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Changes in Dynamic and Kinematic Properties of Saccades in Ocular Myasthenia following Intravenous Immunoglobulin Treatment

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Abstract

We studied the dynamics and kinematics of saccades in a patient with severe ocular myasthenia before and after treatment with intravenous immunoglobulin (IVIG). Before therapy, horizontal saccades were hypometric, but faster than similar-sized saccades made by normal subjects. During a 5-minute test period, saccades decreased in size (fatigue effect), but remained faster than those of controls. Listing's plane of the eye with greater ophthalmoplegia was increased in thickness. After IVIG treatment, the range of eye movements improved, but saccades remained faster than those of controls. Also, no fatigue was observed and the thickness of Listing's plane was reduced towards the normal range. Increased peak velocity, despite progressive hypometria due to fatigue, supports the hypothesis that the pale global extraocular muscle fibers are relatively spared in myasthenia. Involvement of other extraocular muscle fiber types leads to limited range of eye movements and an increase in the thickness of Listing's plane.

Keywords

saccades; fatigue; pale extraocular muscle fibers; Listing's plane

INTRODUCTION

Sustained efforts induce fatigue in the extraocular muscles of patients with ocular myasthenia gravis. Reduction in the size of saccades with sparing of saccadic speed, giving the appearance of limited range of eye movement with hyper-fast saccades (quiver movements), is characteristic of this condition.¹ Neurophysiologic evidence suggests that the pale global fibers of the extraocular muscles, which are likely responsible for the initial acceleration of saccades, could be spared in ocular myasthenia.^{2,3} Study of saccadic dynamics in patients with myasthenia, using phase-plane analysis, supports this hypothesis.⁴ Therefore, on the one hand, it is possible that preservation of normal saccadic speed in ocular myasthenia reflects integrity of the pale global fibers. On the other hand, impaired range of eye movements and gaze-holding ability probably reflects fatigue of the other extraocular muscle fiber types.

While most patients with ocular myasthenia respond to therapies such as acetylcholinesterase inhibitors and corticosteroids, treatment with intravenous immunoglobulin (IVIG) could be considered in more severe cases, although the efficacy of IVIG in ocular myasthenia is unproven.⁵ We report changes in the dynamic and kinematic properties of

saccades in a patient with severe ocular myasthenia who showed prompt improvement following treatment with IVIG.

METHODS

A 62-year-old male with a 10-year history of ocular myasthenia, no longer responsive to treatment with acetylcholinesterase inhibitors, presented with ptosis, worse on the left, and reduced range of horizontal eye movements, with the right eye being more affected. We used the 3-D magnetic search coil technique to measure binocular eye movements, as the patient viewed a laser target on a screen at a distance of 1.2 m, with the head fixed. He initially made saccades to horizontal, vertical, and diagonal target jumps, which enabled us to determine the orientation and thickness of Listing's plane for each eye. He then made saccades to horizontal target jumps at 0.3 Hz for a period of 5 minutes (fatigue test), viewing monocularly with his left eye. He was tested in this way 3 times: before, 5 days after, and 7 weeks after treatment with IVIG (400mg/kg/day). We compared the dynamic features of saccades during the first and fifth minute of testing with those of 10 healthy control subjects.

RESULTS

Before IVIG therapy, the range of eye movement was reduced and saccades were hypometric, especially for his right eye. Nonetheless, saccades were faster than those of similar size made by controls (Fig. 1A, black circles). The amplitude of leftward saccades made by the left eye decreased after 5 minutes of recording (fatigue test), but saccades remained faster than those of controls (Fig. 1A, white circles). Before therapy, Listing's plane of the right eye, which showed greater restriction of movement, was increased in thickness, with standard deviation (SD) of 1.31° (Fig. 2B), compared to the Listing's planes of reported controls.⁶ Seven weeks after IVIG treatment, the range of horizontal eye movements had improved, but saccades still showed peak-velocity values that were greater than those of controls (Fig. 1B). However, there was no decrease in saccade size (*i.e.*, no fatigue) after recording repetitive eye movements for 5 minutes (Fig. 1B, white circles). The thickness of the Listing's plane of the right eye was also reduced towards the normal range (SD of 1.11°, Fig. 2D).

DISCUSSION

Our study shows that there can be improvement in both the dynamic and kinematic abnormalities of saccades in ocular myasthenia following IVIG treatment. At baseline, our patient had horizontal saccades with limited range and abnormally high velocities, which is typical of myasthenia.¹ As the pale global fibers of the extraocular muscles have well developed postsynaptic membrane folding, they are thought to be more resistant to fatigue when compared with other extraocular muscle fibers.³ This may be why myasthenic patients are still able to generate saccades with initial high accelerations, despite the limited range of eye movements.⁴ Here, we show that this characteristic feature is not affected by fatigue induced by repetitive eye movements. Thus, in our patient, the saccadic peak-velocity values were unchanged despite the decrease in saccadic size after 5 minutes of recording (Fig 1A). This finding further supports the hypothesis that the pale global fibers are spared in ocular myasthenia.

Therapy induced an improvement in eye movement range, with persistently increased saccadic peak-velocities, that might reflect a partial recovery of the more affected global fibers. Thinning of Listing's plane after therapy (Fig. 2) further supports this hypothesis. While IVIG therapy has not previously been shown to improve ocular myasthenia,⁵ our study shows that, in cases of severe disease, significant improvement can be observed as

early as 5 days after treatment. Further study of a larger cohort of patients is required to confirm these findings.

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Figure 1.

Plots of peak-velocity versus amplitude of leftward horizontal saccades made by the left eye, before (A) and 7 weeks after treatment with IVIG (400mg/kg/day) (B). Saccades made during the first and the fifth minute of the recording are denoted by black and white circles, respectively. Before therapy, saccades show a decrease in size with time (fatigue effect), but remain faster than those of control subjects (dashed lines indicate 95% prediction intervals) throughout the record. After treatment, saccades do not exhibit fatigue (*i.e.*, no changes in saccades size), but peak velocity values are still higher than normal.

Figure 2.

3-D plots of eye-in-head position, demonstrating Listing's plane during fixations and saccades, from the left eye and right eye prior to IVIG treatment (A and B, respectively) and 7 weeks following IVIG treatment (C and D, respectively). Data are plotted in the pitch (XZ), yaw (XY), and roll (YZ) planes. The range of eye movement of both eyes increased following IVIG treatment and the thickness (SD) of Listing's plane (defined as the standard deviation of data points from the plane of best fit) decreased. (X, naso-occipital axis; Y, inter-aural axis; Z, ventro-caudal axis; (L), left; (D), down; (CW), clockwise.)