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Intellectual Function in Muscular Dystrophies

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Summary. Intellectual function was studied in 28 boys with Duchenne dystrophy, 12 patients with facioscapulohumeral-type and 10 patients with limb-girdle-type muscular dystrophy. A definite relationship between intelligence level and the type of muscle disease was found. The more severe the genetic damage manifested by the rapidity of progression of muscular dystrophy the more definite the affection of the CNS manifesting as mental deficit. The factors influencing the level and structure of intelligence seem to exert their effect before the manifestation of muscle lesions.

Key words: Intellectual function – Duchenne muscular dystrophy – Limb-girdle-type muscular dystrophy – Facioscapulohumeral-type muscular dystrophy

Introduction

Muscular dystrophies have generally been considered as primary disorders of striatal muscles. However, pathological changes outside the skeletal muscle observed in Duchenne muscular dystrophy (DMD) put the matter in a new light. Evidence of the involvement of cardiac muscle [18] and erythrocyte membrane [1, 22] have been described. EEG changes and pathoanatomical abnormalities of the brain suggested involvement of the CNS in that disorder [2, 12, 16, 20].

In recent years a number of studies have shown a fairly consistent picture of an average IQ of around 85 for DMD children [2, 5, 6, 8, 10, 11, 12, 17, 19, 25, 26]. To interpret the results, the consequences of progressive physical hand disability [14, 15] or environmental stimuli deprivation [15] were taken into consideration. Nevertheless, common etiological factors both of mental retardation and muscle disease could not be excluded [4, 5, 14, 17, 20].

Recently systematic studies have concluded that an early and stationary verbal disability reflected by a low verbal IQ is a characteristic sign of DMD [7, 8, 10, 11, 14].

The limb-girdle (LG) and facioscapulohumeral (FSH) types of muscular dystrophies are also considered to be primary muscle diseases representing different nosological entities in relation to heredity, and histological and clinical signs. However, they are generally associated with normal intellectual function. There are few data in the literature on the mental performance in muscular dystrophies of adult life [3, 9].

The purpose of the present study was to investigate:

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– whether there was any difference between the DMD and adult types of muscular dystrophies with respect to verbal, performance and global intelligence level,

– what was the frequency of low (i.e., below 79) IQ values in the different types of muscular dystrophies,

– whether the scores were influenced by hand disability, or by confinement to wheelchair or by familial accumulation,

– whether there was any relationship between progression rate and intellectual function,

– whether there was a special pattern of intelligence damage, i.e., are there characteristic alterations in the subtests of the Wechsler Intelligence Test.

Materials and Methods

Intellectual function was studied in 28 patients with DMD (age 6–13 years), 12 patients with FSH-type (age 14–48 years) and 10 patients (age 18–68 years) with LG-type muscular dystrophy (Table 1). The diagnosis and classification were based on clinical, biochemical, electromyographical, and histological findings.

The severity of muscle damage at the time of investigation was estimated on the basis of the following stages:

I. Mild degree of physical disability (able to walk)
II. Moderate degree of physical disability (able to walk with help)
III. Wheelchair-bound
IV. Recumbent stage

The Wechsler Intelligence Scale for Children (WISC) [23] or for Adults (WAIS) [24] was used on all patients depending on their ages. As no Hungarian standard for WISC was available, this test was also used on a control group of 20 age-matched children with no sign of neuromuscular disease. They were drawn from a similar socioeconomic environment.

Table 1. Characteristics of subjects

	FSH + LG	DMD	Controls for DMD
Number of patients	22	28	20
Mean age in years	35.3	10.8	10.9
Mean duration of disease in years	14.9	7.4	–
Male/Female	16/6	28/0	20/0
Familial/Sporadic cases	12/10	12/16	–

Statistical analyses were done with the help of Student's t-test and the χ^2 test.

Results

IQ levels including full-scale (IQ), performance (PIQ) and verbal (VIQ) quotients were significantly lower in the DMD group than in those with slow progression (FSH and LG). The differences between the DMD group and the control boys were also highly significant ($P < 0.001$). It is remarkable that Hungarian children showed higher VIQ values, roughly by 10, than PIQ values. In agreement with this finding, a VIQ-PIQ discrepancy of 7 points was found in our group of control children (Table 2). The mean difference between the values of VIQ and PIQ was 0.9 points in the DMD group suggesting a relative performance dominance.

The IQ was below 79 in 41% of DMD patients and 23% of the adults (FSH and LG), the difference being significant using the χ^2 test.

Concerning the influence of hand disability on performance, patients were divided into two groups in both types of muscular dystrophy: (a) the first group included patients with mild upper limb weakness without any practical effect on the use of hands; and (b) the second group of patients showed a definite paresis in the upper limbs sufficient to restrict them in daily activities (Table 3). There was no significant difference between the scores of the two groups of DMD patients, moreover the scores on the PIQ scale tended to be slightly higher in the advanced cases. In contrast, the mean IQ of those four patients having restricted use of hands in the adult (FSH and LG) types of muscular dystrophies was significantly lower ($P < 0.01$) in comparison with those having full agility of hands. Since their scores were low on VIQ and PIQ scales this poor performance could not be explained only by paresis.

Analyzing the effect of stimuli deprivation on mental ability, two groups were formed in both types of the disease: (a) patients able to walk; and (b) wheelchair-bound patients (Table 4). There was no difference between the mean scores of the two DMD groups on either scales. The adult (FSH and LG) wheelchair-bound patients showed significantly lower scores on both VIQ and PIQ scales as compared with patients able to walk.

Presuming a common etiological factor of muscle disease and mental disability, the relationship between the mental performance and the familial accumulation of the disease was studied. Accumulation of DMD in a family was observed in 10 cases. In the adult types of muscular dystrophy there were 12 patients with affected relatives (Table 5). No difference was found between the familial and sporadic cases with respect to mean age or time of onset of the disorder in either types of the disease. IQ levels including the PIQ and VIQ scales tended to

Table 2. Comparison between patients with facioscapulohumeral (FSH) + limb-girdle (LG), Duchenne muscular dystrophies (DMD) and controls on full scale, verbal scale and performance scale IQ (VIQ, PIQ)

	IQ (± SD)	VIQ (± SD)	PIQ (± SD)
FSH + LG ($n = 22$)	100.0*** (± 19.4)	100.2** (± 17.1)	102.0*** (± 20.8)
DMD ($n = 28$)	83.2***** (± 19.4)	84.7**** (± 19.7)	85.6**** (± 17.2)
Controls ($n = 20$)	110.2 (± 23.2)	112.0 (± 17.6)	105.0 (± 16.1)

*$P < 0.05$
**$P < 0.01$
***$P < 0.001$ between FSH + LG and DMD patients

****$P < 0.01$
*****$P < 0.001$ between DMD patients and controls

Table 3. IQ, VIQ, and PIQ mean values in patients with FSH + LG and DMD with respect to proper and restricted use of hands

	Use of hands	Mean age in years	IQ (± SD)	VIQ (± SD)	PIQ (± SD)
FSH + LG	Proper ($n = 18$)	31.2	106.4 (± 16.5)	104.1 (± 16.4)	109.0 (± 15.4)
	Restricted ($n = 4$)	53.2	75.2* (± 6.7)	82.5* (± 5.0)	70.5* (± 8.6)
DMD	Proper ($n = 18$)	9.3	81.4 (± 21.4)	82.5 (± 21.7)	84.6 (± 19.0)
	Restricted ($n = 10$)	13.6	86.8 (± 15.6)	88.8 (± 14.1)	87.4 (± 11.8)

*$P < 0.01$ between patients having restricted and proper use of hands

Table 4. Mean IQ, VIQ, and PIQ values in patients with FSH + LG and DMD with respect to mobility

	Mean age in years	IQ (± SD)	VIQ (± SD)	PiQ (± SD)
FSH + LG				
Able to walk ($n = 18$)	31.2	106.4 (± 16.5)	104.1 (± 16.4)	109.0 (± 15.4)
Wheelchair-bound ($n = 4$)	53.2	75.2* (± 6.7)	82.5* (± 5.0)	70.5* (± 8.6)
DMD				
Able to walk ($n = 22$)	9.0	82.3 (± 20.7)	84.5 (± 21.1)	86.0 (± 17.8)
Wheelchair-bound ($n = 6$)	11.6	83.1 (± 15.4)	85.8 (± 14.5)	84.0 (± 15.8)

*$P < 0.01$ between patients able to walk and wheelchair-bound

Table 5. Mean IQ, VIQ, and PIQ values in familial and sporadic cases of FSH + LG and DMD

	Cases	Mean age in years	IQ (± SD)	VIQ (± SD)	PIQ (± SD)
FSH + LG	Familial ($n = 12$)	36.6	91.0** (± 18.5)	92.0* (± 15.2)	91.7** (± 20.7)
	Sporadic ($n = 10$)	33.6	112.5 (± 13.5)	110.0 (± 14.3)	114.3 (± 13.3)
DMD	Familial ($n = 10$)	10.4	80.5 (± 19.9)	83.9 (± 17.4)	81.4 (± 13.0)
	Sporadic ($n = 18$)	10.4	85.0 (± 19.9)	85.6 (± 20.0)	87.9 (± 17.1)

*$P < 0.05$
**$P < 0.01$ between familial and sporadic cases

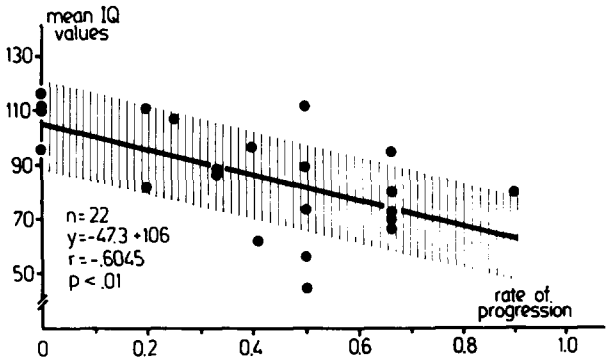

Fig. 1. Linear regression between the progression rate and mean values of IQ in patients with DMD

Table 6. Comparison of subtest scores of the Wechsler test between patients with FSH + LG and DMD and between DMD patients and their age-matched controls

	FSH + LG ($n = 22$)	DMD ($n = 28$)	Controls ($n = 20$)
Information (±SD)	10.2*** (±3.2)	6.9***** (±2.8)	10.8 (±3.2)
Comprehension (±SD)	10.5** (±3.2)	7.6***** (±4.8)	12.3 (±3.9)
Digit span (±SD)	9.6 (±3.2)	9.1 (±5.6)	10.5 (±3.2)
Arithmetic (±SD)	9.1 (±3.8)	9.2 (±5.1)	10.1 (±3.7)
Similarity (±SD)	10.9 (±3.1)	10.9***** (±5.1)	16.1 (±3.1)
Digit symbol (±SD)	12.5* (±4.4)	9.1 (±4.2)	10.8 (±2.3)
Picture arrangement (±SD)	8.8 (±3.2)	8.5 (±4.9)	10.4 (±4.0)
Picture completion (±SD)	10.9 (±4.8)	9.0 (±3.8)	10.4 (±4.0)
Block design (±SD)	10.1* (±3.5)	7.7**** (±2.4)	11.2 (±3.9)
Object assembly (±SD)	9.4 (±3.2)	8.5 (±5.8)	10.6 (±4.1)

*$P < 0.05$
**$P < 0.01$ between FSH + LG and DMD patients
***$P < 0.001$
****$P < 0.05$ between DMD patients
*****$P < 0.001$ and age-matched controls

be lower in familial DMD cases ($P < 0.1$) than in sporadic cases (Table 5).

The connection between the rate of progression of the disease and mental performance in DMD has been discussed elsewhere [7]. The rate of progression was expressed by a ratio, the value of the ratio being 1 when the disease progressed by one stage (one of the four mentioned above) in a year. The slower the progression of the disease the nearer the ratio to 0. A possible relationship was suggested: the more rapid the progression rate the lower the intelligence level in DMD (Fig. 1).

In the present study a similar global tendency seemed to be valid: the rapid progression (DMD)-type of muscular dystrophy was accompanied by a lower intelligence level compared to the cases with slow progression (adult). This observation is roughly consistent with the findings of Karagan and Sorensen [9].

To see whether there was any difference in the pattern of intellectual function, the subtest scores in DMD and adult (FSH and LG) types of muscular dystrophies were investigated (Table 6). The scores of the children with DMD were significantly lower in subtests "information", "comprehension", and "block design" as compared with the adult patients. Mean scores for each verbal subtest except for "arithmetic" and "digit span" were significantly lower in DMD than in age-matched controls. The mean scores of all PIQ subtests except "block design" were not significantly different. The scores of severely disabled adult patients were equally poor in each subtest on both VIQ and PIQ scales.

Discussion

A highly significant shift towards the range of low intelligence levels was found in patients with DMD as compared with the age-matched healthy controls as well as with the patients with LG and FSH dystrophy. IQ values below 79 were found significantly more frequently in DMD than in the LG and FSH types of muscular dystrophies.

A relative performance dominance was shown in cases with DMD as compared with age-matched controls which is roughly consistent with Karagan's findings with the conclusion that an early verbal disability reflected by a low verbal IQ is characteristic of DMD [7, 8]. The high VIQ-PIQ discrepancy is thought to be a poor prognostic sign. Recently Sollee et al. [21] have presented evidence of a cognitive deficit very early in DMD. This deficit could be shown only in cases of young children by low scores in tasks requiring the organisation of attention and verbal skills. It was found not to be stable and tended to disappear in older children. In the present study subtests requiring verbal skills and attention showed significantly lower scores in DMD patients than in healthy controls. Children with DMD aged above 10 years tended to achieve slightly higher scores on the verbal scale than those below 10 years. Subtests "information" and "comprehension" indicating the cognitive attitude and "block design" requiring visuomotor organisation were performed significantly worse by DMD patients than by the adult group with LG and FSH types. Other subtest scores involving purely motor activity were not significantly low. Therefore, the poor achievement measured by the Wechsler test in DMD did not seem to reflect either the stimuli deprivation or the hand disability.

The advanced cases of adult types of muscular dystrophies showed verbal as well as performance quotients below average. Since they became wheelchair-bound at an adult age their mental development should not have been restricted by environmental stimuli deprivation. This finding could be interpreted as the low IQ might be a poor prognostic sign even in the FSH and LG types of muscular dystrophies, although the number of our patients (four cases) was not enough to draw any conclusion.

The mean IQ of dystrophic patients having affected siblings seemed to be lower as compared with those of sporadic cases. This tendency was seen in DMD children ($P < 0.1$) and was highly significant in FSH and LG dystrophy. Similar observations have been published by Leibowitz and Dubowitz [13] and Koziczka et al. [12].

It is well-known that mental retardation is influenced by a great number of different factors, such as abnormality of genes or chromosomes. The various types of muscular dystrophies are inherited as different traits. This may constitute the basis of diverse intelligence levels in different types of muscle diseases. The X-linked rapid progressive DMD is accompanied by the lowest mean IQ level. However, it must be taken into consideration that in the slow progressive group the mean intelligence level of the patients having affected relatives was significantly lower as compared with that of the sporadic cases, reflecting the possibility of more severe genetic damage.

Our data support the hypothesis that there is a relationship between the muscular dystrophies and intellectual function. The more severe the genetic damage manifested by the rapidity of the progression of muscle disease, the more definite the affection of the CNS appearing as an intelligence deficit. The factors influencing the level and structure of intelligence seem to exert their effect before the manifestation of muscle lesions.

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