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LECTURE

# Magnetic resonance imaging in Machado-Joseph disease

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## Abstract

Machado-Joseph disease (SCA3) is the most frequent spinocerebellar ataxia worldwide and caused by abnormal (CAG) expansions within the 10th exon of the MJD1 gene located at chromosome 14q. It is typically an adult onset ataxic syndrome, but there is remarkable phenotypic heterogeneity. Patients often present pyramidal signs, movement disorders (particularly dystonia) and peripheral manifestations. Current research efforts in SCA3 are directed towards understanding the pathophysiology of the disease and also to identify robust biomarkers for clinical trials. In this scenario, magnetic resonance imaging (MRI) emerged as a promising tool. It is a widely available and non-invasive technique that enables the evaluation of structural and functional changes related to the disease. Most available MRI-based studies focused in cerebral abnormalities and employed volumetric techniques. These studies revealed cerebellar (predominantly vermian) and brainstem atrophy in SCA3. More recently, studies using cortical thickness measurements also identified precentral, temporal and occipital volumetric reduction. Diffusion tensor imaging (DTI) is a MRI sequence that enables the evaluation of white matter integrity in the brain. In patients with SCA3, DTI-based studies essentially revealed damage to cerebellar and brainstem tracts, including the cerebellar peduncles. Spinal cord is another neural structure known to be affected in SCA3 from pathological reports. Current high-field scanners and protocols now enable adequate evaluation of the cord in vivo using MRI. Indeed, two reports showed cervical atrophy in the disease, and interestingly the extent of atrophy correlated independently with clinical severity. Overall, these results indicate that SCA3 is associated with multifocal damage to the central nervous system that goes far beyond the cerebellum and connections. It seems, however, that damage distribution is not homogeneous in every single patient. Some recent reports tried to compare MRI findings in patients with different phenotypes, such as dystonic vs non-dystonic. Results indicate that cerebellum is compromised in both situations, but the pattern of cortical and basal ganglia damage is clearly different. There are very few longitudinal MRI data in SCA3. Reetz et al reported progressive caudate and putaminal volumetric reduction after 2 years, but it did not correlate with clinical decline.

In summary, MRI-based studies greatly improved our knowledge about disease mechanisms and genotype-phenotype correlation. The use of MRI parameters as clinical biomarkers for SCA3, however, still needs further studies with a longitudinal design. We strongly believe that DTI might prove more sensitive than volumetric techniques to detect subtle changes in the short-term.

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