



## Selective impairment of the rapid eye movements in myotonic dystrophy

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The patients with myotonic dystrophy (MD) show ocular motor abnormalities including strabismus, vergence deficits, and inaccurate or slow saccades. Two theories have been proposed to explain the oculomotor deficits in MD. The central theory attributes the defects of eye movements of MD to the involvement of the central nervous system while the muscular theory attributes to dystrophic changes of the extraocular muscles. A 58-year-old woman with MD showed selective slowing of horizontal saccades and reduced peak velocities for both horizontal canals in head impulse tests, while smooth-pursuit eye movements and vertical head impulse responses were normal. This case suggests that the extraocular muscles-as a final common pathway of the voluntary saccade and reflexive vestibular eye movements-may better explain the defective rapid eye movements observed in MD.

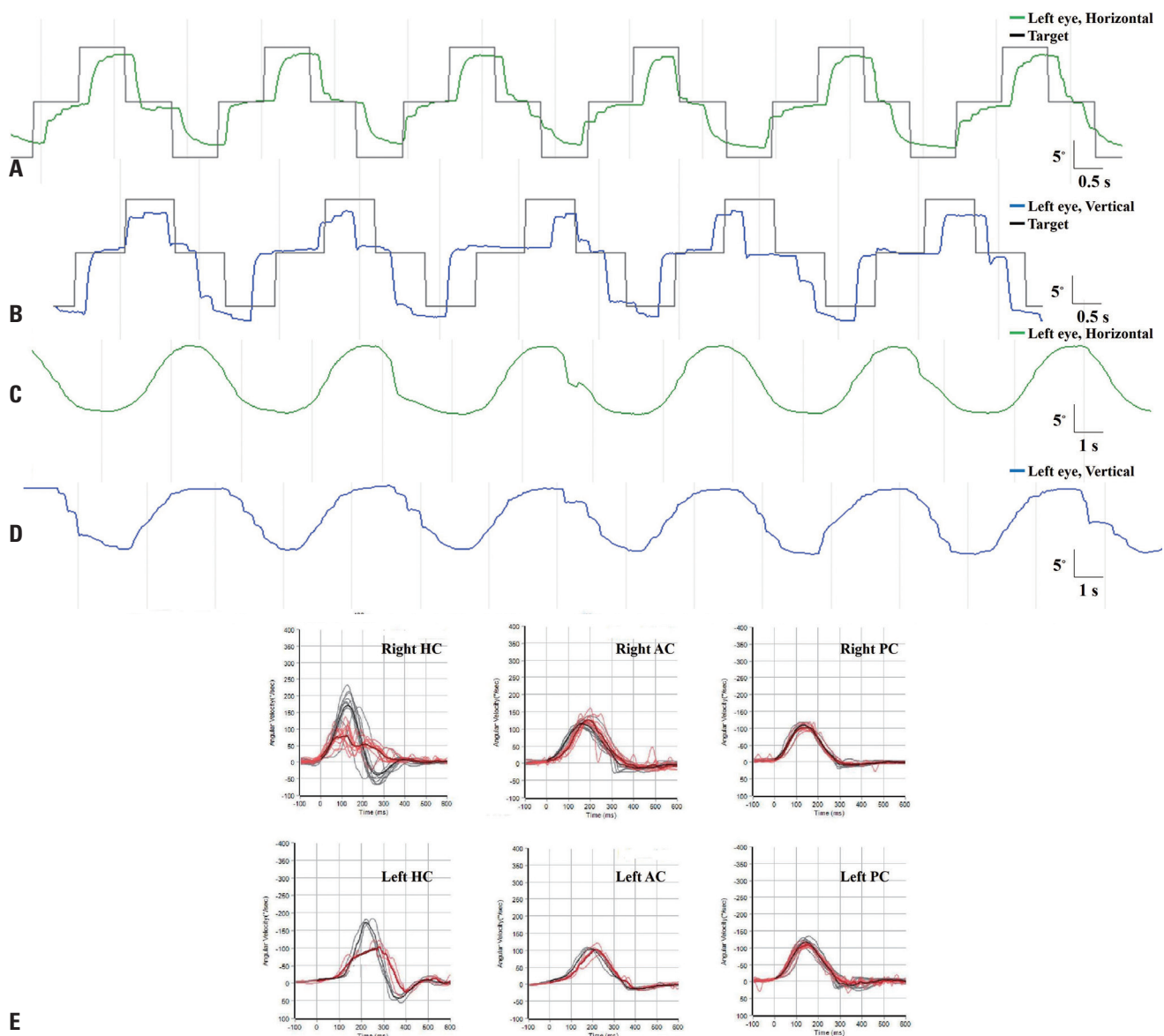
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Myotonic dystrophy (MD) is an autosomal-dominant multisystem disorder that arises from an unstable cytosine-thymine-guanine (CTG) repeat on chromosome 19.<sup>1</sup> MD patients show dystrophic changes prominently in temporal, facial, and distal extremity muscles, and a characteristic delay in muscle relaxation after contraction.<sup>1</sup> Systemic manifestations such as cataract, cardiac conduction abnormality, and endocrine disorders are often evident. While patients with MD seldom complain of oculomotor symptoms other than eyelid ptosis, oculomotor evaluations can disclose various abnormalities including strabismus, vergence deficits, and inaccurate or slow saccades.<sup>2</sup> A decreased saccade velocity in patients with MD is described often in the literature, but its pathophysiology has remained controversial. While dystrophic changes of the extraocular muscles would produce slow horizontal saccades,<sup>2</sup> the involvement of the central nervous system may also explain the oculomotor deficits in MD.<sup>3</sup> This study investigated a patient with MD who showed selective deficits in voluntary and reflexive rapid eye movements.

## CASE

A 58-year-old Korean woman had suffered from gait instability for 13 years. At the presentation she also reported swallowing difficulty, weakness of hand grip, and intermittent dyspnea. A neurologic examination revealed that she had bilateral ptosis and cataracts, and that her primary eye position

was normal. While the ranges of duction and version were normal, both eyes moved notably slowly and conjugately to the eccentric lateral positions. Gaze holding was normal, without gaze-evoked nystagmus. Convergence was impaired. Saccadic eye movements were slow and hypometric in bilateral horizontal directions without a postsaccadic drift (Fig. 1A, Supplementary Video 1). While the leftward centrif-



**Fig. 1.** A 58-year-old woman with myotonic dystrophy showed slowing and hypometria of horizontal saccades (A). The amplitudes and velocities of the vertical saccades were intact, although anticipatory eye movements were frequently observed (B). Smooth pursuit was normal in both horizontal directions (C) and in the upward direction (D). Video head impulse tests revealed decreased peak velocities for bilateral horizontal canals without catch-up saccades, but preserved responses for the vertical canals (E). Upward deflection indicated rightward eye motion in the horizontal plane and upward eye motion in the vertical plane. S, seconds; HC, horizontal canal; AC, anterior canal; PC, posterior canal.

ugal ( $21.6 \pm 4.5^\circ/\text{s}$ , mean  $\pm$  SD) and centripetal ( $66.3 \pm 11.9^\circ/\text{s}$ ) saccades exhibited significantly different velocities, there was no difference between the rightward centrifugal ( $38.9 \pm 8.5^\circ/\text{s}$ ) and centripetal ( $33.8 \pm 16.2^\circ/\text{s}$ ) saccade velocities. The amplitudes and velocities of vertical saccades were normal (Fig. 1B). Smooth pursuit was normal in the bilateral horizontal and upward directions, but mildly impaired in the downward direction and with compensatory catch-up saccades (Fig. 1C, D). Visually enhanced vestibulo-ocular reflexes (VORs) were normal in both the horizontal and vertical planes. There was no positional or head-shaking nystagmus. Optokinetic stimuli rotating to the right elicited small left-beating nystagmus, but with an actual nystagmus visible only occasionally. Optokinetic stimuli rotating to the left elicited relatively faster and greater right-beating nystagmus. Video head impulse tests (HITs) revealed decreased peak velocities for bilateral horizontal canals without catch-up saccades (Supplementary Video 2), but preserved responses for the vertical canals (Fig. 1E). Bithermal caloric tests showed bilaterally reduced responses, with summated slow-phase velocities of the induced nystagmus of less than  $12^\circ/\text{s}$ .

The patient also showed atrophy and weakness of the facial muscles, flaccid dysarthria, percussion myotonia in both hands, weakness of the bilateral lower extremities, and generalized areflexia. Electromyography revealed myotonic discharges in all of the tested muscles. Her nerve conduction velocities were normal. Serum laboratory testing revealed elevated HbA1c and lipid profiles. The findings of brain MRI were unremarkable. The genetic analysis detected 650 CTG-triplet expansion repeats on chromosome 19.

## DISCUSSION

Our patient with type 1 MD showed the selective slowing of horizontal saccades and reduced peak velocities in HITs for both horizontal canals, while smooth-pursuit eye movements and vertical head impulse responses were preserved. These findings were compatible with previous findings of the saccade velocities in the horizontal and vertical directions being significantly lower in patients with MD than in controls, but with the difference being more prominent in the horizontal direction.<sup>2-4</sup> A remarkable deficit in generating rapid eye movements-contrasting with the preservation of

slow-pursuit eye movement-has been described as a consistent feature of MD. Neuro-ophthalmologic examinations including saccade tests are therefore expected to be useful for detecting subclinical symptoms and quantifying the severity of MD.<sup>2</sup>

Two theories have been proposed to explain the oculomotor deficits in MD. First, the involvement of the central nervous system may underlie a dissociation between the deficits in rapid and slow eye movements.<sup>3</sup> A loss of the paramedian pontine reticular formation (PPRF) or a failure to recruit an appropriate number of discharges from the PPRF leads to saccade slowing in the horizontal plane.<sup>4</sup> Even though the PPRF has been considered to include excitatory burst neuron responsible for the ipsilateral horizontal saccades, a bilateral PPRF lesion in human reportedly produced complete gaze palsy in both the horizontal and vertical planes.<sup>5</sup> Moreover, the horizontal VOR was preserved after pathologically confirmed lesions of the PPRF.<sup>6</sup> Since omnipause neurons located in the nucleus raphe pontis are important for generating the high-frequency discharge of burst neurons when their inhibitory signals stop, brainstem dysfunction affecting the omnipause neurons may cause slowing of the saccadic eye movements, also in both the vertical and horizontal directions.

The second muscular theory attributes the dissociative defects of rapid and slow eye movements to a selective abnormality of fibers in the extraocular muscles. Dystrophic changes in the extraocular muscles have been demonstrated histologically,<sup>7</sup> and electromyographic studies have detected myotonic discharges in extraocular muscles.<sup>8</sup> Large-diameter twitch fibers of the extraocular muscles produce saccadic eye movements, while smaller diameter twitch fibers are responsible for tonic maintenance of an eccentric gaze.<sup>9</sup> Therefore, defective saccadic eye movements in MD may be explained by the selective involvement of the large-diameter twitch fibers. Given that HITs are based upon the VOR arc consisting of three neuronal structures (the primary vestibular afferents, vestibular nucleus, and extraocular muscles), the involvement of the PPRF or omnipause neurons seems unlikely to explain the impaired responses to the horizontal head impulses observed in our patient.<sup>6</sup> The extraocular muscles-as the final common pathway of both voluntary saccade and reflexive vestibular eye movements-would account for the defective rapid eye

movements that appeared in our MD patient. If defective responses in the horizontal HIT are due to impairment of the extraocular muscular forces causing the saccadic eye movements in MD, a low peak in video HITs might not indicate low gain of the VOR, but rather suggest insufficient maximum velocities of the eye movements evoked by horizontal head impulses. Indeed, a previous study involving patients with MD found a normal VOR when this was tested using a rotating chair in darkness.<sup>10</sup> Since the catch-up saccades of the HITs and nystagmus induced by caloric stimuli are composed of rapid eye movements, their absence in HITs and bilaterally reduced caloric responses in our patient may also be attributed to impairment of the saccadic eye movements in MD. However, to explain the dissociation in defects of the rapid eye movements between the horizontal and vertical directions, this muscular theory requires the assumption that MD preferentially involves the horizontal extraocular muscles over the vertical muscles. Although a histologic examination of the rectus muscles in patients with MD revealed disorganization in the arrangement of myofibrils with randomly distributed, short, and irregular myofibrils,<sup>7</sup> individual extraocular muscles have not been analyzed. Further studies that include histologic analyses of the extraocular muscles as well as detailed neuro-ophthalmologic tests would help to delineate the origin of the oculomotor abnormalities observed in MD.

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S.H.K. contributed to the analysis and interpretation of the data and drafting of the manuscript. J.S.P. contributed to data collection and manuscript revision.

### Conflicts of Interest

The authors declare that they have no conflict of interest.

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