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A Review of Mathematical Learning Disabilities in Children with Fragile X Syndrome

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The prevalence rate of mathematical learning disabilities (MLD) among children with fragile X syndrome who do not meet criteria for intellectual and developmental disabilities (~50% of female children) exceeds the rate reported in the general population. The purpose of this article is two-fold: (1) to review the findings on MLD in persons with fragile X syndrome; and (2) to discuss fragile X syndrome as a possible model for understanding pathways to MLD.
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Key Words: fragile X syndrome; mathematical learning disability; genetic syndrome

Difficulty with mathematics is well documented among children and adults with fragile X syndrome [Grigsby et al., 1990; Brainard et al., 1991; Bennetto et al., 2001; Mazzocco, 1998, 2001]. Also apparent are deficits in areas of cognitive ability that are associated with mathematics, such as executive function, visual spatial ability, and reading-related skills [as reviewed by Mazzocco and McCloskey, 2005]. The poor mathematics performance associated with fragile X syndrome may reflect a primary deficit resulting from the syndrome or a deficit secondary to difficulty in requisite cognitive skills. Alternatively, a specific profile of mathematical and cognitive deficits associated with fragile X syndrome may be independent of general impairment, as has been proposed for other developmental disorders (e.g., Williams syndrome, this issue). Regardless of the specificity with which it emerges, the fragile X syndrome mathematical learning disability (MLD) profile is a possible model for understanding pathways to MLD [Mazzocco and McCloskey, 2005; Mazzocco et al., 2007; Murphy et al., in press].

The present review focuses on describing MLD in children with fragile X syndrome with a specific emphasis on female individuals without intellectual and developmental disabilities (IADD) (Throughout this review, the term *intellectual and developmental disabilities* (IADD) is used in lieu of the term *mental retardation* to reflect the change in terminology taking place in the field of developmental disabilities research and practice). Cognitive correlates related to MLD, such as executive function, visual spatial skills, and reading-related skills, are also discussed in the context of fragile X syndrome. In the final section, fragile X syndrome is discussed as a model of potential pathways to MLD.

OVERVIEW OF FRAGILE X SYNDROME

Neural development, such as synaptic maturation and neuronal pruning, relies in part on the presence of a specific protein called the *Fragile X Mental Retardation Protein* [FMRP, Oostra, 1996; Greenough et al., 2001]. FMRP is coded for by a single gene on the long arm of the X chromosome. If the production of this protein is disrupted, optimal neural development is impeded resulting in fragile X syndrome.

As the leading genetic cause of inherited IADD, fragile X syndrome affects approximately 1 in 4,000 to 1 in 8,000 live births [Crawford et al., 2001]. The majority of male individuals with fragile X syndrome, but only about half of female individuals, meet criteria for IADD [Rousseau et al., 1994; Bailey et al., 1998]. The range of cognitive abilities among the remaining 50% of female individuals without IADD can vary from no noticeable cognitive deficits to learning disabilities [Rousseau et al., 1994].

Variability in the amount of FMRP produced may affect the extent to which syndrome characteristics are manifest within and across gender groups. Male individuals have only one X chromosome in every cell; whereas female individuals have two X chromosomes. Although only one of the two X chromosomes is active in a female's cells [Lyon, 1972], cells where the unaffected X chromosome is active can still produce FMRP. Thus, female individuals with fragile X syndrome generally, produce more FMRP relative to male individuals, and so may be less affected [Hagerman, 1999]. There can also be variability in the extent to which male individuals with fragile X syndrome produce FMRP [as reviewed by Hagerman, 1999]. Male individuals who have a mosaic pattern of fragile X syndrome have a combination of affected and unaffected cells, and so may produce more FMRP than those individuals

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Table 1. Summary of Implicated Strengths and Challenges in Mathematics and Related Skills in Female and Male Individuals with Fragile X Syndrome[a]

	Females		Males	
	Strength[b]	Challenge[b]	Strength[b]	Challenge[b]
Mathematics skills				
Number sense	Reading/writing numbers[c] Rote counting[c]: Forward by ones Backward by ones Forward by tens Next number in series	Visual/verbal magnitude judgments Mental number line judgments Counting 8 pictured items Applied counting: 1-to-1 correspondence[d] Number constancy Identifying *N*th in set		One-to-one correspondence when counting
Arithmetic operations		Adding sets less than 10		Early math skills as assessed by WJ-R, Applied Problems subtest
Related skills				
Executive function				
Working memory		Performance declines as working memory demands increase	Memory for meaningful information presented in context	Sequential processing
		Limited changes in brain activation in response to increasing task difficulty		Inhibition, selective and sustained attention
Visual spatial		Visual perceptual ability; difficulty recalling object location in array		Visual spatial skills, visual-motor coordination

WJ-R = Woodcock Johnson-Revised.
[a]Table highlights areas of known strength and challenge as well as areas where evidence regarding mathematics and related skills is lacking.
[b]Based on comparisons to children with no known syndrome.
[c]Performance exceeds that of children with MLD.
[d]Indicates area of challenge relative to children with MLD.

with a higher affected to unaffected cell ratio [Bailey et al., 2001].

The majority of research on MLD and fragile X syndrome has focused on individuals without IADD to investigate aspects of the cognitive phenotype independent of global deficits that are associated with IADD. As a result, this review focuses primarily on MLD among female individuals with fragile X syndrome. However, the mathematical abilities and challenges for individuals with fragile X syndrome who meet criteria for IADD is included whenever possible.

Table 1 summarizes what is known about the areas of strength and challenge associated with mathematical skills among female and male individuals with fragile X syndrome. The following section briefly reviews the phenotypic characteristics associated with fragile X syndrome that are relevant to mathematical ability. A complete review of the physical and behavioral characteristics associated with the syndrome is beyond the scope of this article. The reader is referred to Cornish et al. [2007] and Hagerman [2002] for additional information.

Female Individuals with FXS

The cognitive profile of female individuals with fragile X syndrome is characterized by areas of relative strength in verbal skills, such as vocabulary [Jakala et al., 1997], and aspects of visual perception, such as identifying missing parts of concrete objects [Bennetto and Pennington, 1996] and identifying shapes embedded within designs [Mazzocco et al., 2006].

Areas of weakness include visual perceptual skills, such as recalling the location of an object within an array [Mazzocco et al., 2006], and executive function [e.g., Mazzocco et al., 1993; Bennetto et al., 2001]. Executive function includes a range of cognitive abilities related to planning and goal-directed behavior. Specific aspects of executive function that are impaired in fragile X syndrome include working memory [Mazzocco et al., 1993; Kwon et al., 2001], inhibition, sustained attention, and controlled switching of attention [Cornish et al., 2004]. Processing speed per se does not appear to distinguish girls with fragile X syndrome from their peers [Kirk et al., 2005; Mazzocco et al., 2006; Murphy and Mazzocco, 2008a]. However, the performance of girls with fragile X syndrome on working memory tasks declines as the working memory demands of the task increase [Kirk et al., 2005; Murphy and Mazzocco, under review], which suggests that certain tasks may be more effortful for girls with fragile X syndrome relative to their peers [Murphy and Mazzocco, under review].

Male Individuals with FXS

As a group, male individuals with fragile X syndrome tend to have more pronounced cognitive deficits than female individuals [Rousseau et al., 1994; Jakala et al., 1997]. However, areas of strength and weakness are still present. Similar to female individuals with fragile X syndrome, relative strengths among male individuals are apparent in verbal skills [Jakala et al., 1997] and memory for meaningful information that is presented in context [e.g., remembering pictures rather than sequences of numbers [Munir et al., 2000]. Areas of weakness include short-term memory, visual spatial skills, and visual-motor coordination [Cornish et al., 1999], as well as aspects of executive function such as inhibition [Wilding et al., 2002; Scerif et al., 2004], and selective and sustained attention [Cornish et al., 2001]. Along with the select executive function deficits, processing sequential information is an area of relative weakness that may contribute to mathematics performance,

such as counting [Daniel et al., unpublished data].

MLD IN FRAGILE X SYNDROME

Female Individuals with Fragile X Syndrome

Prevalence of MLD

As early as kindergarten, girls with fragile X syndrome are at an increased risk for MLD relative to their peers from the general population [Mazzocco, 2001]. We have found that the percentage of girls with fragile X syndrome who scored in the MLD range, at least once during annual assessments between kindergarten and 3rd grade, was greater (87%) than the rate observed in the K-3rd grade general population (44%) [Murphy et al., 2006]. Even relative to an age and IQ matched comparison group, the ratio of MLD in fragile X syndrome is 2.5–1 [Mazzocco, 2001].

Persistence of MLD

The persistence of MLD during early elementary school among girls with fragile X syndrome has been documented in a single study [Murphy et al., 2006]. In this study, persistence of MLD did not distinguish girls with fragile X syndrome from children in the general population. Approximately 77% of girls with fragile X syndrome (who had MLD) continued to meet criteria for MLD more than once between kindergarten and 3rd grade compared to 70% of children from the general population [Murphy et al., 2006].

Although the MLD persistence rate does not distinguish fragile X syndrome from the general population during early elementary school, poor mathematics performance among female individuals with fragile X syndrome is evident through elementary school [Murphy and Mazzocco, 2008a,b, under review] and into adulthood [Cronister et al., 1991; Mazzocco, 1998; Bennetto et al., 2001]. Moreover, during the early school-age years, girls with fragile X syndrome meet stricter criteria for MLD (score consistently in the bottom 10th percentile on a standardized measure of formal and informal math skills) than children from the general population [Murphy et al., 2006].

Mathematics skills

Mathematics is an area of difficulty for individuals with fragile X syndrome [Grigsby et al., 1990; Brainard et al., 1991; Mazzocco, 1998; Bennetto et al., 2001], but not all aspects of mathematics are impaired. Mathematics ability in fragile X syndrome is characterized by a profile of strengths and challenges, especially in the areas of number sense (e.g., counting) and rational number knowledge [as reviewed by Mazzocco et al., 2007]. Understanding this profile of mathematics ability and its relation to specific cognitive abilities can inform understanding of MLD both in fragile X syndrome and in the general population.

In studying mathematics performance among girls with fragile X syndrome, four types of comparison groups have been employed. The performance of girls with fragile X syndrome has been compared to that of: (1) children from a normative sample of the general population (general population); (2) children from the general population who do not meet criteria for MLD (non-MLD); (3) children from the general population who meet criteria for MLD (children with MLD); and (4) girls with Turner syndrome, another relatively common genetic syndrome. These types of comparisons may inform which characteristics of poor performance can be associated with fragile X syndrome specifically or mathematics learning disability more generally [Murphy et al., in press].

Recent and comprehensive reviews of mathematics skills among females with fragile X syndrome are available elsewhere [see Mazzocco and McCloskey, 2005; Mazzocco et al., 2007; Murphy et al., in press]. This review focuses on selected findings related to number sense, rational number knowledge, and the developmental trajectory of mathematics skills that may best exemplify fragile X syndrome as a model of pathways to MLD.

Number sense

Broadly defined number sense refers to knowledge of numbers and their properties including reading and writing numbers, counting, judging which of two quantities is larger (magnitude judgments), and the ability to manipulate numbers along a mental number line [Berch, 2005]. As early as kindergarten, girls with fragile X syndrome have difficulty with number sense relative to their age, grade, and IQ-matched peers from the general population [Mazzocco, 2001].

Despite generally poor performance, not all aspects of number sense are impaired [Murphy et al., 2006]. Of the multiple aspects of number sense, girls with fragile X syndrome demonstrate relative strengths in written number representation (e.g., reading and writing numbers) and rote counting skills (e.g., counting forward or backwards by one). In fact, rote counting knowledge in fragile X syndrome is comparable to that in the general population and exceeds the performance of children with MLD [Murphy et al., 2006].

The strength in rote counting contrasts with weakness in applied counting knowledge, such as recognizing that rearranging items in a set does not change the quantity of items (number constancy), understanding ordinal numbers (e.g., the ability to correctly identify the *N*th position in an array), and understanding one-to-one correspondence when counting (i.e., recognizing that each object in a set can have only one number name). Overall, girls with fragile X syndrome and children with MLD both perform more poorly than children from the general population on applied counting items [Murphy et al., 2006]. Girls with fragile X syndrome and children with MLD perform at about the same level on applied counting items, except on items measuring understanding of one-to-one correspondence. On these items, the performance of girls with fragile X syndrome lags behind even that of children with MLD [Murphy et al., 2006]. This profile of relative strength in rote counting and weakness in applied counting further distinguishes girls with fragile X syndrome from girls with Turner syndrome, whose performance is in the average range relative to the general population on both rote and applied counting knowledge.

The rote-applied ability distinction is documented during the elementary school years [Murphy et al., 2006]. However, little is known about how this distinction might change over development as a function of maturation or changing curricular demands across grades. In a study of rational number knowledge in middle school, we [Murphy and Mazzocco, 2008b] found a similar pattern of strengths and weaknesses on rote versus applied knowledge. Results from this study are discussed subsequently followed by findings from a study on the developmental trajectory of mathematics development from 1st through 6th grades.

Rational number knowledge

Rational numbers are numbers that can be represented as a fraction or ratio of integers (e.g., 1/2, 2/3). Mastery of rational numbers knowledge

encompasses tasks that can be learned by rote, such as accurate reading of decimal amounts (e.g., using correct place value labels like "tenths" or "hundredths"). Tasks that reflect a conceptual understanding of rational numbers are also important, such as recognizing that the same amount can be represented in different ways; for example, the number words "one-half" can be represented as a fraction (1/2), as a decimal (0.5), or pictorially (◑).

Middle school age girls with fragile X syndrome do struggle with rational numbers, but not on all aspects [Murphy and Mazzocco, 2008b]. In a recent study, we [Murphy and Mazzocco, 2008b] compared the performance of girls with fragile X syndrome to children with and without MLD from the general population on the Ranking Proportions Task [RPT, Mazzocco and Devlin, 2008]. This task includes two subtests that require the participant to rank order amounts that are represented: pictorially (e.g., ◑, ●) or as decimals (e.g., 0.5, 0.25). Participants are also asked to read decimal amounts aloud.

A distinct profile of strengths and challenges emerges across these RPT subtests for girls with fragile X syndrome when compared to children from the general population with and without MLD [Murphy and Mazzocco, 2008b]. Girls with fragile X syndrome do not differ from children in the general population on reading decimals and ranking pictured amounts, and their performance on these tasks exceeds that of children with MLD. Despite these strengths, girls with fragile X syndrome have difficulty ranking decimals; and their performance on this subtest is comparable to that of children with MLD. Thus, a pattern of relative strength on rote skills (e.g., reading decimals, ranking pictorial representations of fractions) coupled with poor conceptual skills is observed among girls with fragile X syndrome. Further, this rote-conceptual performance distinction is consistent with performance on number sense tasks; and is of particular note given that strong rote skills may mask underlying conceptual deficits, thereby hindering mathematics achievement if instructors interpret rote skills as reflecting conceptual mastery [Murphy and Mazzocco, 2008b].

Although findings from this study and others confirm that poor mathematics performance persist through elementary school and into middle school [e.g., Murphy and Mazzocco, 2008a] and beyond [e.g. Grigsby et al., 1990; Bennetto et al., 2001], a developmental perspective is required to understand how poor mathematics performance emerges or resolves during the school years as well as the possible contributions of related cognitive skills to the prediction of mathematics growth and outcomes.

Growth in mathematics skills during the elementary and middle school years

In the only study to date to focus on the growth of mathematical skills among girls with fragile X syndrome [Murphy and Mazzocco, under review], we examined the trajectory of mathematical skills between 1st and 6th grade. Raw scores on the Woodcock Johnson-Revised (WJ-R) calculations subtest were compared between girls with fragile X syndrome and a comparison group from the general population. By 6th grade, girls with fragile X syndrome had lower raw scores on the WJ-R Calculations subtest and a slower growth rate than children in a comparison group from the general population. This is consistent with cross-sectional reports during the elementary school years [Mazzocco, 2001; Kirk et al., 2005; Murphy et al., 2006; Murphy and Mazzocco, 2008a]. However, group differences in both 6th grade math performance and growth rate in math skills disappeared after controlling for FSIQ and working memory performance at 3rd grade. Such findings support the stability of poor math performance as a characteristic of girls with fragile X syndrome and highlight the potential contribution of working memory ability to mathematics achievement over time.

Much less is known about mathematics ability and disability in males with fragile X syndrome than females with fragile X syndrome.

Male Individuals with Fragile X Syndrome

Much less is known about mathematics ability and disability in male individuals with fragile X syndrome relative to what is known about female individuals (see Table 1). Findings from standardized achievement measures suggest that arithmetic is an area of weakness for boys with fragile X syndrome relative to children with Down syndrome or nonspecific IADD, and mental age-matched peers [Dykens et al., 1987; Kemper et al., 1988; Hodapp et al., 1991, 1992]. Roberts et al. [2005] found that early mathematical skills of boys with fragile X syndrome were on par with early reading skills (i.e., letter–word identification), and both areas were strengths relative to dictation. However, early mathematical skills still represents an area of difficulty relative to chronological age-level expectations [Roberts et al., 2005].

Although deficits in mathematics achievement are apparent, little work has been done to characterize the profile of specific formal and informal mathematics skills among boys with fragile X syndrome. Daniel et al. [unpublished data] examined counting and sequential responding in children with fragile X syndrome relative to children with Down syndrome and mental age-matched children with typical achievement. Sequential processing was measured using a computer task in which the child had to complete a series of responses (point to a sequence of stepping-stones) to meet a goal (opening a treasure chest). Variations in the displays included whether the stepping-stones were presented sequentially or simultaneously, spaced regularly or irregularly, and whether the stones vanished once touched. A similar sort of counting task was also used. On these tasks, boys with fragile X syndrome had difficulty applying basic counting principles and inhibiting incorrect responses relative to their peers with Down syndrome and typically achieving peers, whose performance did not differ from one another. Thus, the authors suggest that sequential processing may contribute to counting ability among boys with fragile X syndrome and to a syndrome-specific profile of basic mathematics ability [Daniel et al., unpublished data].

COGNITIVE CORRELATES OF MATHEMATICS PERFORMANCE

Recent and comprehensive reviews of cognitive correlates of mathematics skills, such as executive function, visual spatial ability, and reading-related skills, among females with fragile X syndrome are available elsewhere [e.g., Mazzocco and McCloskey, 2005; Mazzocco et al., 2007; Murphy et al., in press]. There is evidence of specific visual spatial and language deficits among female individuals with fragile X

syndrome, but these deficits may be secondary to deficits in executive function [Bennetto et al., 2001; Murphy et al., 2006]. Thus, the present review focuses on the possible contributions of executive function to mathematics performance in fragile X syndrome.

Executive function encompasses a myriad of skills and abilities, including working memory. The ability to access, hold, and manipulate information in working memory is important for completing a variety of tasks, including those related to mathematics (e.g., counting, calculation). For example, successful counting may depend both on knowledge of counting principles, such as one-to-one correspondence, and the ability to keep track of the items counted to avoid counting the same item more than once. Indeed, the contribution of working memory to mathematics performance is well documented [as reviewed by Geary et al., 2007] and working memory deficits have been associated with MLD [Swanson and Beebe-Frankenberger, 2004].

As discussed previously, deficits in executive function, including working memory, are documented in fragile X syndrome [Bennetto et al., 2001; Kwon et al., 2001; Kirk et al., 2005; Tamm et al., 2002; Murphy and Mazzocco, under review]. Female individuals with fragile X syndrome fail to show increases in brain activation as task difficulty increases on visual spatial [Kwon et al., 2001] or number-processing tasks [Rivera et al., 2002]. For example, females with fragile X syndrome showed no changes in brain activation and were less accurate than their peers at verifying the accuracy of equations when the equations involved three operands (e.g., $2 + 3 + 1 = 5$), but not when they involved two operands (e.g., $2 + 3 = 4$). Such findings may be suggestive of difficulty recruiting the necessary cognitive resources to compensate for increasing task demands [Rivera et al., 2002], or may reflect a lower threshold for working memory tasks relative to the general population [Kwon et al., 2001; Murphy and Mazzocco, under review; Rivera et al., 2002].

Findings from our recent longitudinal study of mathematics and working memory in girls with fragile X syndrome support the notion of a lowered threshold for working memory among girls with fragile X syndrome relative to their peers [Murphy and Mazzocco, under review]. For example, we found that tasks that are not generally considered working memory tasks, such as naming stimuli by color or shape, are more effortful for girls with fragile X syndrome than their peers. On these naming tasks, 3rd grade girls with fragile X syndrome had longer response times than their peers, but their performance was just as accurate. Naming performance contrasted with performance on working memory tasks where girls with fragile X syndrome were just as fast, but less accurate than their peers. We hypothesize that the pattern of trading accuracy for speed observed among girls with fragile X syndrome reflects the difficulty of the working memory tasks. Such speed/accuracy trade-offs are also observed on select mathematics tasks, such as tasks that require verifying the accuracy of arithmetic problems [Murphy and Mazzocco, 2008a].

Working memory performance at 3rd grade predicted 6th grade mathematics achievement and growth rate in mathematics between 1st and 6th grades.

Lower working memory thresholds among girls with fragile X syndrome does not reflect the absence of growth in working memory ability [Murphy and Mazzocco, under review]. Over time from 1st to 7th grades, we found gains in working memory performance among girls with fragile X syndrome, albeit at a slower rate than that of their peers. Improvements in working memory are especially evident between 5th and 7th grades among girls with fragile X syndrome. Moreover, working memory performance at 3rd grade predicted 6th grade mathematics achievement and growth rate in mathematics between 1st and 6th grades. Together, these findings suggest that select tasks that are not traditionally considered to be working memory tasks for children in the general population may indeed be working memory tasks for girls with fragile X syndrome [Murphy and Mazzocco, under review].

The trajectory of working memory and its association with mathematics performance have two important educational implications for girls with fragile X syndrome. First, the emergence of group differences in working memory at 3rd grade and their prediction of 6th grade mathematics performance highlight the importance of early intervention for girls with fragile X syndrome [Murphy and Mazzocco, under review]. Second, depending on the extent to which growth in working memory is directly related to mathematics, these findings also draw attention to the possibility that improvements in working memory observed by 7th grade may contribute to improvements in mathematics performance during the middle school years rather than plateaus in performance [Murphy and Mazzocco, under review]. Additional studies are needed to examine the association between working memory and mathematics, especially during the middle school years.

POTENTIAL PATHWAYS TO MLD

Throughout this review performance and characteristics of individuals with fragile X syndrome as a group are considered rather than drawing attention to individual variability in performance. As evident among other syndromes, such as Williams syndrome (this issue), 22q11.2 deletion (this issue), and Turner syndromes (this issue), individual variability among persons with a given syndrome is evident despite all individuals with a given syndrome sharing a common known etiology. Thus, this relatively homogeneous group of individuals can inform the study of pathways to MLD [Murphy et al., in press]. For example, the co-occurring deficits in executive function and mathematics associated with fragile X syndrome may provide insight into the contribution of executive function to MLD in fragile X syndrome and in the general population [Murphy et al., in press].

There is clear evidence of poor math performance in fragile X syndrome and difficulty with mathematics related cognitive skills. These findings are consistent with the theoretical model of MLD proposed by Geary [1993, 2004]. Figure 1 presents a modified version of Geary's model, which continues to be tested and refined [e.g., Murphy and Mazzocco, 2008b, under review]. According to this model, behavioral characteristics associated with fragile X syndrome (e.g., attention, arousal) may influence performance, including the ability to acquire math skills.

Continued investigation of these relationships among both male and female individuals with fragile X syn-

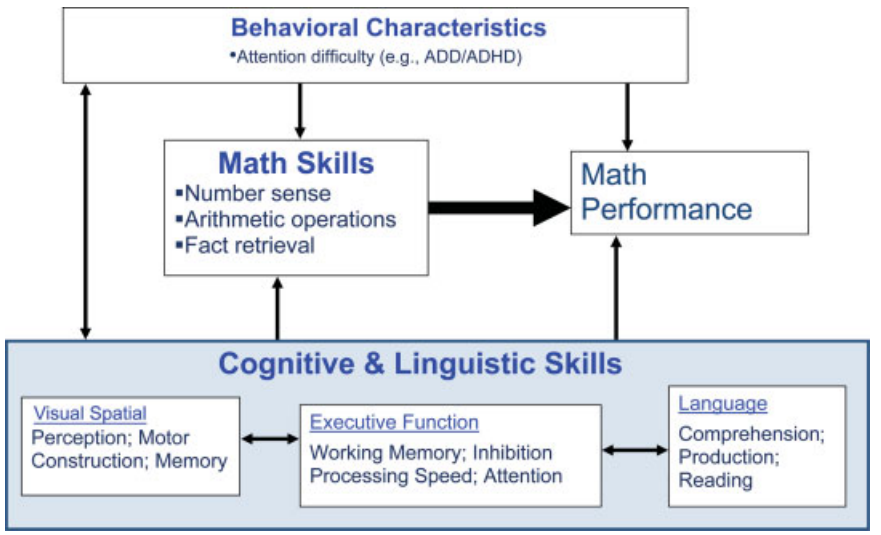

Fig. 1. Conceptual framework for evaluating the contribution of cognitive and behavioral correlates of MLD in fragile X syndrome. Note: given the complexity of each domain and the reciprocal relationships among domains, this figure is intended to broadly focus on the domains and relationships most relevant to the present discussion. This figure is not intended to be all-inclusive, as there are additional areas—such as attention, anxiety, or metacognition—that could influence and be influenced by these domains.

drome will inform the extent to which specific cognitive skills, like working memory, are related to mathematics performance. Another way in which fragile X syndrome can contribute to understanding MLD is as a model of a possible subtype of MLD [Murphy et al., in press]. For example, the association between working memory and mathematic skills can help to further elucidate the specific mechanisms by which working memory contributes to the development of mathematical skills, such as counting or applying procedural knowledge.

Even with the relatively strong support for the contribution of working memory to mathematics performance, it is important to recognize the complexity of both mathematics and working memory. As depicted in Figure 1, there are multiple cognitive skills that can influence mathematical development and multiple pathways through which these cognitive skills can act. For example, visual spatial ability or working memory may facilitate tracking objects when counting such that deficits in either or both areas may contribute to inaccurate counting. Moreover, working memory deficits may be compounded by slow processing speed or difficulty inhibiting related responses [as reviewed by Geary et al., 2007]. Assessing the relative contributions of working memory to mathematics performance in fragile X syndrome is a critical next step towards understanding the syndrome as a model for MLD [Mazzocco and McCloskey, 2005; Murphy et al., in press].

CONCLUSION

Poor mathematics performance associated with fragile X syndrome along with deficits in mathematics-related cognitive skills, including executive functions, provides an opportunity to disentangle the causes of poor mathematics performance. However, much work remains to be done. Along with continuing to explore the profile of mathematics skills of females with fragile X syndrome, there is a need to better characterize the specific formal and informal mathematical skills of males with fragile X syndrome and the mathematics-related cognitive skills of both male and female individuals with fragile X syndrome. Linking these cognitive skills with mathematics performance may help to clarify potential pathways to MLD. Such efforts will be further enhanced by continued comparisons across genetic syndromes to delineate syndrome-specific profiles of skills. Moreover, understanding the sources of performance variation in the development of specific mathematics skills, such as fact retrieval, can elucidate the mechanisms by which learning takes place and inform intervention efforts. Finally, a developmental perspective is needed to understand the interaction of syndrome characteristics and mathematical skill development that may contribute to MLD. ■

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