SHORT REPORT

Neuropsychological deficits in myotonic muscular dystrophy

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Abstract

Twenty patients with myotonic muscular dystrophy (MMD) were compared with twenty controls on a battery of standardised neuropsychological tests measuring motor and cognitive functions. The MMD patients performed significantly poorer on both motor and cognitive tests, particularly those assessing spatial functions. Although both motor and cognitive scores were correlated with age, significant diagnostic group by age interactions were present only for the motor measures. Therefore, while motor deficits in MMD may progress with ageing, cognitive deficits are mainly developmental and relatively stable.

Impairment of higher cognitive functions has been reported as a common clinical feature of myotonic muscular dystrophy (MMD).[1 2] It is well established that muscle degeneration is progressive in MMD, and some authors have suggested that the associated cognitive changes might follow a parallel course. Bird, Follett and Griep[3] found no evidence of progression of cognitive deficits with age. However, their test measures were limited to the Wechsler and Shipley intelligence scales. Portwood *et al*[4] reported that MMD patients with maternal inheritance (and presumably earlier onset of symptoms) had greater deficits on a more comprehensive neuropsychological battery than a paternal inheritance group. Stuss *et al*[5] found that MMD patients performed in the low average range as a group on a neuropsychological battery, but that those with earlier age of onset and longer duration of illness performed significantly more poorly on certain of the tests measuring verbal abilities. They recommended longitudinal research on the cognitive effects of MMD.

Longitudinal research is difficult due to lack of early diagnosis, difficulty in tracking patients over long time spans, and loss of subjects due to geographic changes and mortality. Age of onset is difficult to estimate at best, because patients are usually diagnosed well into the course of the disease and have difficulty judging retrospectively when symptoms began. This study addressed the question of progression in deficits in MMD by sampling cross-sections of MMD patients in ages ranging from young adult to early senescence. Performances of these patients were compared to age-matched normal controls, to ensure that changes in MMD were greater than expected on the basis of normal ageing. Both motor and cognitive abilities were formally assessed, utilising a battery of neuropsychological tests.

Method

Subjects

Experimental subjects consisted of 20 patients being followed for MMD in the Neuromuscular Clinic at the University of Mississippi Medical Center and Jackson Veterans Administration Medical Center. All MMD subjects had had their diagnoses confirmed by a series of tests including electromyography and muscle biopsy. The mean age of the MMD group was 39·6 (SD = 12·6) and the mean education was 11·0 years (SD = 3·0). A group of 20 normal controls matched for age and education were recruited from hospital staff. None of the controls had any history of neurological or psychiatric illness. Subjects in both diagnostic groups were evenly divided into four age-stratified subgroups: ages 20–29, 30–39, 40–49 and 50–65.

Procedure

Subjects were administered a battery of tests measuring both motor and cognitive neuropsychological functions. Motor measures included right and left hand grip strength, finger tapping speed, and grooved pegboard time to completion. Cognitive tests included a short form of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), Wisconsin Card Sorting Test (WCST), Western Aphasia Battery (WAB), Benton's Facial Recognition, Line Orientation, and Three Dimensional Construction Tests, and the Russell revision of the Wechsler Memory Scale. Testing required approximately four hours, and was usually completed in two sessions separated by a rest period.

Results

Two multivariate analyses of variance (MANOVA) were performed with diagnostic group and age group as independent variables. The first MANOVA examined the motor measures as dependent variables, and the second MANOVA used the cognitive measures.

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Table Comparisons of MMD and control groups on motor and cognitive tests

	MMD		Controls		Group	Age	G × A
	M	(SD)	M	(SD)	F (1, 32)	F (3, 32)	F (3, 32)
Motor tests							
Right grip (kg)	8·1	(7·7)	45·0	(9·4)	265·39***	6·54**	1·86
Left grip (kg)	8·4	(7·9)	41·7	(9·9)	183·29***	3·77*	2·97*
Right tap (number/10 s)	26·1	(10·8)	55·5	(9·9)	92·79***	3·12*	0·81
Left tap (number/10 s)	23·9	(9·3)	48·5	(8·9)	78·95***	1·96	1·15
Right pegs (s)	123·4	(68·6)	76·3	(15·9)	16·97***	7·95***	5·29**
Left pegs (s)	125·3	(66·9)	77·3	(17·5)	17·49***	7·45***	4·69**
Cognitive tests							
WAIS-R (FIQ)	84·5	(9·8)	98·1	(11·7)	17·25***	2·16	1·18
Western Aphasia Battery (AQ)	98·6	(1·9)	98·8	(1·4)	0·30	5·40**	0·14
Facial Recognition (number correct)	40·9	(4·9)	46·2	(4·1)	12·98***	1·29	0·38
Line Orientation (number correct)	20·5	(4·1)	26·4	(3·1)	30·47***	3·51*	2·43
3D Construction (s)	186·6	(74·3)	125·6	(34·9)	20·38***	7·66**	2·70
Wechsler Memory Scale							
(Verbal Immediate)	19·3	(6·8)	18·9	(7·1)	0·03	5·05**	0·46
(Verbal Delayed)	15·4	(6·8)	14·9	(6·3)	0·04	4·11*	0·55
(Nonverbal Immediate)	7·9	(3·0)	11·5	(3·4)	19·23***	7·46**	0·42
(Nonverbal Delayed)	6·9	(3·4)	11·0	(3·9)	17·24***	6·96**	0·40
Wisconsin Card Sort (PR's)	27·7	(21·9)	19·1	(15·4)	2·15	2·31	0·48

*p < 0·05
**p < 0·01
***p < 0·001.

The MANOVA testing the motor measures revealed a significant effect for diagnostic group, $F(6, 27) = 45{\cdot}16$, $p < 0{\cdot}001$, for age, $F(18, 76) = 2{\cdot}17$, $p < 0{\cdot}01$, and for the interaction of diagnostic group and age, $F(18, 76) = 1{\cdot}79$, $p < 0{\cdot}05$. The MANOVA testing the cognitive measures revealed a significant effect for diagnostic group only, $F(10, 23) = 5{\cdot}68$, $p < 0{\cdot}001$. These multivariate differences were then examined via univariate F tests on the individual dependent measures.

MMD versus controls

The table presents the average scores for the MMD and the normal groups on motor and cognitive measures, and the results of the univariate F-tests from the MANOVA. As one would expect in a disease involving muscle degeneration, the MMD group performed significantly worse on all motor tests, including measures of motor strength, fine motor speed, and visuomotor coordination. These deficits were severe and bilateral, with no significant differences between right and left hand performance.

Similarly severe deficits are noted on many cognitive tests. The MMD subjects produced significantly lower IQs than the controls (see table). Eight of the MMD subjects had IQs in the dull normal range (80–89), six fell in the borderline range (70–79) and one fell in the retarded range (69 and below). Thus while there was little evidence of "mental retardation" per se, the disease clearly resulted in lowered intellectual abilities for most patients.

Tests of language and of verbal memory were normal for the MMD group, while spatial and nonverbal memory abilities were significantly impaired. Comparing the Verbal and Performance subtests with the WAIS-R revealed a similar pattern, with the sum of scaled scores for Block Design and Picture Arrangement significantly lower than the sum of Vocabulary and Arithmetic, $t(18) = 2{\cdot}53$, $p < 0{\cdot}02$. Despite evidence of motor deficits which might implicate frontal systems, prefrontal executive functions measured by the WCST appeared intact.

Progression of deficits with age

As the table indicates, older subjects performed significantly poorer than younger subjects on most motor tests, memory measures, and time to complete the 3D construction task. The older subjects were also worse on the WAB-AQ, an unexpected finding. Significant diagnostic group by age group interactions were found on left hand grip strength and pegboard. However, no such interactions were noted on cognitive tests. Thus while there was evidence of progression of motor deficits in MMD, there was no evidence for a similar abnormal age-related cognitive decline in these patients.

Motor versus cognitive deficits

Certain cognitive tests require motor speed and coordination for normal performance, and hence scores might be depressed due to basic motor problems (rather than cognitive deficits) in MMD patients. The performance subtests of the WAIS-R (which require manipulation of test materials), the nonverbal memory subtests (which require drawing), and the 3D construction task were most likely to be effected by motor problems. The remaining tests had no significant motor component which could compromise results. Multivariate analyses of covariance was therefore performed comparing the groups on these measures, controlling for scores on the pegboard task (our best measure of psychomotor speed and coordination). When motor abilities were controlled, we again found a significant effect for diagnostic group, $F(4, 25) = 4{\cdot}40$, $p < 0{\cdot}001$, and for age, $F(12, 66) = 2{\cdot}21$, $p < 0{\cdot}02$, but not for the interaction of group and age.

Discussion

As expected in a disease involving myotonia and muscle degeneration, the MMD group performed significantly worse on all motor tests, including measures of motor strength, fine motor speed, and visuomotor coordination. It was also not surprising that age by

diagnosis interactions were found for some of the motor measures, since motor problems are known to progress in MMD. Our results demonstrate that these changes exceed those found on the basis of normal ageing.

Of greater interest were the findings on neuropsychological tests of intellectual and cognitive functions. Early studies had suggested a high incidence of retardation in MMD patients, ranging from 21% to 69%, whereas more recent investigators have suggested that these estimates are too high.[6] While our results did show mild intellectual impairment in the sample as a whole, only one of twenty MMD subjects actually displayed an IQ in the retarded range.

The pattern of results on neuropsychological tests of specific cognitive and memory abilities indicated greater impairment of nonverbal, spatial tests, suggesting greater right hemisphere involvement in the disease. It is also of interest that age-related progression in motor abilities was found only on left hand grip strength and on grooved pegboard (a motor task with significant spatial demands), which may also reflect right hemisphere deficit. Previous studies have been inconsistent with regard to laterality indices. Bird *et al*[3] and Portwood *et al*[6] also found relative impairment of nonverbal or spatial abilities, whereas Stuss *et al*[5] reported the opposite pattern of greater verbal skills impairment, and Woodward *et al*[1] reported generalised deficits on all tests. These studies are difficult to compare directly, since they utilised different test batteries, and generally examined younger patients than our study.

In summary, the present investigation provided evidence for progression of MMD symptoms only in the motor domain. These findings suggest that cognitive deficits are mainly congenital or developmental and relatively stable in MMD. True longitudinal study following MMD patients over a significant period of time will be necessary to confirm these findings. The most practical method for accomplishing this difficult goal may be to identify patients with infantile onset subtype of MMD, who can be identified early in life.

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