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A muscle biopsy study in patients with Autism spectrum disorders and neuromuscular clinical signs

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Autism spectrum disorders (ASD) are neurodevelopmental disorders, with heterogeneous aetiology, characterized by deficiencies in social interaction and communication and by repetitive and stereotyped behaviours.

The frequent association of ASD with other neurological and extra-neurological signs suggests that autism could be considered as a multiorgan systemic disorder with a primary central nervous system involvement.

Evidence of mitochondrial dysfunction (MD) and other neuromuscular disorder (dystrophinopathies and congenital muscular dystrophy due to mutations of POMGnT1 gene) has been documented in a subset of patients affected by syndromic ASD, however, only few case reports and small samples studies with specific features have been reported in literature.

During our clinical activity, in order to identify the etiopathogenesis of patients with ASD, we selected 12 patients (10 males and 2 female) with ASD (2 with autism and 10 with ASD NOS) presenting also additional signs suggestive of neuromuscular disease. For these patients we carried out muscle biopsy for further histological, biochemical and genetic investigations.

All patients presented MR and muscle hypotonia. Blood CK was elevated in 2 patients and lactic acid was increased in 5. EMG was myogenic in 5 and neurogenic 5 subjects. EEG findings were abnormal in 8 patients. Brain MRI showed variously associated malformative, atrophic changes and white matter alterations in 9 patients.

On histological examination of skeletal muscle we found myogenic or neurogenic changes in 10 patients, 6 of them presented also other morphological abnormalities, such as lipid accumulation, and/or mitochondrial proliferation, and/or COX deficient fibers. At biochemical investigations deficiency of the respiratory chain complex I, complex IV, and complex I, II and II+III was detected in 3 patients respectively.

Finally, genetic studies revealed multiple deletions of mtDNA in 1 patient with normal histological and biochemical findings, the already known homoplasmic C4320T in $tRNA^{Ile}$ in 1 patient and a new nucleotide change A9234G (M10V) of COX 3 gene in a patient with COX deficient fibers.

Muscle involvement was found in almost all patients (10/12) and mitochondrial dysfunctions in the 50% (6/12) of the samples examined. Additional studies in a larger group of subjects are needed, in order to confirm the hypothesis of an aetiological link between autism, mitochondrial dysfunction and other different neuromuscular diseases.