmetic, yet are slower than their peers on many of these tasks, and are both slower and less accurate than their peers on complex calculations and numerical estimation [see Mazzocco, 2009]. Compared to their peers, females with fragile X syndrome are as quick and as accurate when performing tasks such as reading numerals, reciting common math facts, and naming decimals, but show weak numerical understanding [see Murphy, 2009]. In persons with Williams syndrome, the pattern of assets and deficits varies with development such that abstract representations of quantity appear intact during infancy and yet fail to show the typical developmental trajectory during childhood, whereas preverbal approximate number skills are deficient throughout the life course [see O'Hearn and Luna, 2009].

In other developmental disorders, a profile of math strengths and weaknesses is less clear. Math deficits in children with NF-1 include math calculations and math word problems [see Moore, 2009]. However, because some children with NF-1 have highly developed math skills, there is no apparent group pattern of relative or absolute assets and deficits. Math deficits (whether measured by absolute age-based standings or by discrepancy with intelligence) are apparent in children with very low birth weight or very preterm birth (VLBW/VPTB) on a range of math tasks, even when excluding children with mental retardation or neurosensory disorders [Taylor et al., 2009].

In some developmental disorders, MLD is accompanied by reading deficits [such as in fragile X syndrome, see Murphy, 2009], whereas in a number of other disorders, deficits in math are disproportionately greater than those in reading. In both children and young adults with SBM, math skills are poorer than reading skills [English et al., 2009]. Children with VLBW/VPTB have more pronounced impairments in math than in reading [see Taylor et al., 2009]. Children with 22q11DS show considerable difficulties in math, despite relatively normal reading [De Smedt et al., 2009], and girls with Turner syndrome have mathematical difficulties despite reading skills that are often above average [Mazzocco, 2009]. In both fragile X and Williams syndromes, although reading levels are impaired commensurate with moderate developmental disabilities reported for this population, deficits in mathematics contrast with relatively intact verbal skills, and children with either syndrome have a relative strength in reading numerals compared to intelligence quotient (IQ)-matched peers [Murphy, 2009; O'Hearn and Luna, 2009]. Collectively, children with NF1 exhibit the full range of performance levels for verbal and mathematics skills [see Moore, 2009].

Individual Differences in MLD Within Conditions: Error Variance or Principled Phenotypic Differences?

The mathematical skills phenotype within each of the developmental disorders studied is characterized by considerable individual variability. Mathematical abilities in children and adolescents with NF-1 are highly variable, and this variability is expressed over the full range of ability; that is to say, children with NF-1 may have either poor or superior math skills [see Moore, 2009; Mazzocco, 2001]. Likewise, some children with extreme degrees of VLBW/VPTB function well academically despite high-risk birth [Anderson and Doyle, 2003]. In this respect, variability in math in NF-1 is unlike that in 22q11DS, SBM, or Williams, fragile X and Turner syndromes, in which superior math performance is not typically observed.

Significant individual differences might initially suggest that it is not group membership in the developmental disorder that produces MLD. Of itself, this would not entail that individual differences represent error variance or problems in measurement. As a group, children with SBM have attenuated inhibition of return whereby (unadaptively and unlike typically developing children) they repetitively orient to the same location [Dennis et al., 2005]; as individuals, attenuated inhibition of return is related, not to group membership, but to the presence of a specific midbrain anomaly that is one of the common neuroanatomical stigmata of the condition. For inhibition of return, individual differences seem to be principled, not random, and related to neuroanatomical variation in the disorder.

Individual differences in math have also been related to variations in the genetic and brain features of different developmental disorders. In NF-1, physical and cognitive variability has been related to variability in DNA sequences in the NF-1 gene [Moore and Slopis, 2008]. In SBM, physical variability (in mobility) and cognitive variability have been related to the level of the spinal cord lesion [Fletcher et al., 2005], which in turn is associated with mutations in the genetic regulation of the folate metabolic pathways [Volcik et al., 2000]. For fragile X syndrome, which results from a single gene mutation [Verkerk et al., 1991], variability of cognitive impairment is associated with X-inactivation levels that, in turn, influence expression of this gene and its associated protein [Bailey et al., 2001]. There are several influences on the variation observed for the physical and cognitive phenotype of Turner syndrome, including karyotype characteristics [Davenport et al., 2007], specific haplotypes resulting from partial deletion karyotypes [Ross et al., 2000], maternal versus paternal origin of the intact X chromosome [Cutter et al., 2005] and sex hormone levels throughout development (as reviewed by Ross et al. [2006]). What is not yet clear is whether and how MLD is part of the systematic variability associated with these and other factors in these disorders.

Factors related to poorer math outcomes have been well specified in children with VLBW or VPTB, and include lower birth weight and gestational age, neonatal complications, and abnormalities in brain structure [Taylor et al., 2009]. Because these factors are also associated with outcomes in other areas of achievement, their specificity to mathematics is unclear. The specificity question also arises in evaluating the impact of factors associated with poverty, as discussed by Jordan and Levine [2009].

The Natural Course Progression of MLD Over the Life Course

A life course approach to mathematics ability and MLD is difficult to implement, and the approaches adopted to date have sometimes been typological (e.g., establishing whether a “classification of nonverbal learning disabilities” holds in adult life as well as in childhood [Tsatsanis and Rourke, 2008]). The papers in the special issue contribute importantly to understanding the life course phenotype of MLD in developmental disorders, showing that

number deficits frequently appear early, generally project a history of later math deficits, and typically develop into a lifetime of math disability.

English et al. [2009] make both cross-sectional and longitudinal contributions to specifying the MLD phenotype over the life course. Reviewing cross-sectional studies, they show that poor math characterizes preschoolers, school-aged children, and young adults with SBM. Compared to age peers, preschoolers with SBM have less well developed understanding of one to one correspondences, are less skilled at rote counting, and are less able to match on the basis of quantity. Compared to age expectations, young adults with SBM exhibit difficulty with computation accuracy and speed, problem solving and functional numerosity. Reporting on a longitudinal study of infants with SBM followed for 8 years, these authors identify cognitive predictors of math outcomes at 5 and 7 years of age, and also show that the longitudinal predictors of math are different from those of reading.

Murphy [2009] and Mazzocco [2009] both draw similar inferences from longitudinal studies of fragile X and Turner syndrome, respectively. Each of these X-chromosome related disorders demonstrates a risk for MLD evident by the early school years and persisting through elementary and middle school. Cross-sectional data indicate life long mathematical challenges well into adulthood. The trajectory of math and working memory skills of girls with fragile X differs from that of their peers, but working memory predicts math achievement and growth in math performance over time for both groups; rote skills appear to be a strength throughout the school years Murphy [2009]. Among girls with Turner syndrome, rates of growth on math and related skills, such as working memory and rapid naming, are slower than that of their peers, and typically rote tasks remain more effortful for girls with Turner syndrome throughout the school years [Mazzocco, 2009].

Some life course math difficulties are expressed as a failure to make age-appropriate developmental changes. In children with Williams syndrome [O'Hearn and Luna, 2009], intact preverbal numerical acuity skills fail to develop along the typical trajectory, and thereby interfere with math learning by the school age years.

Mathematics deficits in VLBW/VPTB cohorts are evident from the early school-age years and persist into adolescence and young adulthood. Several cross-sectional and longitudinal studies of VLBW/VPTB [Taylor et al., 2009] indicate that cognitive abilities in early childhood skills predict later math function in childhood and in adolescence; studies of longitudinal changes in math have suggested stability of deficits from age 11 to adolescence as well as increased deficits from age 8 to adolescence [Taylor et al., 2009].

CROSS-DISORDER COMPARISONS

The diversity of disorders addressed in this special issue provides not only descriptive information about these different conditions, but also the opportunity to make principled comparisons across disorders. These comparisons address a number of issues, including whether cognitive and behavioral comorbidities across conditions provide clues about the pathways to MLD, and whether commonalities in brain dysmorphology are associated with common math profiles.

There are many challenges in making cross-disorder comparisons. One is that, for a given mathematics skill, developmental disorders have been evaluated at different discrete points along what is actually a continuum. Another is the difficulty of establishing clear definitions for constructs used to describe mathematics skills, such as *number sense*.

Consider the continuum from subitizing to enumeration. Individuals with 22q11DS can subitize and enumerate small sets but experience difficulty enumerating larger sets [De

Smedt et al., 2009], suggesting difficulty with formal number skills. Children with SBM have immature counting strategies that include counting up, suggesting a related difficulty [English et al., 2009]. Women with Turner syndrome revert to counting earlier (that is, for smaller quantities) than their peers [Bruandet et al., 2004], suggesting difficulty with more automatic, informal number sense and reliance on a more controlled process of counting.

Studies making direct comparisons of the basic processes involved in number sense across disorders would help evaluate the plausibility of these interpretations and establish whether a deficit in number sense is common to all three conditions. Moreover, such studies may help differentiate this particular referent of the term from more formally acquired number knowledge skills, which are often also referred to as number sense by some researchers and educators [see Berch, 2005 for a detailed discussion of these very different interpretations]. The range of skills allegedly subsumed in the number sense construct is illustrated by the different types of number sense tasks referred to throughout the papers in this special issue. An equally wide-ranging set of tasks is evident among number sense testing batteries and intervention programs proposed to date [e.g., Griffin, 2007; Jordan et al., 2008; Lawson, 2008].

Cognitive and Behavioral Comorbidities Across Conditions

Children with MLD have a range of cognitive deficits and co-morbid behavioral disorders, raising the question of how these cognitive and behavioral co-morbidities are related to mathematics. We will consider how the papers in this special issue bear on this topic, using as examples one (albeit, very broad) domain of cognitive deficit (spatial disability) and one behavioral co-morbidity (attention disorder).

In some subtyping schemes [Geary, 1993; Rourke, 1993], mathematical difficulties of children with MLD are related to difficulties in spatial representation, and hence, to spatial deficits. According to English et al. [2009], children with SBM provide little support for this view, although the validity of this conclusion could well be dependent on how this relationship is assessed: Visual-spatial skills account for very little of the variance in single-digit arithmetic for children with SBM with math but not reading difficulties; and in multi-digit arithmetic tasks, these children do not commit a disproportionate number of visual-spatial or visual monitoring errors involving misreading or miswriting numbers, crowding written work, or spatial misalignment of numbers in columns. Spatial deficits do not predict math in girls with fragile X syndrome [Mazzocco, 1998], and the spatial types of errors described above occur more frequently in girls with Turner syndrome relative to girls with fragile X syndrome but not relative to the general population. Even so, spatial and mathematics scores are frequently uncorrelated with one another in girls with Turner syndrome. In contrast, spatial ability is highly predictive of academic achievement in reading and math calculations in children and adolescents with NF-1 [Moore, 2009]. Spatial deficits also predict mathematics problems in children with 22q11DS [De Smedt et al., 2009; Simon, 2008]. Among other cognitive deficits, spatial problems are associated with math deficits in children with VLBW/VPTB [Taylor et al., 2009].

Spatial deficits predict mathematics scores in some but not all developmental disorders. To be sure, *spatial deficits* is a term that covers a range of complex, sometimes language-driven tasks, and has not been investigated across developmental disorders using the well-operationalized basic processes envisioned by current researchers studying the commonalities of space, time, and number [e.g., Simon, 2008]. For the moment, *spatial deficits*, referring to a range of complex tasks, cannot be shown to represent a single common pathway to math disability, but as the papers in this special issue illustrate, the lack of support for this pathway may result from how spatial skills are conceptualized and measured.

Geary's [1993] earliest rendering of this subtype characterized spatial deficits primarily in terms of *behavioral* or *performance* features, such as misaligning numbers when setting up multidigit arithmetic problems. However, his more recent delineation of spatial deficits has focused predominantly on the spatial *representation* of numerical magnitude information as arrayed along the mental number line [Geary and Hoard, 2005]. Additionally, Geary et al [2008] have provided compelling evidence that children with idiopathic MLD are comparatively poor at estimating number placements in a linear fashion along a physical number line, which may be attributable in part to difficulty inhibiting primitive, logarithmically-spaced number-magnitude representations when having to make linear placements. Concomitantly, others [e.g., Simon et al., 2008] have expanded on the spatial subtype as consisting of a form of spatial *attention*. Consequently, it must be recognized that evidence regarding the role and importance of spatial deficits in the mathematical difficulties exhibited by children with neurodevelopmental disorders is highly dependent on the nature and definition of the spatial component(s) at issue, the underlying theoretical perspective, and the measures of the spatial constructs employed in a particular study.

Several of the developmental disorders addressed in this special issue report difficulties in attention, in addition to, and/or related to, deficits in math. It is useful to articulate the various forms of inattention associated with the different disorders. For example, NF-1, fragile X syndrome, Turner syndrome, VLBW/VPTB, 22q11DS, and SBM are each associated with poor attention. For NF-1, there is some suggestion that the mechanism of attention deficit is dopaminergic, which would be consistent with the presence of hyperactivity as part of the attention profile [Moore, 2009]. For SBM, dopaminergic-mediated attention functions appear to be essentially intact, there is only a 2% incidence of hyperactivity, and the attention deficit is related to stimulus orienting, not response control [Dennis et al., 2008]. For 22q11DS, the attention profile involved deficient spatial orienting [Simon, 2008], which appears more similar to attention deficits in SBM than to those described in NF-1. The nature of attention problems in children with VLBW/VPTB has been less fully identified.

On the face of it, it is unlikely that different biological and behavioral manifestations of attention deficits would bear the same relation to MLD across disorders. However, in order to address the role of attention as a pathway to MLD, it will be necessary first to articulate a model of attention, including components related and unrelated to mathematics, and compare these components across disorders.

Are Commonalities in Brain Dysmorphology Associated with Common Mathematics Ability Profiles?

Laterality appears to have a principled relation to mathematical abilities in children, with left-sided brain lesions or activation being more relevant for math than right-sided lesions or activation. Recent studies in typically developing children have implicated left-sided white matter tracts in mathematical skills. van Eimeren et al. [2008] conducted diffusion tensor imaging (DTI) on typically developing 7 to 9-year-old children and measured their math skills, finding that the left superior corona radiata was associated with numerical operations and math reasoning and fractional anisotropy in the left inferior longitudinal fasciculus was specifically correlated with numerical operations. Individuals with SBM have reduction in white matter volumes and developmental compromise of key white matter tracts, including the inferior longitudinal fasciculus [Fletcher et al., 2005; Hasan et al., 2008]. A high prevalence of abnormalities in white matter has been observed in individuals with NF-1 [Filho et al., 2008] and children with VLBW/VPTB [Edgin et al., 2008]. The association of these white matter anomalies with math in these developmental disorders remains unstudied.

Neurocognitive models of mathematical abilities distinguish between a verbal retrieval code and a quantitative code. The prototypical function of the verbal retrieval code involves math fact retrieval, and the prototypical functions of the quantitative code include numerosity and estimation. This distinction has served as a basis for a number of studies with the populations addressed in this special issue (but see Ansari [in press] for an in-depth discussion of the limitations associated with using adult neurocognitive models of math processing to interpret the findings regarding mathematical difficulties in children with neurodevelopmental disorders).

Impairment in the code for quantity and magnitude seems to be a common pathway to MLD, in that nearly all the disorders discussed in the special issue have some form of this impairment and many have concurrent compromise or atypical development of posterior parietal regions, bilaterally or on the left. In children and adolescents with VLBW/VPTB and discrepancy-based MLD, Isaacs et al. [2001] observed a reduction in brain volume isolated to the left parietal lobe. In children and adolescents with 22q11DS, individual differences in mental arithmetic were correlated with left parietal white matter structures that are adjacent to gray matter regions of the intraparietal sulcus [Barnea-Goraly et al., 2005]. Brain growth in SBM affects posterior more than anterior cortical structures as it proceeds in a back-to-front progression following ventricular dilation and hydrocephalus, producing selective reduction in posterior cortical volume [Juranek et al., 2008], and children with SBM have spatial attention problems that are correlated with posterior brain volumes [Dennis et al., 2005]; although the relation of posterior parietal dysmorphology to mathematical function has not been studied.

O'Hearn and Luna [2009] also describe atypical parietal development in persons with Williams syndrome, which, coupled with evidence of mathematics processing and parietal lobe activation, suggests that studies of this disorder may provide insights into the nature of this relationship. The same can be said for Turner syndrome and 22q11DS, which Simon has shown exhibit a similar deficit in spatial attention [Simon et al., 2008].

Understanding the neurobiology of math fact retrieval is perhaps more challenging. English et al [2009] suggest that difficulty in math fact retrieval is a core deficit in children with SBM and, more broadly, children with MLD, further suggesting that efficiency of math fact retrieval may be a marker of computational skill across the general population, not simply a marker of MLD. This notion is consistent with Baroody et al.'s characterization of MD. In contrast, among children with 22q11DS, math fact retrieval is preserved, despite a range of math disabilities [De Smedt, 2009]. Rote basic math skills are a reported strength for girls with fragile X syndrome [Murphy, 2009], despite poor reading skills. And accurate but slow responses to "math fact" items are common among girls with Turner syndrome, such that it is unclear if "retrieval" truly describes the processing used to achieve this level of performance in this group. The status of math fact retrieval in NF-1 and VLBW/VPTB is not clear; as Taylor et al. [2009] indicate, research on VLBW/VPTB to date has not differentiated the effects of VLBW/VPTB on different types of mathematics skills, such as the ability to retrieve mathematics facts, carry out procedures for solving written or story problems, or apply mathematics concepts.

Recent analyses of math fact retrieval in the left angular gyrus have shown that increased activation of the left angular gyrus is related, not only to a switch from direct calculation to fact retrieval, but also to a transfer of learned math facts between different arithmetic operations [Ischebeck et al., 2009].

Deficient math fact retrieval cannot be the single path to MLD in neurodevelopmental disorders, because, as the papers in this special issue indicate, MLD with significant

difficulties in a number code can occur with either intact (22q11DS, Williams syndrome), slow but accurate (Turner syndrome, SBM), or inaccurate (fragile X) math fact retrieval. Activation patterns differ not only in degree, but also in areas of function, which in turn may interact with the type of math tasks presented. For instance, girls with Turner syndrome engage more resources than do their peers—including engagement of the angular gyrus—during technically easy arithmetic problems such as those that are typically solved by fact retrieval; and compared to these “easy” problems, during more difficult problems (such as those that require working memory) girls with Turner syndrome do not show the increase in activation that is observed among their peers [Kesler et al., 2006]. Comparison of left angular gyrus activation under the two conditions (switch to fact retrieval and transfer of learned math facts) in the disorders with intact and slow but accurate fact retrieval would clarify whether poor number sense but intact fact retrieval is a distinct pathway to MLD.

MATHEMATICAL LEARNING DISABILITIES RESEARCH BY THE YEAR 2019

As we read the papers in this special issue, we found ourselves reflecting on what a second edition of this issue might look like a decade from now. Our thoughts about this question, which amount to a wish list for the future, include theoretical gains, advances in methodology, and principled intervention studies. Theoretical approaches to MLD stand to benefit from more fully articulated models of the normal mathematical process and increased focus on delineating core deficits (we emphasize the plural form here, as it appears that a single core deficit is unlikely to account for the multifaceted nature of mathematical learning disabilities [see Pennington, 2006, for a detailed and thoughtful treatment of this issue with respect to dyslexia]). Methodological gains may range from approaches in study design (participant matching, including multiple disorders in a single study), and experimental tasks based on theoretical advances. Theoretical and methodological advances are not mutually exclusive—consider their integration in research focused on parallel conceptualizations of mathematics as passive versus active processing (e.g., passive storage of information versus active, on-line construction of mathematical “meaning”). Moreover, as these advances contribute to intervention research, we stand to gain a greater understanding of the interplay among the genetic, biological, and environmental pathways that produce MLD and mediate its manifestation and outcome.

Theoretical Advances by 2019

Models of the normal mathematical process—The papers in this special issue highlight some lacunae in our understanding of the normal process of mathematics. In this context, we will consider the role of executive function, notably the executive resource of working memory, in current models of math.

Working memory is an important feature of many models of mathematical cognition, although its role in specific components of mathematical processing is currently under debate [Landerl et al., 2004; LeFevre et al., 2005; Butterworth and Reigosa Crespo, 2007; Swanson and Kim, 2007; Berch, 2008]. Certainly, working memory does not account for the particular math disabilities in some developmental disorders such as 22q11.DS [De Smedt et al., 2009]. Because there is almost no complex cognitive process that does *not* involve working memory, it is important to move toward a fuller specification of how working memory operates in models of math. Geary [2004] has probably made the most significant progress to date in this regard, spelling out precisely how deficits in the central executive, phonological loop, and visuo-spatial sketchpad (as per Baddeley’s [1998] model) may contribute to impairments in various components of math performance exhibited by children with MLD. In the present issue, English et al. propose that working memory might foster the acquisition of math skills in iterative cycles of mastery, and they suggest that breakdowns in various points in the cycles might lead to math deficits and perpetuate a cycle of academic

underachievement. Finally, as Berch [2008] has pointed out, the working memory model of Unsworth and Engle [2007] which emphasizes the important role played by the context in which the retrieval of information takes place may have important implications for studying children with MLD. According to this view, individual differences in working memory capacity may arise in part because of variation in the ability to retrieve relevant information from secondary memory in the presence of highly distracting information. Consequently, as Berch notes, the comparatively poor recall by children with MLD in complex span tasks (e.g., counting span) may be partially attributable to a poorer discrimination process at retrieval.

For the most part, the models of mathematics that currently inform our research function primarily as useful heuristics. In contrast, the models we would hope to review ten years hence will most likely be more comprehensive and fully articulated. Some of the issues we would want to have clarified by 2019 include: Do the domains of mathematical processing that require working memory operate in the same way? Do capacity-limited executive resources (such as working memory) and knowledge structures of executive function (such as planning and problem solving) play distinct roles in mathematical thinking? Is a deficit in working memory capacity a necessary or sufficient pathway to MLD, and can we make a principled distinction between MLD with and without a serviceable working memory pathway? Are alternative models of working memory better suited to delineating MLD, specific MLD subtypes, or specific genetic etiologies of MLD than are the commonly studied capacity-limited models? (see a recent, in-depth treatment of the latter issue by Berch [2008]).

Increased focus on understanding deficits rather than on generating typologies—Categorical and typological classifications continue to be sought for MLD, just as for other forms of LD. What the articles in the special issue illustrate is that some traditional typologies provide an imperfect characterization of the math phenotype in several different developmental disorders. Moore [2009] points out that learning disabilities in NF-1 would be poorly characterized as nonverbal learning disabilities [Harnadek and Rourke, 1994], being neither nonverbal nor restricted to mathematics. English et al. [2009] report a mathematics profile in children with SBM that includes relative preservation of mechanical arithmetic skills, a cardinal deficit in the nonverbal learning disabilities framework. In 22q11DS, the characteristic nonverbal learning disabilities IQ pattern (Verbal IQ > Performance IQ) is attenuated or reversed [De Smedt et al., 2009]. For these and other disorders (such as Turner syndrome), the framework fails to specify within-disorder specificity, much less to differentiate these disorders from each one.

In ADHD research, an earlier focus on typologies has largely given way to a search for core deficits and endophenotypes, [Gottesman and Gould, 2003], hypothetical constructs intervening between genes and behaviors [Almasy and Blangero, 2001] that are common in affected individuals (sensitive), relatively unique to the disorder (specific), and comparatively uncommon in the normal population [Biederman et al., 1995; Crosbie et al., 2008]. The search has been productive in identifying a limited number of candidate endophenotypes (e.g., response inhibition) that are deficient in individuals with ADHD (however typologized) and that are demonstrably related to some of the genetic anomalies (e.g., in dopamine transporter genes) and brain pathways (e.g., prefrontal-dorsal striatum and orbitofrontal-ventral striatum circuits) associated with the ADHD phenotype.

The papers in this special issue have demonstrated not only the range of skills we think of as “mathematical,” but also how dissociable combinations of these skills may be within and across disorders. Looking forward, it is possible that a special issue in 2019 might elaborate on the myriad of explanations as to why a core deficit (or most likely a set of core deficits)

cannot adequately characterize a disorder as complex as MLD. Alternatively, the 2019 special issue might include an update on the status of current core deficits and impaired processes (e.g., fact retrieval, poor number knowledge, spatio-temporal resolution, spatial orienting, and nonsymbolic magnitude representation), as well as new information about whether systematic comparisons across disorders has provided us with sufficient data about sensitivity and specificity to consider any or all of these deficits as candidate endophenotypes.

Advances in MLD subtyping—Over the past 15 years, we have witnessed a progression from the earliest models of MLD, which focused on differentiating subtypes, toward models aligned with advances being made in other areas of mathematical cognition. This transition can be characterized as a shift from examining specific skills in the context of a proposed MLD subtype to delineating the broader conceptualization of a subtype *per se*.

For instance, response time (RT) is a dimension of math performance that is poorly articulated in subtyping schemes. Often considered evidence of a process loosely referred to as “fact retrieval”, researchers have already demonstrated the variability in types of “processing” involved in the act of “retrieval” (as discussed further, below [also see LeFevre et al., 1996]). Yet slow RT during arithmetic calculations is a proposed characteristic of an MLD subtype (semantic memory), and a proposed core characteristic of children with mathematical learning difficulties [Baroody et al., 2009]. RT and fact retrieval are overlapping, but separate, issues. For some disorders (22q11DS), RT problems seem relatively non-salient; for others (Turner syndrome, SBM) slower RTs are apparent on mathematical and non-mathematical tasks, such as stimulus orienting. The specificity of RT slowing to mathematics is not always obvious, because slower RTs among a wide range of tasks suggests a general processing speed deficit rather than deficits with mathematics *per se*, as was proposed for the Turner syndrome phenotype in the 1980s. But further studies revealed selective slow responding in Turner syndrome [e.g. Simon et al., 2008]. The reason under-specification of RT in math models matters is that conditions such as Turner syndrome and SBM sit uneasily as a Semantic math subtype [Geary, 1993]. This lack of fit occurs because although math fact retrieval is accurate in persons with SBM or Turner syndrome it is also slow [English et al. 2009; Mazzocco, 2009].

Advances in conceptualizing constructs like RT will likely be crucial for making further progress in delineating subtle processing deficits that may accumulate over time and eventuate in impaired or inaccurate mathematical performance. A recent example of such an approach comes from a study of *transcoding*—translating from one numeric code to another, such as reading (i.e., verbalizing) a visually presented Arabic numeral. van Loosbroek et al. [2009] measured the so-called “planning time” in seconds, needed by 9-year-old children with or without MLD to begin writing an Arabic numeral (e.g., 7) in response to a dictated number word (“seven”). Not only were the children with MLD slower overall in planning time, but unlike their typically achieving peers, they exhibited a problem-size effect for numbers smaller than 10—taking an increasingly (linear) amount of time to begin writing the numerals as the magnitude of the numbers increased! The authors argue that these findings suggest an inefficient semantic linking of numerical symbols to analog numerical representations, rather than transcoding via a more direct, nonsemantic route as appeared to be carried out by the typically-achieving children.

Finally, future research assessing RTs must take into account the methodological complexities associated with the multiple factors that contribute to measures of processing time. For example, slower RTs in a math fact retrieval task can be partially attributed to slower, global processing speed, search time, response preparation, and the like. Furthermore, developmental changes in such processing components can complicate the

interpretations of age-related differences in RT. Indeed, Kiselev et al. [2009] have recently demonstrated process-specific, age-related differences in processing speed for simple discrimination, and choice reaction-time tasks (that did not require reading). As these authors point out, such findings are consistent with the principle of the “heterochronicity” of brain development during childhood—that “different brain structures and areas follow temporally distinct maturational trajectories that should be manifest on tasks that demand the concomitant distinct cognitive processes subserved by these brain structures” [Kiselev et al., 2009, p. 163].

Advances in Models of MLD subtypes are likely to see gains during the next decade of MLD research. Some of these advances will come not from the study of MLD itself, but from better-articulated cognitive models that can be exploited to understand pathways to MLD.

In the domain of attention, the prototypical disorder is attention deficit hyperactivity disorder (ADHD), which is dopaminergically mediated and characteristically involves intact stimulus orienting but poor response control. More recent models of childhood attention deficits [e.g., Dennis et al., 2008] have identified a contrasting profile of disordered attention that concerns poor stimulus orienting, with difficulty disengaging and shifting attention. It remains to be seen whether the non-ADHD stimulus orienting attention disorders observed in SBM and acute lymphoblastic leukemia (and apparently also in 22q11DS) are related to mathematics skills in these conditions.

We have already seen advances in clarifying the construct of the Spatial subtype of MLD, which has progressed from its original focus on overtly spatial products (misalignment of numbers during paper and pencil calculations) and scaffolds (using graph paper to help maintain proper alignment) during mathematics [Geary, 1993] to its more current emphasis on spatial components of basic mathematical cognition including the mental number line and the conceptual understanding of place value (i.e., the base-10, positional meaning of multidigit numbers) [Dehaene et al., 2003; Geary and Hoard, 2005; Simon et al., 2008].

The evolution of the Spatial subtype, in its short history, illustrates not only how advances in characterizing basic mathematical processes can inform research on MLD, but also how the lack of evidence based on a single construct could not definitively rule out a potential theoretical pathway. As such the field needs to be as mindful of its potential false negatives in research outcomes as of its tantalizing “hits.”

Methodological Advances

Defining comparison groups—One source of potential false negatives in phenotype research is the methodological approach to defining comparison groups, or in defining MLD. In learning disabilities (LD) research (as seen in the papers included in this special issue), one important distinction in the approaches used is between the use of low achievement criteria (defined in terms of age norms or age expectations) and discrepancy definitions (defined relative to IQ or some other measure of cognitive development). At the broadest level, the choice of one definition of MLD (or other mathematical difficulties) over another represents an implicit view of a long-standing controversy about discrepancy versus low achievement definitions of LD [see Francis et al., 1996, for a discussion]. In developmental disorders with a shorter MLD research history, such as very low birth weight and very preterm birth (VLBW/VPTB), discrepancy definitions, IQ controls, or mental age matching have played a role in helping define the phenotype of mathematical abilities. In disorders with a longer MLD research history such as 22q11DS and Turner syndrome, studies have moved towards a focus on comparing index groups on developmentally

appropriate skills like reading and on experimental tasks of functions, such as the representation of quantity, that have theoretically-specified and testable relations to math.

Children with MLD, as a group, often have lower IQ scores than their typically achieving peers. To the extent that the same neurodevelopmental events that produced the low IQ also produced the MLD, IQ and MLD are not fully separable, which means that one cannot be subtracted from, or covaried out of, the other (for a discussion, see Dennis et al. [in press]). This erroneous assumption may be most obvious when an arithmetic subtest is included in the IQ measure, and although omitting such a subtest would be an improvement in the right direction, it fails to fully account for the central issue, which is that, especially in genetic and brain disorders, lowered IQ and MLD are tied to each other and to their shared condition.

The existence of IQ differences forces the MLD researcher to consider low achievement and discrepancy measures of the construct, the choice of which, in turn, presupposes one type of control or comparison group rather than another. In some studies, only one measure is used to assess mathematical difficulties or disabilities; in others, both measures are used and produce different results with different math measures [Taylor et al., 2009]. In the papers of this special issue, comparison groups may include mental age comparisons, matching on age, or matching on age and IQ, comparison to children with other developmental disorders, or some combination of the above. Although a researcher's confidence in the findings that emerge when IQ matching is employed may not necessarily be unwarranted, the risk of false negatives may inadvertently lead us to exclude MLD from a phenotype when absolute performance differences are significant. A number of researchers have adopted reporting absolute and relative outcomes in a single study [e.g., Mazzocco et al., 2006], which, while perhaps cumbersome, at least allows the reader to consider both types of outcome. Analyses of different definitions of the MLD construct should serve to make us more mindful of our interpretations. The advantages and disadvantages of each approach hinder any single one from emerging as the "best" approach, but explorations of the outcomes of each approach can promote advances in this area.

The choice of how we define control and comparison groups has consequences for establishing the incidence of MLD. Even within the confines of disorders for which superior performance does not occur, there is variability in the frequency with which members of a population meet criteria for MLD, and how relative frequency compared to a control group varies further as a function of how that control group is defined. For instance, the incidence of MLD among young girls with Turner syndrome is four times greater than the rate observed in an age- and IQ-matched group of girls without Turner syndrome; whereas the difference in rates for girls with versus without fragile X syndrome is 2.5:1. This suggests a higher incidence of MLD in Turner syndrome than fragile X, but the reverse is true because of different characteristics of the IQ-matched comparison groups used across these two analyses [Mazzocco, 2001].

Of practical importance, somewhat different conclusions about MLD treatment might be shaped by focusing on whether deficits in math are absolute or relative to IQ. For instance, compared to those from more advantaged backgrounds, children with unrelieved socioeconomic disadvantage may have lower IQ scores. If IQ discrepancy scores are used to identify mathematical learning difficulties, such children will be less likely to be targeted for remedial mathematics education that might enhance their number competence and foster greater mathematical learning.

Math as both storage of learned math facts and active, on-line construction of number solutions—Some of the advances to be gained in MLD research can be guided by the lessons learned from research on reading disabilities. Much of an earlier research era

in reading disabilities was concerned with failures of word decoding as the defining deficit of dyslexia. This constituted a reasonable focus at the time, given the importance of understanding why word decoding could become a rapid, obligatory, and automatic process for most children—but not for those with dyslexia. More recently, reading research has been broadened to include issues concerned with the active, on-line construction of meaning in texts, including the process by which inferences are made from the textual “facts,” from the situation described by the text but not literally “in” the text, and from real-world knowledge. Contemporary research focuses on the process by which the individual’s reading goals modify how a text is read.

An important contribution of the current special issue is to show that both fact retrieval and active construction are important for math, even for such seemingly basic math skills as math fact manipulation [Baroody et al., 2009]. In other words, although proficiency in arithmetic and higher forms of mathematics demonstrably requires adequate storage and efficient retrieval of math facts in semantic memory, memorizing these facts in a meaningful manner (i.e., active construction) can lessen the amount of time and practice needed to achieve mastery, minimize retrieval errors, and permit existing knowledge to be applied to the learning of new arithmetic combinations [Baroody, 2009].

We predict that future research will devote increased attention to the study of active constructive processes in mathematical learning, including such questions as: Which kinds of inferences do children make using math facts they have successfully retrieved? Do inferences play a greater role in intuitive, informal numerical skills than in formal math ability and achievement measures? How does a child construct mental models involving number and extent, and how do these mental models constrain the inferences the child makes about possible numeric solutions? Are measures of executive top-down control associated with how children adjust their mathematical problem solving in accordance with different goals? And finally, how can children with MLD be successfully taught to engage in more active construction for learning basic math facts if such an approach seems to simultaneously require both of the following: A deeper understanding of mathematical concepts (including a well-interconnected knowledge of arithmetic facts, principles, and processes) that are quite difficult for these individuals to comprehend, and a comparatively unstructured, inquiry-based learning environment (where they may be expected to take advantage of opportunities for “*discovering* patterns and relations”), in which children with LD typically fare poorly?

Studying the neural correlates of MLD—Despite some recent advances in the cognitive neuroscience of both typical and atypical cognitive development (see a recent review by Ansari et al. [2008]), there remain numerous conceptual, methodological and statistical challenges in characterizing not only the neural correlates of MLD, but also the confluence of factors that may play a causal role in producing the phenotypic impairments in performance described throughout the current collection of papers. Future progress in this area will require careful attention to recent advances being made in the use of various neuroimaging and related modalities. For thoughtful treatments of the complex issues associated with the study of developmental changes in mathematical cognition both in children with and without MLD, future researchers should consult the recent papers by Ansari et al. [2008] and Kaufman [2008].

Interplay Among Genetic, Biological, and Environmental Pathways to MLD

Variation in mathematical abilities has been associated with differences in endogenous features within children, such as genetic polymorphisms, genetic mutations, and brain dysmorphisms, as well as with factors exogenous to the child, such as poverty and

socioeconomic disadvantage [Jordan and Levine, 2009]. The home environment and early learning experiences are important influences on subsequent mathematics achievement at 10 years of age [Melhuish et al., 2008]. Although endogenous and exogenous pathways to MLD have largely been considered separately, recent research in other domains suggests that they are interrelated. For example, the brain systems with the most protracted postnatal development (e.g., the perisylvian areas important for language) are most susceptible to environmental influences and show the strongest associations with socioeconomic status [Noble et al., 2005; Farah et al., 2006], so it is important to understand that unrelieved poverty and socioeconomic disadvantage will change, not only the environment for learning math, but also the brain resources of the mathematics learner. Ten years from now, we would hope that the interplay between genetic, brain, and environmental pathways to MLD will be better understood.

A FINAL THOUGHT

Those of us working with developmental disabilities have sometimes supposed that the cascading changes in development that involve defective genes and alterations in neurogenesis, cell migration and neuronal connectivity must project a permanently bleak cognitive outcome, and that any mutability in outcome can only exist in disorders whose origins lie in exogenous factors, such as environmental disadvantage. Genetics researchers caution against such an interpretation, emphasizing that etiology need not predetermine a definitive outcome for developmental profiles and trajectories. Instructional interventions should clearly be a focus of future studies, but recent animal models of neurodevelopmental disorders show, somewhat surprisingly, that reversing underlying molecular defects may improve function, even if treatments begin only in adulthood [Ehninger et al., 2008]. In the future, cognitive deficits, including those in math, may prove to be more malleable, and through more diverse pathways, throughout the life course of individuals with neurodevelopmental disorders than we currently imagine.

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