Temporal lobe biochemistry and non-verbal neurocognitive function in Myotonic Dystrophy Type I

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Introduction

Myotonic Dystrophy type I (DM1) is characterized by myotonia with muscle wasting and weakness related to a mutation leading to expansion of the triplet repeat CTG of the DMPK gene on chromosome 19. Additional impairments are found in the ocular, endocrine, cardiac and cognitive realms. Cognitive impairments include a general decrease in full scale IQ (FSIQ) compared to normals with a tendency toward a non-verbal learning disability with lower performance IQ (PIQ) than verbal IQ (VIQ)[1]. Attempts have been made to identify the underlying mechanism of cognitive impairment through the use of MRI. Some studies have found correlations between brain MRI findings (cerebral atrophy and/or white matter lesions)[2,3] though not all found such a relationship[4]. Others have used MR spectroscopy to identify increases in myoinositol, total creatine, and choline-containing compounds as well as a reductions in the N-acetyl aspartate (NAA) to Creatine (Cr) and NAA/Choline ratios in patients with myotonic dystrophy compared to normals, although the relationship between these metabolite levels and cognitive performance was not measured[5,6]. This study explores the correlation between performance on a comprehensive neuropsychological assessment battery and brain metabolites measured across the temporal lobe with proton magnetic resonance spectroscopic imaging (^{1}H-MRSI) in patients with DM1.

Design/Methods

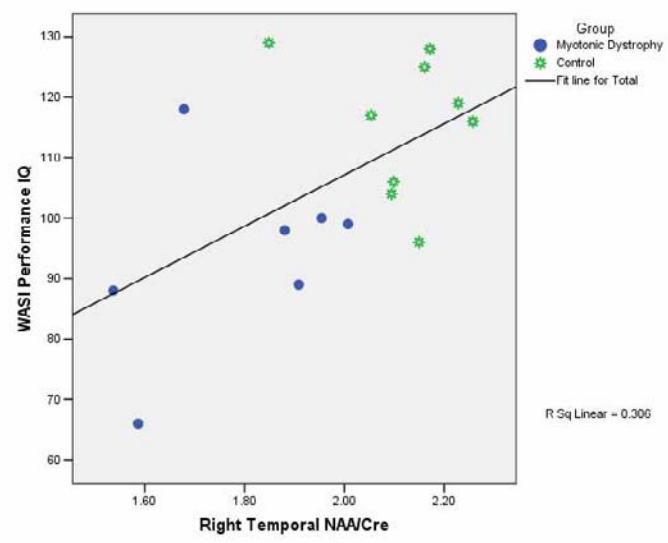
Seven adult subjects with DM1 and nine healthy controls completed a comprehensive battery of neurocognitive tests and magnetic resonance spectroscopic imaging (MRSI) at 1.5 tesla. The neurocognitive battery consisted of: 1) Wechsler Abbreviated Scale of Intelligence (WASI), 2) California Verbal Learning Test (CVLT), 3) Rey Complex Figure Test (RCFT),43) Facial Recognition from the Wechsler Memory Scale – III (FR-WMS), 5) Judgment of Line Orientation (JLO), 6) Trail Making Test – Parts A & B (TMT), 7)Wisconsin Card Sorting Test (WCST), 8) Grip Strength (GRIP), and 9) Grooved Pegboard Test (PEG). The MRS grid was placed in horizontal sections on an oblique angle along the hippocampus, across the temporal lobes. MRS data were analyzed using LCModel with the outcome measure being the NAA to Cr ratio. Patients were compared to age and gender matched control subjects. Comparison was made between groups on NAA levels and cognitive performance, differences in NAA levels between cerebral hemispheres (left versus right), and correlations were measured between NAA and cognitive performance. We hypothesized that neurocognitive measures of memory functioning, dependent upon temporal lobe integrity, would be related to metabolic measures of temporal lobe neurochemistry in patients with DM1 but not controls.

Results

The groups did not differ on age or gender distribution (Mean age DM1 = 37.1 +/- 11.9; Mean age controls = 37.1 +/- 15.0; DM1 = 4 males/3 females; controls = 4 Males/5 Females). A non-significant trend towards higher education in controls was evident (Education DM1 = 12.7 +/- 1.8; Education controls = 14.1 +/- 1.6) . The patients had a lower NAA/Cr ratio across the temporal lobes compared to controls (Right NAA/Cre – t = 4.2, p = .001; Left NAA/Cre – t = 2.7, p = .018). There was no group difference on VIQ, but the controls had a significantly higher PIQ (t = 3.2, p = .007) which lead to a group difference in FSIQ (t = 2.5, p = .023). A significant correlation was found between right temporal lobe NAA/Cr and WASI Performance IQ in the combined sample (Figure 1). In addition, there was a significant correlation between Right Temporal NAA/Cr and delayed recall of the Rey Complex Figure (r = ..89, p = .007) and Facial Recognition subtests (r = .80, p = .03), both non-verbal memory tasks thought to measure right temporal lobe function; this relationship was not present in the control group. There were no differences in NAA/Cr ratios between the cerebral hemispheres in either group.

Discussion

The patients showed an overall reduction in NAA/Cr compared to controls. Interestingly, there was a positive correlation between right temporal lobe NAA/Cr and Performance IQ in the combined sample, but only the patients with myotonic dystrophy exhibited a correlation between NAA/Cr and specific non-verbal tasks designed to tap right temporal lobe functioning. The patient group used in this study confirmed previous results of lower FSIQ compared to age, gender and education matched controls. These findings support the notion of a non-verbal learning disability in patients with DM1 and provides insight into a possible biochemical mechanism for this dysfunction.



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