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Original article

Profile of cognitive function in adults with duchenne muscular dystrophy

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Abstract

Background: Several studies have examined intellectual functioning of boys with duchenne muscular dystrophy (DMD). However, little is known about the remaining cognitive weaknesses in adults with DMD.

Objective: The purpose of this study was to investigate the profile of cognitive functioning that is characteristics of adults with DMD.

Methods: Twenty-four subscales from the Wechsler Adult Intelligence Scale III (WAIS-III), the Clinical Assessment for Attention (CAT), and the Wechsler Memory Scale Revised (WMS-R) were used to assess participants with DMD ($N = 15$; mean age = 30.4 years).

Results: Scores for Picture Completion, Arithmetic, Matrix Reasoning, Symbol Search, Letter-Number Sequencing, and Digit Span of the WAIS-III; all CAT scores, and Logical Memory and Delayed Logical Memory from the WMS-R were significantly deficient in adults with DMD in comparison to the normal population.

Conclusion: The ability to sequentially process auditory and visual information remains impaired in adults with DMD.

Keywords: Duchenne muscular dystrophy; Cognitive function; Neuropsychological profile; Sequential processing

1. Introduction

Duchenne muscular dystrophy (DMD) is a genetic disease of the muscles caused by deficits in the Dystrophin–Glycoprotein Complex (DGC). It is known that DGC deficits are related to cognitive dysfunction [1]. In the brain, the DGC is involved in the organization of $GABA_A$ receptors ($GABA_ARs$) and aquaporin-4 (AQP4)-containing protein complexes in neurons and glia, respectively. Therefore, it is possible that defects in processing and assembling in the DGC are associated with a spectrum of brain abnormalities, ranging from mild cognitive impairment to neuronal migration disorders, in addition to muscle impairment [1].

Loss of dystrophin is associated with a complex set of physiological and anatomical adaptations that are known contributors to the cognitive deficits observed in patients with DMD and related disorders. Moreover, DGC is known to be associated with disorders other than DMD [1]. There is evidence of disordered CNS architecture, abnormalities in dendrites, and loss of neurons in boys with DMD [2]. These boys show EEG

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abnormalities [2] and the prevalence of epilepsy is higher in DMD (6.3%) than in the general population [3]. CT [4] and MRI [5] studies report that brain atrophy is observed in patients with DMD. These reports suggest that functional and morphological abnormalities are affected by the absence of dystrophins.

A number of studies have assessed the intellectual functioning of boys with DMD. It is known that their mean IQs are about one standard deviation lower than those of the general population [6–9]. It has also been demonstrated that boys with DMD have lower verbal IQs (VIQ) than Performance IQs (PIQ) [7,10–13]. Furthermore, Hinton et al. [14] administered a battery of neuropsychological tests and indicated that boys with DMD did poorly on Story Recall, Digit Span, and Auditory Comprehension compared to an unaffected sibling. They concluded that this profile suggests that verbal working memory skills were selectively impaired. In addition, cognitive abilities such as sequential processing are more impaired than simultaneous processing in boys with DMD [11,15].

Cotton [16], based on a meta-analysis of 1224 children and boys with DMD, reported that all children had both a mean Full-scale IQ (FIQ) and a PIQ score of approximately 80. However, mean VIQ scores, particularly in the verbal subtests including Information, Similarities, Arithmetic, Comprehension, and Digit Span improved with age. Moreover, deficits in logical verbal abstract reasoning, language development, and mathematical/computational ability were less evident in older age groups. These data lend support to the premise that intellectual functioning in the DMD changes with age and that such changes are mainly confined to verbal and language skills [16], rather than more global changes. They suggested that there is a need to adopt more specific, directed, and prospective neuropsychological assessments to further delineate age-related changes in cognition in DMD populations [16].

Therefore, the purpose of this study was to investigate whether the above described cognitive weaknesses remain in adult patients with DMD, by using a wide range of neuropsychological assessment instruments.

2. Methods

2.1. Participants

Fifteen patients with DMD (mean age = 30.4 years, age range = 19–44 years) participated in this study. Inpatients admitted to our hospital or outpatients who visited us regularly during the assessments were included. Their clinical diagnosis was confirmed by molecular assessment of the skeletal muscle and/or by DNA analysis of lymphocytes from peripheral blood using the multiplex ligation-dependent probe amplification (MLPA) method. Patients who were not diagnosed with definite DMD, those who did not give informed consent, and those who could not tolerate the assessment were excluded.

All the participants were briefed about the study and after the briefing, they gave their signed informed consent for participation. The Institutional Review Board (IRB) of the Okinawa National Hospital approved this study.

2.2. Assessment of cognitive functions

We used twenty-four subscales from the Wechsler Adult Intelligence Scale III (WAIS-III), the Clinical Assessment for Attention (CAT) [17], and the Wechsler Memory Scale (WMS-R) for assessing the participants. Nearly all the participants had restricted hand movements, and therefore, we excluded subsets of assessment instruments that required hand movements in order to respond, such as Block Design and Picture Arrangement from the WAIS-III. In the case of participants that were unable to move their hands at all, with the exception of their fingers, we adopted a new response method. For example, in the CAT Auditory Detection Task, the assistant placed his palm under the participant's fingers and the participant communicated his response by pushing the assistant's palm with his fingers. The assistant then tapped the table strongly to notify the participant's response. The tester recorded the sound of tap as the response of the participant.

2.3. Assessment instruments

In this study, 10 WAIS-III subscales were used: (1) Picture Completion, (2) Vocabulary, (3) Similarities, (4) Arithmetic, (5) Matrix Reasoning, (6) Information, (7) Comprehension, (8) Symbol Search, (9) Letter-Number Sequencing and (10) Digit Span. Seven CAT subscales were administered, including (11) Auditory Detection, (12) Symbol Digit Modalities, (13) Memory Updating (3-span) (14) Memory Updating (4 span), (15) Paced Auditory Serial Addition Test (PASAT; 2 s.), (16) PASAT (1 s.), (17) Position Stroop, and finally seven WMS-R subscales: (18) Logical Memory, (19) Visual Paired Association, (20) Verbal Paired Associate, (21) Figural Memory, (22) Delayed Logical Memory, (23) Delayed Visual Paired Association, and [24] Delayed Verbal Paired Associates. WAIS-III scores are standard scores, CAT scores indicate percentage of correct answers, and WMS-R scores were raw scores. The relationship between the subscales used and intellectual abilities required is shown in Table1.

2.4. Data analysis

All assessment instruments described above have been standardized for use in Japan, and therefore, the