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Characteristic Eye Movements in Ataxia-Telangiectasia-Like Disorder: An Explanatory Hypothesis

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Objective: To investigate cerebellar dysfunctions and quantitatively characterize specific oculomotor changes in ataxia-telangiectasia-like disorder (ATLD), a rare autosomal recessive disease caused by mutations in the *MRE11* gene. Additionally, to further elucidate the pathophysiology of cerebellar damage in the ataxia-telangiectasia (AT) spectrum disorders.

Methods: Saccade dynamics, metrics, and visual fixation deficits were investigated in two Italian adult siblings with genetically confirmed ATLD. Visually guided saccades were compared with those of 40 healthy subjects. Steady fixation was tested in primary and eccentric positions. Quantitative characterization of saccade parameters, saccadic intrusions (SI), and nystagmus was performed.

Results: Patients showed abnormally hypermetric and fast horizontal saccades to the left and greater inaccuracy than healthy subjects in all saccadic eye movements. Eye movement abnormalities included slow eye movements that preceded the initial saccade. Horizontal and vertical spontaneous jerk nystagmus, gaze-evoked, and rebound nystagmus were evident. Fixation was interrupted by large square-wave jerk SI and macrosaccadic oscillations.

Conclusion: Slow eye movements accompanying saccades, SI, and cerebellar nystagmus are frequently seen in AT patients, additionally our ATLD patients showed the presence of fast and hypermetric saccades suggesting damage of granule cell-parallel fiber-Purkinje cell synapses of the cerebellar vermis. A dual pathogenetic mechanism involving neurodevelopmental and neurodegenerative changes is hypothesized to explain the peculiar phenotype of this disease.

Keywords: ataxia-telangiectasia-like disorder, saccade hypermetria, granule cells, parallel fibers, Purkinje cells

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INTRODUCTION

Autosomal recessive cerebellar ataxias with DNA-double strand break repair deficits are a group of severe neurodegenerative and systemic diseases featuring early-onset ataxia and radiosensitivity including ataxia-telangiectasia (AT), the most common disorder of this group, and ataxia-telangiectasia-like disorder (ATLD) (1). ATLD is a very rare autosomal recessive disease due to mutations in the *MRE11* gene (2). This gene encodes a protein (Mre11) with nuclease and DNA-binding activity;