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BILATERAL INO: UNUSUAL PATTERNS OF SACCADIC INTRUSIONS

The signals for adduction during conjugate horizontal eye movements are carried through the medial longitudinal fasciculus (MLF). Lesions in this pathway cause internuclear ophthalmoplegia (INO), characterized by impaired ipsilesional adduction, often with nystagmus of the contralateral abducting eye. Usually with INO straight-ahead fixation appears steady. Here we demonstrate quantitative recordings and videos of 2 unusual patterns of saccadic intrusions in a patient with bilateral INO and discuss a plausible mechanism.

Case report. A 49-year-old woman with multiple sclerosis was admitted to the hospital for evaluation of elevated JC virus serologies. The workup was negative for progressive multifocal leukoencephalopathy. Ocular motor examination revealed exotropia, bilateral INO, and intermittent, spontaneous, monocular-appearing abducting movements. The brain MRI showed widespread hyperintensities on a fluid-attenuated inversion recovery sequence with lesions in the brainstem (figure e-1 on the *Neurology*[®] Web site at Neurology.org).

Oculography. An infrared video goggle system (RealEyes xDVR system, Micromedical Technologies Inc., Chatham, IL) was used to record eye movements at a frame rate of 100 Hz. Recordings were performed at the bedside with the patient seated, looking straight ahead at a handheld stationary target. A behavioral calibration of eye movements was unreliable and, instead, we assumed average values of 24 mm for the diameter of the globe and 12 mm for the diameter of the iris.¹ Eye movements were analyzed using custom pupil tracking software.

Findings. Recordings showed spontaneous bursts of saccades at frequencies of 1–2 Hz, up to 10° in amplitude, and 200 deg/s peak velocity in the abducting eye. Two patterns were observed: (1) spontaneous binocular couplets of back-and-forth saccades with an intersaccadic interval of approximately 200 ms (figure 1, A and C, and video 1) and (2) spontaneous salvos of abducting saccades followed by a drift of the abducting eye, with a decreasing velocity waveform, toward the initial position (figure 1, B and D, and

video 2). At the same time, the adducting eye showed a slow, small amplitude movement followed by a slower return to the initial ocular position. In both patterns, eye movements also had a small vertical component and ptosis was present, especially in the left eye (videos 1 and 2).

What would be a plausible explanation for these patterns of saccadic intrusions in the context of bilateral INO? A horizontal saccade is generated by a pulse discharge from neurons in the paramedian pontine reticular formation (PPRF). Subsequently, the neural integrator network—including the nucleus prepositus hypoglossi and the medial vestibular nucleus—generates a step discharge to sustain the new eye position. With MLF lesions, saccades present a characteristic disconjugate waveform. The pulse is affected in the adducting eye, which consequently makes a slow saccade, often with limitation of adduction. In the abducting eye, the pulse is directly transmitted to the abducens motoneurons avoiding the MLF pathway. The step, however, may not match the pulse command to sustain the new eye position and thus the eye may drift quickly toward the orbital position specified by the step. This pulse-step mismatch in the abducting eye is likely due to an adaptive increase in the duration of the pulse discharge, which is generated in the PPRF and would also involve the motoneurons that project directly to the lateral rectus muscle in an attempt to overcome impaired transmission in the MLF.^{2–4} In our patient, horizontal saccades in both directions showed a pulse-step mismatch (figure e-2). There were also bursts of spontaneous disconjugate saccades away from and back to a fixation point, with intervals of approximately 200 ms, consistent with square wave jerks (SWJ)⁴ (figure 1A). Another pattern showed a saccade in the abducting eye with a deficient step, and instead of a return saccade after several hundred milliseconds, there was a drift toward the midline (figure 1B). A slow drift may occur after saccadic intrusions but it is usually binocular.⁵ In both patterns, the abducting eye behaved similarly, but the adducting eye was different depending on its position in the direction of action of the paretic medial rectus. The intersaccadic interval in the first pattern appeared longer after the abduction of the left eye and shorter after the

Supplemental data
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Figure 1 Sample recordings of saccadic intrusions

(A) Disconjugate waveforms with spontaneous binocular couplets of back-and-forth saccades with intersaccadic intervals (see video 1). (B) Salvos of abducting saccades followed by a drift of the abducting eye back to the midline (see video 2). (C, D) Corresponding velocity traces for data shown in (A, B), respectively.

abduction of the right eye, perhaps reflecting a preference for the right eye for fixation. The lack of a return, abducting saccade in the second pattern may also reflect a preference for fixation by the right eye, which was now closer to the midline.

Monocular, stepless saccadic intrusions with bilateral INO were reported previously.⁶ Our patient also showed saccadic intrusions but they were not monocular, albeit markedly disconjugate. Some of these movements were followed by a return saccade producing the distinctive pattern of SWJ. Since saccadic intrusions are usually not part of the INO pathophysiology, their presence suggests involvement extrinsic to the MLF pathway (e.g., lesions involving the pause neurons within the pontine reticular formation).⁴ The unusual patterns of saccadic intrusions shown by our patient, however, may reflect the markedly disconjugate effects of INO.

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1. Riordan-Eva P, Whitcher J. Vaughan & Asbury's General Ophthalmology. New York: McGraw Hill Professional; 2008.
2. Baloh RW, Yee RD, Honrubia V. Internuclear ophthalmoplegia: I: saccades and dissociated nystagmus. *Arch Neurol* 1978;35:484–489.
3. Zee DS, Hain TC, Carl JR. Abduction nystagmus in internuclear ophthalmoplegia. *Ann Neurol* 1987;21:383–388.
4. Leigh RJ, Zee DS. *The Neurology of Eye Movements*. New York: Oxford University Press; 2015.
5. Abadi RV, Gowen E. Characteristics of saccadic intrusions. *Vision Res* 2004;44:2675–2690.
6. Herishanu YO, Sharpe JA. Saccadic intrusions in internuclear ophthalmoplegia. *Ann Neurol* 1983;14:67–72.