Brain metabolites in myotonic dystrophy type 1: A 3.0 T proton magnetic resonance spectroscopy study

Y. Takado[1,2], H. Igarashi[1], K. Terajima[1,2], T. Shimohata[2], M. Okubo[1,3], K. Okamoto[1,4], M. Nishizawa[1,2], and T. Nakada[1]

[1]Center for Integrated Human Brain Science, Brain Research Institute, University of Niigata, Niigata, Japan, [2]Neurology, Brain Research Institute, University of Niigata, Niigata, Japan, [3]Institute of Medicine and Dentistry Basic Radiological Technology, School of Health Sciences, University of Niigata, Niigata, Japan, [4]Neurosurgery, Brain Research Institute, University of Niigata, Niigata, Japan

Background: Myotonic dystrophy type1 (DM1) is a multisystem disease characterized by progressive muscular weakness, central nervous system (CNS) impairment, and many other extramuscular manifestations. While there were some reports on cognitive impairment in DM1 patients(1, 2), the mechanism is not fully determined even by research in neuropathology(3, 4). Proton magnetic resonance spectroscopy (^{1}H-MRS) is a useful method which can analyze brain metabolites in living patients. While there were some reports on metabolites of the brain in DM1 patients(5-7), the distribution of brain damage and the exact change in metabolites are not understood well. Furthermore, there were no reports on brain metabolites in DM1 analyzed by a 3.0 T scanner.

Objectives: To seek cerebral abnormalities and factors that cause them in DM1 patients using ^{1}H-MRS at a 3.0 T scanner.

Design: Thirteen DM1 patients were compared with thirteen healthy age matched control subjects. Single-voxel ^{1}H-MRS (frontal white matter and frontal cortex) and two slices of MRSI (basal ganglia level and centrum semiovale level) were performed. The concentrations of metabolites were calculated using LCModel (Stephen Provencher Inc., Oakville, Ontario, Canada). Metabolites were evaluated in multiple brain regions (frontal white matter, frontal cortex, parietal white matter, putamen, thalamus, insular cortex, posterior internal capsule). Metabolites were correlated with clinical parameters such as frontal assessment battery (FAB) and Mini-Mental State Examination (MMSE). All DM1 patients had DNA analysis for trinucleotide cytosine-thymine-guanine (CTG) repeats.

Results: *Single voxel MRS.* Compared with control subjects, DM1 patients had decreased levels of NAA (in the frontal white matter region and frontal cortex), Cho (in the frontal white matter region) and Glutamate (in the frontal white matter region) ($p < 0.05$). Cho, Glutamine and Glx in the frontal white matter increased significantly in DM1 patients compared with control subjects.

MRSI. Compared with control subjects, DM1 patients had decreased levels of NAA/Cr (in the frontal white matter, insula cortex, putamen, parietal white matter, posterior internal capsule and thalamus) and Cho/Cr (in the frontal white matter and posterior internal capsule) ($p < 0.05$). Cho/Cr in the thalamus increased significantly in DM1 patients.

Correlation between metabolites and clinical parameters. The ratio of NAA/Cr in the frontal cortex negatively correlated with the number of CTG repeats ($r = -0.67$, $p < 0.05$). The ratio of NAA/Cr in the frontal white matter was positively correlated with FAB ($r = 0.62$, $p < 0.05$).

Conclusions: This is the first study about brain metabolites analyzed at a 3.0 T scanner in DM1 patients. Diffuse CNS impairments were detected in multiple brain regions by ^{1}H-MRS. These results probably reflect the microenvironment of the CNS impairment in DM1 which cannot be detected by research in pathology(8).

References:

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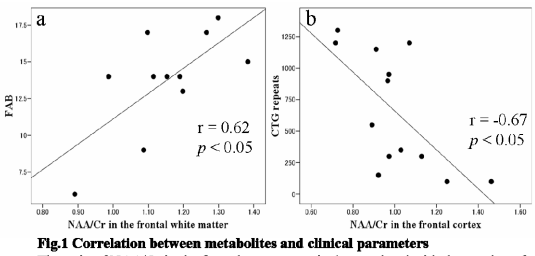
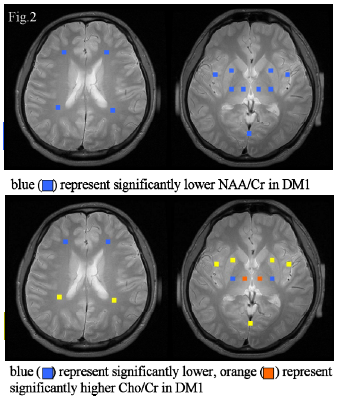


Fig.1 Correlation between metabolites and clinical parameters
The ratio of NAA/Cr in the frontal cortex negatively correlated with the number of CTG repeats ($r = -0.67$, $p < 0.05$) (a). The ratio of NAA/Cr in the frontal white matter was positively correlated with FAB ($r = 0.62$, $p < 0.05$) (b).
CTG: cytosine-thymine-guanine, FAB: frontal assessment battery



blue (■) represent significantly lower NAA/Cr in DM1

blue (■) represent significantly lower, orange (■) represent significantly higher Cho/Cr in DM1