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Investigation of Poor Academic Achievement in Children with Duchenne Muscular Dystrophy

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Abstract

Duchenne Muscular Dystrophy (DMD) is a neurogenetic developmental disorder that presents with progressive muscular weakness. It is caused by a mutation in a gene that results in the absence of specific products that normally localize to muscle cells and the central nervous system (CNS). The majority of affected individuals have IQs within the normal range, generally with lower verbal than performance IQ scores. Prior work has demonstrated selective deficits on tests of verbal span and immediate memory. For the current study, 26 boys with DMD (and normal intellectual function) and their unaffected siblings were evaluated. Paired comparisons demonstrated that the children with DMD had significantly poorer academic achievement scores than their siblings, even though their vocabulary levels and home and educational environments were comparable. Children with DMD also had more behavioral concerns, physical disabilities, and poorer verbal memory spans. Linear regression indicated that behavioral concerns, executive function, and physical disability did not contribute substantially to academic performance, whereas performance on verbal span did. DMD presents with a selective developmental aberration in verbal span that has wide-ranging consequences on learning skills.

Duchenne Muscular Dystrophy (DMD) is a neurogenetic developmental disability. DMD is known mainly as a genetic disease of muscle, although it also has developmental consequences on the central nervous system. DMD is caused by a mutation of a gene on the X chromosome (Koenig et al., 1987). It occurs in about 1/3,200 boys and results in progressive muscular weakness. DMD is the most common fatal childhood inherited disorder, and affected individuals rarely live past their late -20s.

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Ever since its original characterization by Duchenne (1872), boys with DMD have been known to be at increased risk of mental retardation, although the majority of boys with DMD are not mentally retarded. Whether impaired cognitive function in individuals with DMD resulted from the stresses of living with a chronic, progressive, physically disabling disorder or from the underlying etiology affecting the development of the nervous system was uncertain. Yet, well before discovery of the gene that causes the disorder, decreased academic achievement scores were documented, prompting investigators to write that "an investigation of intelligence and academic achievement should be a routine part" of care for all children with DMD (Worden & Vignos, 1962).

The discovery that the mutated gene in DMD codes for multiple protein products that localize to separate tissue types, including muscle and brain, offers a potential explanation for the cognitive manifestation of the DMD phenotype (for reviews see J. L. Anderson, Head, Rae, & Morley, 2002;Mehler, 2000). In the brain, dystrophin isoforms normally localize to circumscribed cerebral and cerebellar cortical regions and are absent in autopsied brains of individuals affected with DMD. Brain dystrophins are found primarily in the cortex rather than in lower brain structures, and they have been localized to specific cell types as well. In neurons, it has been most clearly identified in pyramidal, stellate, and Purkinje cells (Gorecki et al., 1992;Lidov, Byers, Watkins, & Kunkel, 1990;Tian et al., 1996;Uchino, Teramoto, Naoe, Miike, et al., 1994;Uchino, Teramoto, Naoe, Yoshioka, et al., 1994), and appears to be concentrated primarily in the post-synaptic region (Jancsik & Hajos, 1998;Kim, Wu, Xu, & Black, 1992). Although the contribution of the dystrophin brain products to brain function is unknown, they have been hypothesized to play a structural role that aids in synaptic transmission (e.g., Jancsik & Hajos, 1998). Study of brain function has demonstrated cerebellar hypometabolism as well as variable involvement of association cortices (Lee et al., 2002). Given the selective localization of the dystrophins in normal brains, it is thought that their absence may result in selective cognitive deficits.

Examination of correlation of IQ scores with deletion position in the DMD gene has not demonstrated a one-to-one relationship, but evidence suggests that some regions are more highly associated with mental retardation than others (Bushby et al., 1995). Specifically, cases of mental retardation have been observed only when the deletion is above the 5′ breakpoint of exon 30. However, deletions in those regions are also found in individuals with normal intellectual function, suggesting that deletion location may be necessary, but not sufficient, to impair cognitive development.

There is tremendous individual variation in general intellectual function across affected boys. In a meta-analysis of 32 published papers examining IQ among a total of 1,146 individuals with DMD, the mean full-scale IQ value was 80.2 with a standard deviation of 19.3 (Cotton, Voudouris & Greenwood, 2001). Although scores are shifted down more than one standard deviation from the normative population, the frequency distribution did not differ significantly. Thus, as a result of this downward shift, 35 percent of the children in the DMD sample had IQ scores in the "mentally retarded" range (or scores less than 70), while 6 percent had scores in the "high average" or above range (scores above 110).

Notably, boys with DMD have been reported to have significantly lower verbal IQ scores than performance IQ scores. Because this has been repeatedly demonstrated, it appears to be a reliable finding across the spectrum of intellectual levels. When available data were collapsed across studies in a sample of 878 individuals affected with DMD, the mean group difference between the two scales was five points, which was statistically significant (Cotton et al., 2001). Given the motor and speed demands on many performance (but not verbal) subtests, the finding of higher performance scores among a motor-impaired group is suggestive of even greater verbal-performance discrepancies than are reported.

Examination of more specific cognitive skills has demonstrated mixed findings, but overall most studies have found that individuals with DMD have limited immediate verbal memory (S. W. Anderson, Routh, & Ionasescu, 1988;Billard et al., 1992;Billard, Gillet, Barthez, Hommet, & Bertrand, 1998;Dorman, Hurley, & D'Avignon, 1988;Hinton, Nereo, DeVivo, Goldstein, & Stern, 2000,2001;Karagan, Richmond, & Sorenson, 1980;Karagan & Zellweger, 1978;Leibowitz & Dubowitz, 1981;Marsh & Munsat, 1974;Ogasawara, 1989;Smith, Sibert, & Harper, 1990;Whelan, 1987). The methods used to examine cognitive skills differed across the studies, and many studies had small samples with inadequate or no comparison groups. Nonetheless, most studies report poor performance on tests that require listening to and accurately repeating back verbal information presented only once.

Perhaps the most characteristic example of this is digit span; almost invariably individuals with DMD have demonstrated poor digit recall. Limited digit span has been observed across multiple studies when boys with DMD were compared to normal controls, children with a different neuromuscular disorder (spinal muscular atrophy), or to sibling controls (S. W. Anderson et al., 1988;Billard et al., 1992,1998;Dorman et al., 1988;Hinton et al, 2001;Ogasawara, 1989;Whelan, 1987). Moreover, boys with DMD present with a selective profile such that subtests that tap verbal immediate recall (e.g., Digit Span and Story Memory) are consistently lowest, regardless of general intellectual function (Hinton et al., 2000). Although we have previously referred to the digit-span-related deficit as one of poor "verbal working memory," we have revised our description to call it instead limited "verbal immediate memory" or limited "verbal span." Evaluation of maximum span lengths for both forward and backward recall are similarly diminished in DMD, suggesting that it is span length, rather than mental manipulation of the information, that is impaired (Hinton et al., 2001). Across the age span from 6 to 16 years, boys with DMD recall one to two digits fewer than published norms and their siblings of comparable age on both forward and backward span (Batchelder, Fee, Stern, & Hinton, 2003;Hinton, Fee, De Vivo, Golstein & Stern, in preparation).

Fewer studies have examined academic skills among boys with DMD. An early study by Worden and Vignos (1962) demonstrated that academic achievement was commensurate with overall IQ, such that for boys with DMD mean scores on academic tests were again about one standard deviation lower than the general population. Evaluation of 38 boys with DMD on the Stanford Binet Intelligence Test, the Metropolitan Achievement Test in Arithmetic, and the Gilmore Oral Reading Test provided academic education and achievement quotients for both reading and math skills. For the DMD group, the mean IQ score was 83, and the mean educational quotients (designed to examine how children perform relative to others of their same age) were 84 for math and 87 for reading. The mean achievement quotients (designed to examine how children perform academically relative to their intellectual level) were 96 for math and 101 for reading. These data indicate decreased performance on academic achievement tests, but do not support a discrepancy-based characterization of a specific learning disability, as IQ scores and academic scores are comparably depressed. The authors concluded that the boys with DMD are "achieving within the average expectancy for children of their mental ability" (Worden & Vignos, 1962, p. 971).

Other researchers who have focused solely on reading skills have suggested that children with DMD present with a form of developmental dyslexia. Liebowitz and Dubowitz (1981) tested 42 boys on the Burt Revised Reading Test and found the group had a mean standard score of 82 that was almost identical to their WISC-R V IQ mean score of 83. The authors noted that the reading scores were skewed, such that half of their sample did very poorly on the reading test. Dorman et al. (1988) tested 15 boys with DMD on reading tests and also found limited reading skills in about half the children. Similarly, Billard et al. (1992) demonstrated that among a group of 24 older boys with DMD about half the children with DMD had severe reading disabilities, while none of the comparison group of children affected with a different

neuromuscular disorder (i.e., spinal muscular atrophy) did. Further, the mean standard score on the Reading Index of the DMD group was about one standard deviation lower than that of a children with spinal muscular atrophy. Thus, across studies, children with DMD demonstrated reading difficulties, yet group mean scores on reading tests were not substantially different from the mean IQ scores.

In more detailed examinations of the components of reading, both Dorman and Billard reported that phonological processing is particularly impaired in DMD. In Dorman's sample, the children with DMD had significantly reduced phonetic word-attack skills (Dorman et al., 1988). Billard reported that the overall error rate was highest for the DMD group when reading nonwords, also implicating poor phonological-processing skills (Billard et al., 1998). Billard's analyses compared boys with DMD to either children with spinal muscular atrophy or normal controls who were matched on age and socioeconomic level. They found the children with DMD had a reading age of about two years behind the comparison children. In discussing possible contributions to the poor reading skills among the children with DMD, they noted that poor attention, difficulty with graphophonological conversion, reduction in short-term memory, a deficit on the level of speech production, or psychoaffective and cultural processes might each limit reading ability in the DMD group. After careful consideration of each, they concluded that "a deficit in graphophonological process seems to be the principal explanation of the reading disability" (Billard, et al., 1998, p. 18).

Our work comparing 41 nonretarded boys with DMD to their unaffected sibling controls on a wide battery of tests (Hinton et al., 2001) indicated that the children with DMD performed significantly more poorly than their siblings on Woodcock-Johnson broad composite scores of mathematics and writing, in addition to reading. Even though the two subject groups did not differ on mean age, grade and vocabulary level, nonverbal reasoning, or on the majority of neuropsychological measures given, the group with DMD did consistently worse on all academic achievement tests. The mean standard scores for reading, mathematics, and writing were more than 10 points lower in the DMD than the control group, with the biggest overall effect seen on performance on mathematics tests. The group with DMD also did more poorly than their siblings on tests of immediate verbal memory, including both forward and backward Digit Span and Story Memory. We noted that many potential contributions to poor academic achievement exist in this group, including physical, psychosocial, intellectual, and environmental factors, yet proposed that the limited verbal span may have the most pronounced effect.

The current study tests the assertion that limited verbal span significantly modifies academic achievement among boys with DMD. Sibling pairs (one child affected with DMD and one child unaffected) were carefully selected from the above-mentioned group (Hinton et al., 2001). Their performances on the IQ and achievement measures were analyzed in greater depth to examine the nature of the academic difficulties associated with DMD. Only children who were a minimum of eight years old were included to ensure that basic academic achievement skills had been covered in their education. Only children of estimated "average" or above intellectual ability were included to investigate specific learning disabilities, rather than widespread developmental delays. Only children living at home with unaffected biological siblings, sharing similar home and school environments, family resources, and genetic backgrounds were included. Additionally, only data from measures believed, in general, to significantly impact on academic achievement were included. This careful subject and measure selection based on *a priori* criteria allowed for rigorous scrutiny of contributions to performance on academic achievement tests. We hypothesized that in DMD, limited verbal memory span would be the most salient factor that contributes to academic achievement across subject areas.

METHOD

Subjects

Twenty-six sibling pairs (one boy with DMD and one unaffected sibling) were studied. All children were between 8 and 16 years of age, in good general health (other than the diagnosis of DMD), lived at home, spoke English as their primary language, were of average or above intellectual function, and were willing to participate. Twenty-four families were self-described as Caucasian; two as Hispanic. Twenty-five of the children's mothers and 20 of the children's fathers were high school graduates; six mothers and five fathers were college graduates. All families had incomes in the middle-class or above range.

All children with DMD were male. Diagnosis of DMD was based on clinical onset of progressive weakness before five years of age, elevated serum creatine kinase levels, and either molecular assessment of mutation in the DMD gene or muscle biopsy that was deficient in dystrophin and compatible with DMD. Subjects were recruited from private physicians associated with the Muscular Dystrophy Association clinics in New York (New York Presbyterian Medical Center (NYPMC)), and Atlanta, GA (Scottish Rite Children's Medical Center) and from responses to announcements and mailings sent through the Muscular Dystrophy Association and the Parent Project Muscular Dystrophy. For those families where more than one boy met criteria for inclusion, only one affected male was included. The selected proband was chosen randomly; preference for the elder and then the younger boy alternated between families.

Twenty-six unaffected sibling comparison children whose age was within four years of the proband's age also participated. Where more than one comparison child was available, preference was given first to male gender and then to closeness of age. Fourteen control children were male and 12 were female. Nine siblings were older (four male and five female) and 17 subjects were younger (ten male and seven female) than their brother with DMD.

Procedures

After giving informed consent, all subjects received a battery of neuropsychological tests. The current analyses were drawn from an ongoing study of cognitive skills in children with DMD. Measures with a minimal amount of motor demands were included to minimize the potential confounding effects of impaired physical agility. All measures for the current analyses were chosen based on *a priori* hypotheses regarding potential contributions to academic achievement in this population. Data from some of the participating individuals, on some of the measures, have been described in previously published research reports (Hinton et al., 2000,2001). Data were collected at the hospital clinic (n = 6 sibling pairs), or in the subjects' homes (n = 20 sibling pairs). All subjects were individually assessed in a quiet room, and each assessment took about three hours. Subjects were given breaks as needed. Testing was done in English. All tests were scored twice (once by the person who administered them and once by a research assistant who had not had direct contact with the subject) to ensure validity of the data. Discrepancies were resolved by consensus.

Measures

Academic achievement was assessed using the Woodcock-Johnson (WJ) Achievement Battery (Woodcock & Johnson, 1977). Selected subtests included the Letter-Word, Passage Comprehension, and Word Attack subtests to determine a Broad Reading composite score, the Calculation and Applied Problems subtests to obtain a Broad Mathematics composite score, and the Dictation subtest. The selection of the 1977 edition of the Woodcock-Johnson tests was based on the fact that the subtests had been translated and standardized on a Spanish-speaking population as well as an English-speaking one. At the time of initial data collection,

the 1977 edition was selected as the best tool of academic achievement in a heterogeneous population because we intended to compare data from our bilingual (Spanish/English) subjects to our solely English-speaking subjects. For the purposes of the current analyses, only data from primary English speakers were included.

Measures of select cognitive functions and behavior were included. Intellectual function was estimated using the Ravens Coloured Matrices (Raven, Court, & Raven, 1990). Vocabulary knowledge was assessed using the Peabody Picture Vocabulary Test—Revised (Dunn & Dunn, 1981). Elementary phonological awareness was assessed using the Wepman Auditory Discrimination Test (Wepman & Reynolds, 1987). Executive function was assessed using the Child Category Test (Boll, 1992). Verbal span was assessed using the Digit Span subtest from the WISC-III (Wechsler, 1991). Children's behavior was assessed using the Child Behavior Checklist completed by the children's parents (Achenbach, 1991). All children in the group with DMD were demonstrating increased physical weakness relative to their siblings. Wheelchair dependency was used as a gross marker of physical disability, and 11 of the boys with DMD, but none of the siblings, were using wheelchairs at the time of the examination.

Data Analysis

Between-group paired *t*-tests were run on all primary outcomes, the academic achievement test scores. Since the 1977 edition of the Woodcock-Johnson tests provides standard scores only for the broad composites, raw-score data were analyzed for the individual subtests. The Bonferoni correction was applied to set an alpha that was appropriate for the number of individual analyses (or 0.05/9 ~ 0.005).

Within-group paired *t*-tests were run to examine the discrepancies between intelligence and. academic achievement. Three paired *t*-tests were run for each group, comparing the Ravens standard score with each of the academic achievement composites. The Bonferoni correction was applied to set an alpha that was appropriate for the number of individual analyses (or 0.05/6 ~ 0.008).

Between-group paired *t*-tests were also run on all measures believed *a priori* to be possible confounders of the academic achievement scores. These included age, wheelchair use, a measure of nonverbal intellectual function, vocabulary skill, executive function, phonological awareness, verbal span, and behavior. The Bonferoni correction was not applied, as the goal was to set liberal criteria to find measures that should be included in the regression models. All measures found to differ between groups at the 0.05 level were then included in the model examining academic achievement in the DMD group.

Three linear regression analyses were run, examining reading, mathematics, and dictation composite scores as outcomes, and simultaneously entering the items found to differ significantly between the matched groups as independent variables. Data from all subjects were included to rule out any bias of group membership.

RESULTS

Results from paired *t*-tests are presented in Tables 1, 2, and 3. Table 1 shows that significant between-group differences were observed on all academic composite scores and on each individual academic subtest, even when applying the stringent alpha of 0.005. Standardized composite scores, based on a mean of 100 and a standard deviation of 15, were about one standard deviation different between the groups in each of the three areas. The biggest between-group difference (21 points) was on the mathematics composite. Thus, children with DMD did more poorly than their siblings across academic areas.

Table 1 also shows that raw scores on each individual subtest were also significantly lower in the DMD group. Because of the edition of the measures used, no standardization data were available for the individual subtests. Across the reading subtests, there was no evidence of a selectively greater phonological deficit; rather, children demonstrated phonological-processing difficulties, as evidenced by their poor performance on Word Attack, and also did comparably poorly on other reading subtests.

Table 2 shows within-group comparisons examining performance on intellectual and academic measures. All three comparisons for the DMD group were significantly different. Across reading, mathematics, and dictation, children with DMD scored significantly more poorly on their academic tests than they did on their nonverbal intellectual measure, with mean difference scores being between 8 and 14 points. In contrast, siblings' scores on all three academic composites were not significantly different from their nonverbal intelligence estimate. Their mean difference scores ranged from 0.6 to 1.9.

Table 3 shows between-group findings across potential confounding measures. The groups did not differ on age or vocabulary level (Peabody Picture Vocabulary Test) or elementary phonological discrimination (Wepman). As anticipated, there was a between-group difference on a measure of verbal span (Digit Span), with the DMD group demonstrating poorer performance than their siblings. Additionally, groups differed on intellectual level (Raven's Coloured Matrices) and executive function (Children's Category Test), findings that were unexpected, given prior analyses. Prior analyses had not run paired comparisons with well-matched subject groups, so the current statistics were more sensitive to minor differences. Of note is that the scores of the DMD group were all well within the average range, (e.g., mean standard score on the Ravens was 99), yet children with DMD consistently scored below their siblings on these nonverbal measures. The DMD group also had higher ratings on the Total Behavior Problem Scale of the Child Behavior Checklist, which might reflect some of the psychosocial aspects of the illness, and this effect size was larger than those observed on the cognitive measures. Other significant between-group differences were reflected in the study design: only children in the DMD group used wheelchairs ($n = 11$), and only children in the sibling group were of mixed gender (14 males and 12 females).

Because of the unexpected finding of the between-group differences on the Ravens Test, an analysis of variance (ANOVA) was run on the achievement scores, co-varying for the effects of intellectual function to determine whether the between-group differences remained after the effects of intellectual function were controlled. A 2 group by 3 measure (Reading, mathematics, and dictation) ANOVA, with Ravens scores entered as a covariate, was run. The omnibus F was significant ($F = 4.16$, $p = 0.007$), confirming that academic skills were selectively depressed in DMD, and that the effects were not due solely to depressed intellectual function. Further, between-group differences for the individual composite scores, controlling for intellectual function, were significant for both mathematics and dictation (math $F = 13.69$, $p = 0.001$; dictation $F = 5.24$, $p = 0.027$). Surprisingly, for the reading composite score, the between-group difference approached, but did not reach, significance (reading $F = 3.54$, $p = 0.067$).

To determine which variables might influence academic achievement, three linear regression analyses were run. Reading, mathematics, and dictation composite scores were outcomes, and the items found to differ significantly between the matched groups (Ravens, Digit Span, Children's Category Test, CBCL Total Behavior Problem scale, wheelchair use, and gender) were entered simultaneously as independent variables. The results are presented in Table 4. For each analysis, the overall F value was significant (Reading $F = 10.38$, $p = 0.000$; math $F = 10.91$, $p = 0.000$; dictation $F = 14.31$, $p = 0.000$). Further, for each analysis, intellectual-function and verbal-span measures both contributed significantly to academic scores, but

measures of executive function, behavior, physical function, and gender did not. Thus, among a group of children from similar environments who were close in age, factors related to cognitive function rather than physical disability distinguished the groups' performance on academic skills.

DISCUSSION

The results of these analyses replicate the findings of nonspecific decreased academic achievement in boys with DMD. Across academic areas, boys with DMD performed more poorly than their siblings. Further, for the boys with DMD, academic scores were significantly depressed relative to their estimated intellectual level, but this was not true for their siblings. For the DMD group, the largest effect was for mathematics, where the mean Raven versus math composite score was 14 for the group with DMD and only 0.59 for their siblings. Individual math data are displayed graphically in Figures 1 and 2. Ravens scores are arranged from lowest to highest, and for both groups fall across a similar range. Math scores are arranged relative to the Ravens score for each individual subject. In the DMD group, all but 1 percent of the group scored lower on the math test, while for the siblings there was a fairly even distribution of scores, with 41 percent of the group scoring higher in math than on the Ravens.

Further, the results support the hypothesis that there is a significant relationship between performance on digit-span and on academic-achievement tests in boys with DMD. Although numerous factors contribute to any individual's academic achievement—from underlying genetic makeup, to physical health, mood and intellectual ability, to daily environment and school opportunities—only intellectual function and verbal span were found to be significant influences on children's test scores in analyses that attempted to tease out the contributions of multiple factors. The ability to listen to verbal material and hold it in immediate memory contributed between 25–39 percent of the variance observed on academic scores in reading, writing, and arithmetic. Wheelchair use, behavior problems, executive function, and gender did not significantly contribute to the outcome scores.

We propose that immediate verbal memory is the core deficit in DMD. Across studies, children with DMD have been shown to do poorly on a variety of tests that tap into the ability to listen to verbally presented information and accurately respond, whether by saying back a series of digits, words, nonwords, or sentences just heard, or by performing a multistep task that has been verbally directed, without benefit of repetition (Billard et al., 1992,1998;Dorman et al., 1988;Hinton et al., 2000,2001, unpublished data; Karagan et al., 1980;Leibowitz & Dubowitz, 1981;Marsh & Munsat, 1974;Smith et al., 1990). The deficits observed do not, however, depend on the manipulation of the information (the most simple case being that forward and backward digit spans are similarly limited), suggesting that the problem is not "working" memory. Additionally, the problems experienced by the children with DMD appeared to be somewhat more focused than generalized attentional deficits. Of note is that the Attention Problems scale on the Child Behavior Checklist is not significantly elevated in the children with DMD when compared to their siblings, (Hinton, Nereo, & Fee, submitted). The problem observed in individuals with DMD appears to be one of limited verbal storage capacity, or possibly limited space within the hypothetical "phonological loop" (Baddeley, 1986).

This limited verbal storage capacity is believed to be a developmental consequence of the etiology of the disorder. In DMD, the genetic mutation prohibits selective dystrophin protein products from being made. As a result, affected individuals' brains develop without dystrophin products that are normally there. The exact function of these products is unknown, but they may well normally provide the biological substrate necessary for optimal performance on tests of immediate verbal memory. Thus, we propose that as a result of having a mutated dystrophin

gene, children with DMD have limited immediate verbal memory, which in turn contributes to their falling behind in their academic skills.

Other investigators have discussed DMD as being a type of developmental dyslexia that presents with a core deficit in phonological processing that interferes with acquisition of reading skills (Billard et al., 1992,1998;Dorman et al., 1988). We did not find any between-group differences on a measure of phonological processing, the Wepman Auditory Discrimination Task; children with DMD were able to distinguish simple words from one another. Additionally, we found that performance on the Wepman test did not contribute to performance on the academic-achievement measures. However, we are concerned that those data may reflect limited test sensitivity and are not a sufficient means to rule out phonological-processing deficits in this group. We are currently examining children using more comprehensive tests of phonological processing, including tests of nonword repetition and sound blending, and initial results indicate that the children with DMD show difficulties on these measures. Further, our Woodcock-Johnson data support the claim that children with DMD have reading difficulties, and that they are not proficient in their phonological-processing skills, as evidenced by their limited word-attack abilities. Our findings, much like those of Worden and Vignos (1962), indicate that the academic impact is more far ranging than solely reading skills, and that children with DMD have difficulty in other academic areas, such as mathematics. We propose that the “core” deficit is the limited verbal span associated with DMD, which, in turn, might hamper phonological-decoding skills. Even in the elegant study of reading ability in DMD by Billard et al. (1998), which concluded that graphophonological difficulties were the major source of reading disability, Digit Span and Arithmetic scores were the only significant contributions to reading scores in a regression analysis. The interdependent relationship between phonological processing and phonological memory (as measured by digit or sentence recall) has been well characterized by the model put forth by Wagner, Torgensen, and Rashotte (1999).

The idea that a child who does not “grasp” verbally presented material as readily as his or her peers may fall behind in all areas of school progress makes intuitive sense. If the child attends the same classroom and listens to the same lessons, but is unable to “catch” the information as well as his or her classmates, then the consequences may be profound. Indeed, there is extensive literature documenting the association of verbal memory span and academic achievement. Verbal memory span has been found to correlate with word-learning and reading and math-achievement scores in heterogeneous student populations (e.g., Adams & Gathercole, 2000;Daneman & Carpenter, 1980;Gathercole, Hitch, Service, & Martin, 1997;Hitch, Towse, & Hutton, 2001). Among groups of children characterized by their academic difficulties (such as those with dyslexia or learning disabilities), performance on Digit Span has been repeatedly found to be poor when compared to non-reading or learning disabled groups (e.g., Hulme & Roodenrys, 1995;Siegel & Ryan, 1989). Further, when groups of children with school-identified learning disabilities are reviewed, between 13–20 percent have been found to have isolated significant difficulties on verbal-span tasks (e.g., Lyon, 1985;Siegel & Ryan, 1989;Speece, 1987;Torgensen, 1988). Early performance on tests of verbal span have been found to be predictive of later reading and math attainment (e.g., Ashcraft, 1995;Shaywitz et al., 1999;Wagner et al., 1997). Additionally, measures of phonological awareness and memory are found to contribute to the shared variance in reading and math (Hecht, Torgenson, Wagner, & Rashotte, 2001). Although a thorough review is beyond the scope of this article, the association of performance on measures of verbal span (and measures of phonological memory) and measures of academic skill is very well established.

There are a number of issues that clinicians and educators should consider when working with a child with DMD. First, awareness that cognitive deficits are associated with DMD is crucial to the best treatment of all affected children. Because most educators are likely not familiar

with the disorder, understanding that what presents as a disease of physical disability also can affect cognitive development is the first step toward tailoring an appropriate curriculum. Additionally, awareness of the range of cognitive components involved in learning and awareness that selective deficits occur across the IQ range will aid in the recognition that children who are not mentally retarded may have learning disabilities that affect their academic achievement. Second, the results suggest that all children with DMD would benefit from an individualized neuropsychological evaluation to determine whether specialized educational interventions may be warranted. Among the children in the current study, even those with above-average estimated IQs performed significantly worse on their academic achievement tests. Thus, all children with DMD are presumed to be at risk for learning disabilities. The individual child's assessment should emphasize academic skills, verbal abilities (especially including measures of phonological processing and memory), working memory, and attention.

Appropriate educational interventions include breaking detailed verbal instructions into smaller segments, repeating verbal information, and phonological-awareness training. In general, classroom techniques that have been adopted for children with developmental dyslexia and attentional deficits will likely be effective learning strategies for children with DMD.

Our ongoing work will examine in greater detail the interrelationships between digit span, phonological processing and memory, and academic skills in children with DMD. The current study supports the hypothesis that limited digit span contributes to poorer academic performance. Nonetheless, the study does not allow for careful examination of the aspects of digit span that are most salient. Thus, although we argue that it is immediate verbal span that is compromised, the study has admittedly limited measures of phonological processing, working memory, and attention, making it impossible to rule out the contributions of these cognitive constructs. Further, understanding of academic performance in this group of children is somewhat hampered by the use of out-dated measures that do not allow for detailed evaluation of different academic processes. The choice of test was based on a methodological decision to make the test battery appropriate and equivalent for children who were either primarily English or Spanish speakers. However, this constraint was not necessary for the current analyses, as only English-speaking children were studied, and it is unfortunate not to have data on the most current test measures. Our ongoing studies are using the most recent test editions and we hope to be able to extend and replicate the current findings in a new group of children with DMD.

The strengths of the current work lie in the careful design, which, in particular, involved comparing children with a known etiology and normal intellectual level to well-matched controls. Unlike the majority of research in the field of learning disabilities where the physical cause of the cognitive problems is unknown, this work provides a neuroscience reductionist model for relating gene, brain development, and behavior. The combination of known etiology associated with selective cognitive deficits has the potential to improve our understanding of various contributions to poor academic achievement. Children are grouped based on characteristics other than their learning disabilities, avoiding some of the confounds necessarily encountered by examining cognitive skills in groups selected based on their cognitive performance.

Thus, study of DMD provides an etiology-based model of a common problem—limited verbal span—that affects academic achievement. Further study of children affected by DMD might yield insight into the underlying brain function and cognitive manifestation of such learning disabilities and might improve the quality of life for each affected individual.

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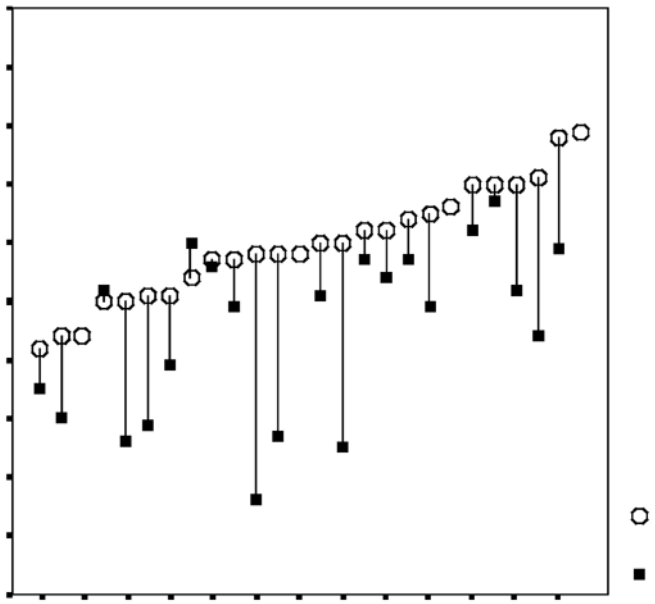

FIGURE 1

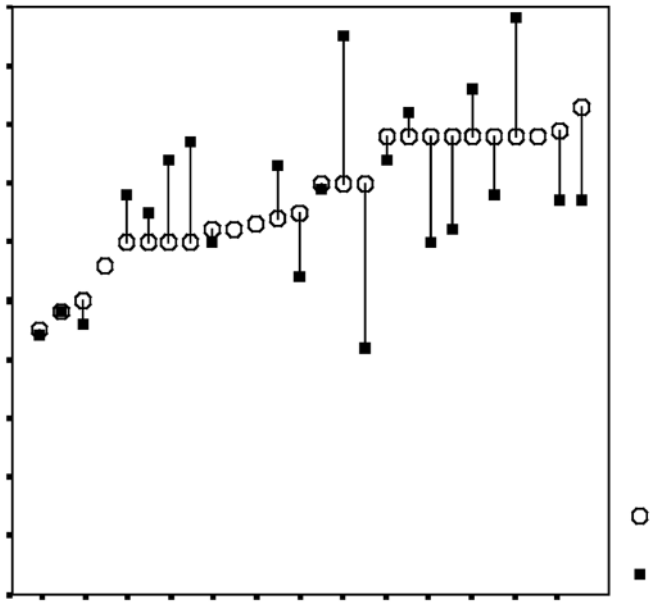

FIGURE 2

FIGURES 1 and 2.

Relationship of individual subjects' IQ and academic scores. Individual data points from subjects with DMD are displayed in Figure 1 and data from siblings are in Figure 2. The circles represent the Ravens IQ estimate and have been arranged in ascending order for each group. Filled squares represent W-J Mathematics composite scores. Individual subjects' data points are connected by a line. Note that for children with DMD, math scores generally fall below their IQ estimates, whereas for the sibling comparison group, math scores are more variably dispersed.

TABLE 1

Between-Group Paired *t*-Tests of Academic Achievement Scores

Variable	DMD Mean ± SD	Sibling Mean ± SD	t-Value	p
Standard Scores				
READ SS	91.08 + 14.86	105.56 + 11.77	4.86	0.000
MATH SS	85.27 + 14.46	106.36 + 13.62	4.44	0.000
WRITING SS	91.23 + 15.95	108.45 + 14.86	5.32	0.000
Raw Data				
Letter Word	34.27 + 6.89	40.50 + 4.46	4.49	0.000
Passage Comp.	14.73 + 4.63	18.81 + 2.76	4.69	0.000
Word Attack	13.08 + 7.27	19.00 + 4.38	4.14	0.000
Applied Problems	27.73 + 4.62	33.63 + 4.64	4.53	0.000
Calculation	16.00 + 5.98	22.23 + 6.32	3.74	0.001
Dictation	19.50 + 7.08	24.23 + 6.39	3.04	0.006

TABLE 2

Within-Group Paired *t*-Tests of IQ Versus Academic Scores

	Difference Mean ± SD	t-Value	p
DMD Group			
Ravens SS-Read SS	8.32 + 12.36	3.36	0.003
Ravens SS-Math SS	14.00 + 12.25	5.36	0.000
Ravens SS-Write SS	8.04 + 12.98	2.91	0.008
Sibling Group			
Ravens SS-Read SS	1.88 + 10.28	0.93	ns
Ravens SS-Math SS	0.59 + 13.41	0.21	ns
Ravens SS-Write SS	0.64 + 10.61	0.28	ns

TABLE 3

Between-Group Paired *t*-Tests of Potential Contributing Variables

Variable	DMD Mean ± SD	Sibling Mean ± SD	t-Value	P
Age	10.96 + 1.77	11.81 + 2.02	1.78	ns
PPVT SS	109.00 + 15.73	113.65 + 15.93	1.53	ns
RAVENS SS	99.65 + 9.90	107.34 + 10.81	2.83	0.009
DIGIT SPAN ScS	8.19 + 2.67	9.96 + 2.79	2.21	0.037
Wepman raw data	26.52 + 2.50	26.90 + 2.23	0.53	ns
CC T T score	46.15 + 9.84	51.73 + 9.00	2.27	0.032
CBCL total T	54.56 + 11.78	41.84 + 9.88	4.84	0.000

Note. SS is standard score. ScS is scaled score.

TABLE 4

Summary of Regression Analysis for Variables Predicting Academic Achievement Scores

W-J Composite	Variables	B	SE	Beta	p
Reading	Ravens SS	0.72	0.18	0.53	0.000
	Wheelchair use	0.01	4.37	0.00	ns
	CBCL total T	0.04	0.15	0.04	ns
	Digit Span ScS	1.22	0.58	0.25	0.04
	Category test	0.12	0.17	0.08	ns
	Gender	7.83	4.29	0.21	ns
Math	Ravens SS	0.55	0.21	.33	0.010
	Wheelchair use	−6.06	5.15	−0.14	ns
	CBCL total T	−0.02	0.17	−0.01	ns
	Digit Span ScS	2.15	0.67	0.36	0.003
	Category test	0.38	0.19	0.21	ns
	Gender	7.07	4.99	0.16	ns
Writing	Ravens SS	0.84	0.19	0.53	0.000
	Wheelchair use	0.98	4.73	−0.03	ns
	CBCL total T	−0.01	0.16	0.01	ns
	Digit Span ScS	2.21	0.61	0.39	0.001
	Category test	0.12	0.18	0.07	ns
	Gender	6.62	4.58	0.15	ns

Note. SS is standard score. ScS is scaled score.