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Saccadic oscillations and intrusions preceding the postnatal appearance of congenital nystagmus

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ABSTRACT. Saccadic intrusions and oscillations (square wave jerks and oscillations, double saccadic pulses and multiple double saccadic pulses) are rare in infants. They have been observed in both normal adults and those afflicted with central nervous system diseases. The authors recorded saccadic oscillations in a normal 4½-month-old infant. Five months later they recorded both saccadic oscillations and congenital nystagmus (CN) waveforms. A complete neurological examination did not show nervous system abnormality.

There is only one report of an adult with documented saccadic oscillations and whose longitudinal evaluation failed to show other abnormalities. Some types of saccadic oscillations may represent a benign condition in infants. The subsequent developing of CN in this patient results in questions regarding the interrelationship of fast eye movement and slow eye movement system abnormalities. The authors hypothesize that the saccadic oscillations precluded the early appearance of the developing CN.

Key words: saccadic oscillations; square wave oscillations; saccadic intrusions; square wave jerks; congenital nystagmus

INTRODUCTION

The more common ocular oscillations seen in childhood and infancy include; congenital nystagmus (CN), latent/manifest latent nystagmus and the nystagmus accompanying spasmus nutans. Some of these oscillations are associated with known systemic abnormalities (Dell'Osso, 1984). Pendular and jerk nystagmus have been observed with disorders of the visual system including albinism, achromatopsia and aniridia (Dell'Osso, 1984; Dell'Osso & Daroff, 1985). Oscillations commonly called 'searching nystagmus' in the ophthalmic literature are associated with central nervous system and visual defects (Kestenbaum, 1961). Opsoclonus is a saccadic abnormality associated with childhood

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neuroblastoma and other diseases (Daroff, 1977).

Because of the subtle differences in the many types of ocular oscillations, accurate ocular motility recordings are necessary to distinguish between them. We documented a significant change in the ocular oscillations of an otherwise neurologically normal infant.

CASE REPORT

Our patient was a 4½-month-old white male, the full term product of an uncomplicated labor and delivery. His birth weight was 3,515 g, one and five minute Apgars were 6 and 9 respectively. His past medical history was significant for pyloric stenosis corrected by a pyloromyotomy at six weeks of age. His pediatrician observed the onset of 'nystagmus' at four months of age. The family medical history was unremarkable for any neurologic or ocular motor abnormalities.

The infant had normal growth and development. His physical examination was unremarkable. His neurologic examination revealed no abnormalities except a possible left hand preference and the ocular motor instability. A head CAT scan was normal.

At 4½ months the infant could fix and follow well with both eyes; the external examination, anterior segments, and fundi were unremarkable. The ocular motor examination showed the infant to be orthophoric with full versions and ductions. The ocular oscillations consisted of horizontal, conjugate, small amplitude, moderately high-frequency movements. There appeared to be periods of quiescence and it was difficult on gross examination to make the distinction between pendular and jerk movements. There was no damping with convergence and no change with gaze position or optokinetic stimulation. Our clinical impression was either CN or periodic alternating nystagmus.

At 9½ months of age the infant returned for a repeat examination and recording. The evaluation was unchanged except for the ocular motor examination. He had a small-angle esotropia in the left eye without the gross appearance of amblyopia. Versions and ductions were full. The oscillations were horizontal, conjugate, slightly larger amplitude movements. They were now continuous, pendular, and damped with convergence. The subsequent ocular motor examination was consistent with a diagnosis of CN.

METHODS

The patient was seated comfortably on his mother's lap and various toys were used as fixation objects. His eye movements were recorded using infrared oculography. The sensors, mounted on spectacle frames, were held in place over the infant's eyes by an examiner and adjusted to the infant's pupillary distance. Eye movements were electronically differentiated and both position and velocity traces were recorded on a modified Beckman Type R612 Dynograph. The bandwidth of the entire system (position and velocity) was DC-100 Hz. Eye movements were recorded with the patient fixating straight ahead. It was impossible to calibrate exactly for position; the calibration shown in the illustration is only approximate. Relative calibration of the two eyes was achieved by setting the saccadic movements of both eyes equal to each other.

RESULTS

Fig. 1A is representative of the ocular motility recording at 4½ months of age. The saccadic nature of the instability is demonstrated by saccades away from fixation with brief intersaccadic intervals and subsequent saccades back towards fixation ('corrective saccades'). The oscillations were sporadic, conjugate, and interrupted fixation. There was no nystagmus; there were square wave oscillations (SWO) and square wave jerks (SWJ). The slow changes in eye position are common in recordings of infants and here, may also reflect some head movement during fixation of the hand-held toy used as a fixation target.

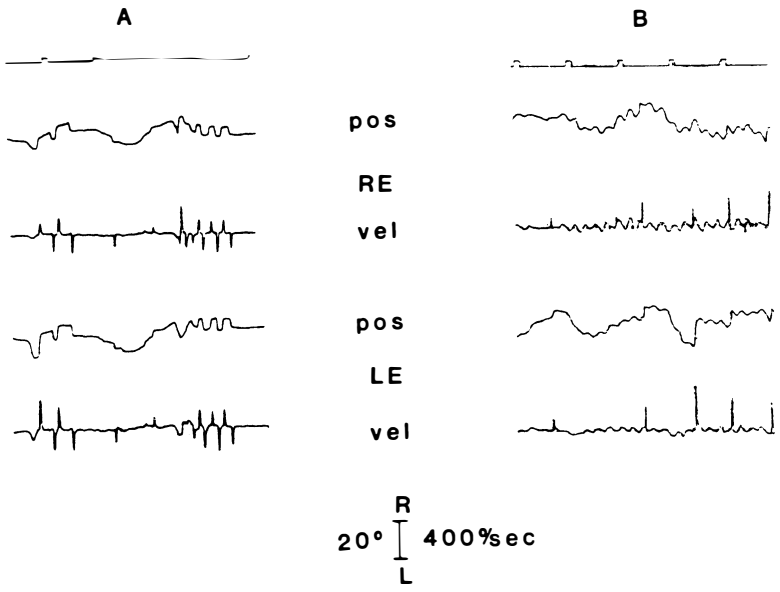

Fig. 1. Representative sections of the infrared oculographic recordings taken from our patient at A, 4½ months and B, 9½ months of age. Part A shows saccadic oscillations consisting of fast phases taking the eyes off target to the right with a subsequent intersaccadic interval and fast phase back on target. These are horizontal, conjugate, intermittent, high-frequency, small-amplitude (approximately 5 degrees), and interrupt fixation. Part B, segment chosen to show the horizontal, pendular, moderately high-frequency, small-amplitude, more persistent oscillation consistent with congenital nystagmus. RE – right eye, LE – left eye, pos – position, vel – velocity, R – right, L – left and timing marks are at one-second intervals.

The infant was 9½ months old when the recording shown in Fig. 1B was obtained. The oscillation was a horizontal, conjugate, pendular nystagmus. Pendular, jerk, jerk with extended foveation, and dual jerk waveforms were seen throughout the recording. These waveforms are consistent with CN (Dell'Osso & Daroff, 1975). Also present in other parts of the recording was an intermittent background saccadic instability identical to the oscillations and intrusions seen at 4½ months of age. Thus, at 9½ months of age, this infant had CN, SWO, and SWJ.

DISCUSSION

The appearance of ocular oscillations in infants has been described previously by Kestenbaum (1961), and others. Most of these oscillations occur in the context of some other pathology, either visual system or central nervous system (Lavery *et al.*, 1984).

Table 1 is the current classification of ocular oscillations which result from disorders in the saccadic system (Dell'Osso, 1984). The saccadic instabilities of our patient are included in 'square wave jerks/oscillations' (Dell'Osso, 1984; Abel *et al.*, 1984). Some conditions associated with SWJ include acute and chronic cerebellar disease (Dell'Osso, 1984; Daroff, 1977), cerebral disease (Daroff & Troost, 1985; Sharpe *et al.*, 1982; Leigh & Zee, 1983), progressive supranuclear palsy (Abel *et al.*, 1984; Dell'Osso, 1984; Daroff, 1977; Daroff & Troost, 1985; Leigh & Zee, 1983), Alzheimer's disease (Jones *et al.*, 1983),

TABLE 1. Saccadic oscillations and intrusions

1. Bobbing/dipping
2. Convergence-retraction 'nystagmus'
3. Double saccadic pulses (single/multiple)
4. Dynamic overshoot
5. Dysmetria
6. Flutter
7. Flutter dysmetria
8. Macro saccadic oscillations
9. Macro square wave jerks (bursts/single)
10. Myoclonus
11. Opsoclonus
12. Psychogenic flutter
13. Saccadic lateropulsion
14. Saccadic pulses/pulse trains
15. Square wave jerks/oscillations
16. Superior oblique myokymia

schizophrenia (Levin *et al.*, 1982), non-paralytic strabismus (Ciuffreda *et al.*, 1979), and multiple sclerosis (Daroff, 1977). SWO have only been reported with progressive supranuclear palsy (Abel *et al.*, 1984) and Parkinson's disease combined with alcoholic cerebellar degeneration (Sharpe & Fletcher, 1984).

It is apparent from our experience with ocular motility recordings that clinical impressions do not always correlate with the oscillations recorded. Although experienced observers may be able to distinguish a slow pendular nystagmus from a fast jerk nystagmus, differentiation of most saccadic oscillations and intrusions can only be consistently accomplished with accurate eye movement recordings. The main differences are the presence or absence of an intersaccadic interval, whether or not the instability interrupts fixation or occurs on refixation, and characteristic waveform patterns (Dell'Osso *et al.*, 1977; Abel *et al.*, 1984; Doslak *et al.*, 1983). These differences, invisible to the observing eye, imply unique pathophysiological mechanisms for the initiation of each saccadic instability.

Herishanu & Sharpe found that 24% of their normal young adult subjects had SWJ (1981). They stated that more than 9 SWJ per minute was outside the '95% confidence limit' and indicative of pathology. Other characteristics for 'normal' SWJ have been proposed. These include: occurrence only under closed lids (Sharpe *et al.*, 1982; Feldon & Langston, 1977); fixation not interrupted (Daroff, 1977); and amplitudes of less than 5 degrees with short intersaccadic intervals (100-400 msec) (Sharpe *et al.*, 1982; Feldon & Langston, 1977).

Several theories regarding the origin of these oscillations have been proposed. It has been suggested that they were a disorder of 'microsaccades', an amplified version of normally occurring micromovements of the eyes (Feldon & Langston, 1977). However, a more attractive hypothesis was proposed by Zee & Robinson, who used control systems modeling and neurophysiology (1979). They hypothesized that square wave jerks are initiated supranuclearly by a spurious error signal which, after a latency equivalent to a normal saccade, brings the eyes back on target. Flutter, flutter dysmetria, and saccadic pulses are initiated at the level of the brainstem centers in the 'pause cells'. This instability leads to back-to-back saccades without an intersaccadic interval.

Our study of this patient raises two important points. The first is that like CN, SWJ and/or SWO in infancy and childhood may also represent a benign condition. We know of one other case; a young girl in whom this saccadic instability has been present for more than six years without other pathology manifesting (personal communication, Zee, 1986). The second is the observation of the evolution of CN in a patient with another, and theoretically unrelated, ocular oscillation. The current theories of the generation of CN and saccadic oscillations differ in that the former is an instability of the 'slow eye move-

ment system', while the latter is an instability in the 'fast eye movement system' (Dell'Osso & Daroff, 1974, 1985; Dell'Osso, 1984; Abel *et al.*, 1984; Doslak *et al.*, 1983).

Before discussing further the development of both the saccadic oscillation and CN waveforms it should be made clear that, although the latter were not present at birth, they do represent CN. Several types of nystagmus can be present at birth. The three most common are: CN, latent/manifest latent nystagmus and spasmus nutans. While all may be truly congenital (*i.e.*, present at birth) they are different types of nystagmus. Their waveforms, variation with gaze angle and basic underlying mechanisms are different. If these different disorders are lumped under one name, 'congenital nystagmus', then understanding of the underlying pathophysiological mechanisms may be lost. This is especially true since, in any particular subject, any of the three may appear weeks or months after birth. The important criterion, in terms of physiological mechanism, is not whether the nystagmus was present at birth but what kind of nystagmus it is; that determines prognosis and therapy. Thus, by all criteria that define CN, our subject developed CN some time after birth, between the times of the first and second recordings.

It is probable that the two different oscillations seen in this case are coincidental rather than the result of some unique relation. We documented the absence of CN at 4½ months of age and its presence at 9½ months. The SWO, although frequent at 4½ months, were not constantly present and there were many instances in the first record where CN would have been recorded if present. We, therefore, speculate that either the presence of SWO delayed the manifestation of the CN, or that this was a rare case where the CN was slow to develop, independent of other abnormalities. The SWO did not evolve into CN; both CN and SWO were evident throughout the second record. This is consistent with the difference in ocular motor systems responsible for the two oscillations. It is known that the saccadic system develops before the pursuit system but this is not a likely explanation for the differences in time course of the developments of SWO and CN in this case; many cases of CN have been seen at birth despite the later development of smooth pursuit. Based only on the data from this unique case, we cannot conclude which of the two above hypotheses is correct; the rarity of the second however suggests that the SWO delayed the development of the CN.

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REFERENCES

ABEL, L. A., TRACCIS, S., DELL'OSSO, L. F., DAROFF, R. B. & TROOST, B. T.: Square wave oscillation. The relationship of saccadic intrusions and oscillations. *Neuro-ophthalmology (Amsterdam) 4*: 21-25, 1984

CIUFFREDA, K. J., KENYON, R. V. & STARK, L.: Saccadic intrusions in strabismus. *Arch. Ophthal. 97*: 1673-1679, 1979

DAROFF, R. B.: Ocular oscillations. *Ann. Otolaryng. 86*: 102-107, 1977

DAROFF, R. B. & TROOST, B. T.: Supranuclear disorders of eye movements. In: *Clinical Ophthalmology*, Vol. II (T. Duane, ed.), pp. 1-18. Harper and Row, Hagerstown 1985

DELL'OSSO, L. F.: Nystagmus and other ocular motor oscillations and intrusions. In: *Neuro-Ophthalmology-1984,* Vol. III (S. Lessell and J. T. W. Van Dalen, eds.), pp. 157-204. Excerpta Medica, Amsterdam 1984

DELL'OSSO, L. F., ABEL, L. A. & DAROFF, R. B.: 'Inverse latent' macro square wave jerks and macro saccadic oscillations. *Ann. Neurol. 2*: 57-60, 1977

DELL'OSSO, L. F. & DAROFF, R. B.: Functional organization of the ocular motor system. *Aerospace Med. 45*: 873-875, 1974
DELL'OSSO, L. F. & DAROFF, R. B.: Congenital nystagmus waveforms and foveation strategy. *Docum. ophthal. 39*: 155-182, 1975
DELL'OSSO, L. F. & DAROFF, R. B.: Eye movement characteristics and recording techniques. In: *Clinical Ophthalmology*, Vol. II (T. Duane, ed.), pp. 1-16. Harper and Row, Hagerstown 1985
DOSLAK, M. J., DELL'OSSO, L. F. & DAROFF, R. B.: Multiple double saccadic pulses occurring with other saccadic intrusions and oscillations. *Neuro-ophthalmology (Amsterdam) 3*: 109-116, 1983
FELDON, S. E. & LANGSTON, J. W.: Square-wave jerks: a disorder of microsaccades? *Neurology (NY) 27*: 278-281, 1977
HERISHANU, Y. O. & SHARPE, J. A.: Normal square wave jerks. *Invest. Ophthal. vis. Sci. 20*: 268-272, 1981
JONES, A., FRIEDLAND, R. P., KOSS, B., STARK, L. & THOMPKINS-OBER, B. A.: Saccadic intrusions in Alzheimer-type dementia. *J. Neurol. 229*: 189-194, 1983
KESTENBAUM, A.: *Clinical Methods of Neuro-ophthalmologic Examination*, 2nd edn., pp. 160-200. Grune and Stratton, New York 1961
LAVERY, M. A., O'NEILL, J. F., CHU, F. C. & MARTYN, L. J.: Acquired nystagmus in early childhood: a presenting sign of intracranial tumor. *Ophthalmology 91*: 425-435, 1984
LEIGH, R. J. & ZEE, D. S.: *The Neurology of Eye Movements.* F. A. Davis, Philadelphia 1983
LEVIN, S., JONES, A., STARK, L., MARRIN, E. L. & HOLZMAN, P. S.: Identification of abnormal patterns in eye movements of schizophrenic patients. *Arch. gen. Psychiat. 39*: 1125-1130, 1982
SHARPE, J. A. & FLETCHER, W. A.: Saccadic intrusions and oscillations. *Canad. J. neurol. Sci. 11*: 426-433, 1984
SHARPE, J. A., HERISHANU, Y. O. & WHITE, O. B.: Cerebral square wave jerks. *Neurology (NY) 32*: 57-62, 1982
ZEE, D. S. & ROBINSON, D. A.: A hypothetical explanation of saccadic oscillations. *Ann. Neurol. 5*: 405-414, 1979