# Variable Waveforms in Downbeat Nystagmus Imply Short-Term Gain Changes

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**A patient with downbeat nystagmus subsequent to ankylosing spondylitis was studied. His nystagmus was found to exhibit both increasing- and decreasing-velocity exponential slow phases as well as the linear form more often reported. Alternation between waveforms sometimes occurred on a beat-to-beat or even intrabeat basis. Possible explanations for all three waveforms are presented in terms of short-term gain changes in cerebellar compensation for leaky brainstem neural integrators. A computer model was developed and its results are discussed.**

Abel LA, Traccis S, Dell'Osso LF, Ansevin CF: Variable waveforms in downbeat nystagmus imply short-term gain changes. Ann Neurol 13:616–620, 1983

One of the key features used to distinguish between congenital nystagmus (CN) and acquired forms of nystagmus has been an observation of the slow-phase waveform. Over the past 10 years, accurate eye movement recordings have identified three different slow-phase shapes of jerk nystagmus: increasing-velocity exponential (runaway) slow phases caused by high-gain instability of the slow eye movement subsystem [7]; linear slow phases caused by tone imbalance [10]; and decreasing-velocity exponential slow phases caused by defective tonic innervation [1].

Acquired jerk nystagmus has been found to have either linear or decreasing-velocity exponential slow phases. In contrast, the jerk types of CN have always been observed to have increasing-velocity exponential waveforms. CN does not include manifest latent nystagmus, which, although it may be a congenital form of nystagmus, is entirely different mechanistically, clinically, and oculographically [9]. These observations have held for all cases of horizontal nystagmus; they have also been applied to vertical nystagmus. Recently, however, Zee and colleagues [16] discussed a patient with an acquired downbeating nystagmus stemming from cerebellar degeneration related to ovarian carcinoma. The slow phases showed an exponentially increasing velocity. Also, Pedersen and co-workers [12] discussed a patient with intermittent downbeat nystagmus consequent to an Arnold-Chiari malformation; their recordings showed similar waveforms. These findings are important because the different nystagmus waveforms reflect different instabilities in the ocular motor pathways. These differences could have diagnostic meaning; for example, in the horizontal plane an increasing-velocity exponential slow phase was believed to be pathognomonic of CN.

This article describes a patient with an acquired downbeating nystagmus characterized by exponentially increasing and decreasing and linear slow phases, sometimes changing on a beat-to-beat basis. Primary position downbeat nystagmus is often associated with disorders of the craniocervical junction, such as Arnold-Chiari malformations [4]. It has also been described in patients with presumed parenchymal cerebellar disease [18], in alcoholic patients [5], and in those with drug intoxication [2], brainstem encephalitis [14], and demyelinating disease [11]. This is the first report in which downbeat nystagmus has been associated with ankylosing spondylitis. We have developed a computer simulation of the patient's nystagmus, based on a model of cerebellar and brainstem pathways [17].

## Case Report

A 62-year-old man had a 40-year history of ankylosing spondylitis. He first noted "jumpy vision," described as a "vertical quiver" which gradually became more noticeable and constant, in January 1980.

Over the next 1½ years his oscillopsia became more severe, being most noticeable when he arose in the morning and lessening as the day progressed. His balance became somewhat more unsteady. He complained of generalized fatigue, mild tremor on lifting a glass of water, and increasingly severe and constant occipital headaches.

On physical examination he was well-developed and in no acute distress. He had downbeat nystagmus in primary position which increased in amplitude on looking laterally and

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Received Aug 16, 1982, and in revised form Nov 2, 1982. Accepted for publication Nov 6, 1982.

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downward. There was no nystagmus on upgaze, and his extraocular movements were otherwise intact and full. His pupils were equal and reactive to light, and funduscopic and visual field examinations were within normal limits. Facial sensation, corneal reflexes, and gag reflex were intact. Grimace was symmetrical. He had a high-tone hearing loss bilaterally. Sternocleidomastoid and trapezius strengths were normal. The tongue deviated slightly to the right on protrusion. Muscle bulk, tone, and strength were normal except for very mild weakness in the grip and opponens muscles bilaterally. Sensation was intact to pinprick, light touch, proprioception, and vibration. On finger-to-nose examination there was a slight bilateral intention tremor. Heel-to-shin examination and gait were difficult to evaluate because of a fused spine and prosthetic hips, but there was no marked ataxia. Deep tendon reflexes were brisk bilaterally, with a slight increase in the right knee and ankle jerk as compared with the left. There was no clonus, and reflexes were brisk and symmetrical in the upper extremities. Plantar responses were flexor.

Skull roentgenography was normal, including basilar views of the foramen magnum. Tomograms of the atlantoaxial junction showed about 2 mm of subluxation with flexion and extension. The odontoid process was hypertrophied, and a small posterior spur was noted. The cervical spine appeared fused except for the C1-C2 junction. Computed tomographic scan showed no abnormalities, with the tip of the odontoid below the foramen magnum.

High metrizamide myelography with computed axial tomography showed the small spur off the posterior aspect of the odontoid which appeared to be pressing on the spinal cord at the C1-C2 level. The cerebellar tonsils did not appear to be displaced downward, and the radiologist noted no evidence of Arnold-Chiari malformation. Because of the possibility of atlantoaxial or vertical subluxation and the progression of his symptoms (with occipital headaches and more marked oscillopsia), the patient underwent odontoidectomy and the cervical spur was removed in October 1981. The patient tolerated the procedure well, and there has been no progression of his symptoms postoperatively. The oscillopsia and downbeat nystagmus have persisted, however.

## Methods

Eye movements were recorded using infrared oculography, modified for use with vertical eye movements. In horizontal recordings, the phototransistors are aimed at the limbus on the left and right of each eye. This positioning is impossible in the vertical plane because of the eyelids, so the patient's lower lids were held slightly retracted with adhesive tape, leaving the entire lower portion of the iris visible but permitting him to blink. The optoelectronic assembly was positioned well below the center of the pupil, with the phototransistors angled sharply toward the center of the lower margin of the iris. The outputs of the transistors were summed rather than used differentially. With this technique, linearity was obtained over a range of approximately ± 10° vertically.

The patient sat 1.14 m from a vertical arc of the same radius. Calibration was carried out using light-emitting diodes at ± 10°. Eye movements were recorded on a modified Beckman Type R rectilinear Dynograph. The bandwidth of the entire system (both position and velocity) was DC to 100 Hz.

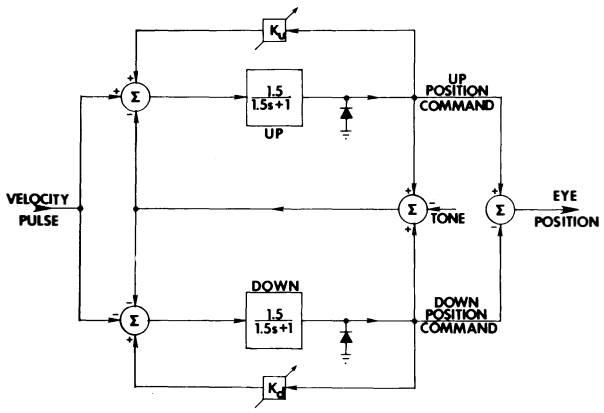


*Fig 1. Block diagram of the computer-simulated up and down brainstem leaky integrators and their cerebellar compensatory feedback loops* ($K_u$ *and* $K_d$, *respectively). Redrawn from Zee and colleagues [17].*

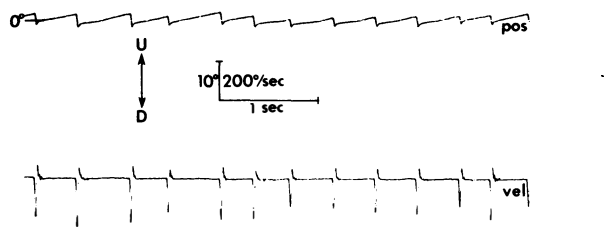


*Fig 2. Eye movements of patient as seen during his first recording session in the laboratory. Waveforms are linear with occasional increasing-velocity beats.* (U = *upgaze;* D = *downgaze;* pos = *position;* vel = *velocity.)*

During recording, the patient's head was restrained with a headrest and chin support.

The computer simulation was performed on a Systron-Donner SD-80 analog computer. The saccadic pulse generator was represented using the computer's repetitive operation model. The model concentrated on the up and down integrators, connected in push-pull and with variable positive feedback present to compensate for their inherent leakiness. The feedback and severity of leak for both integrators could each be controlled by the operator. A block diagram of the model, adapted from Zee and colleagues [17], is shown in Figure 1.

## Results

Examples of the patient's nystagmus as seen during his first recording are illustrated in Figure 2. Although linear slow phases predominate, occasionally nystagmus beats with increasing-velocity exponential slow phases are seen. These were evident in all positions of gaze but were most common in upgaze. Also of note are the pronounced dynamic overshoots (i.e., immediate, small-amplitude return saccades) seen in the nystagmus fast phases.

This patient was recorded again 3 months later, using the same techniques. Several changes were noted in his

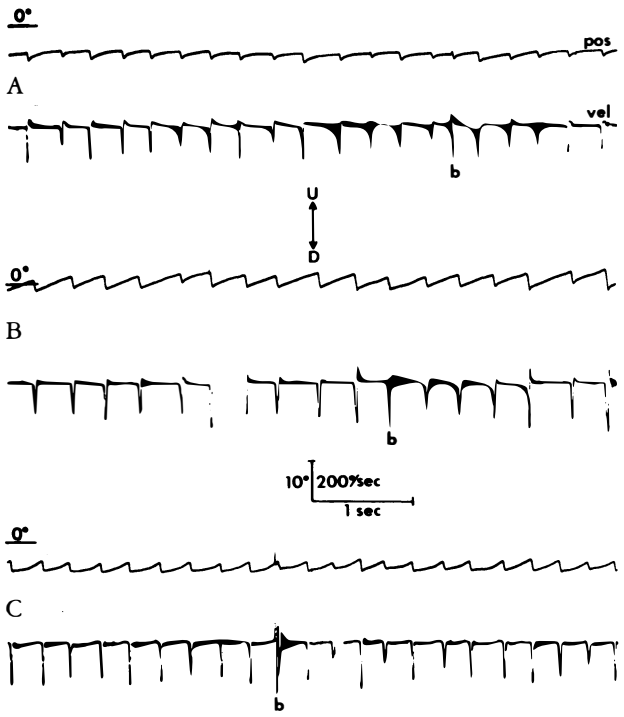


*Fig 3. Patient's nystagmus, showing (A) decreasing-velocity, (B) linear, and (C) increasing-velocity slow phases, all seen during one recording session.* (b = *blink; other abbreviations as in Figure 2.)*

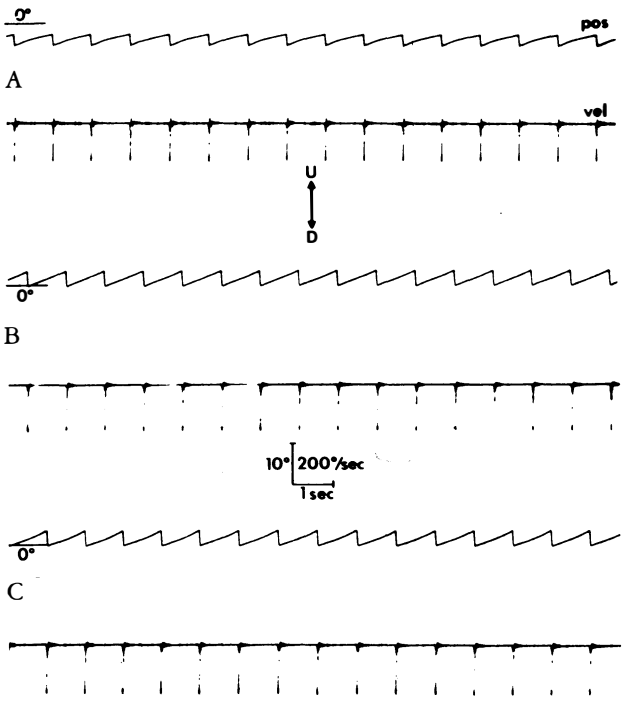


*Fig 5. Model simulations of (A) decreasing-velocity (feedback parameters: $K_d$ = 0, $K_u$ "normal"), (B) linear (feedback parameters: $K_d$ "normal," $K_u$ twice "normal"), and (C) increasing-velocity (feedback parameters: $K_d$ "normal," $K_u$ three times "normal") waveforms. Compare with patient's eye movements as shown in Figure 3. (Abbreviations as in Figure 2.)*

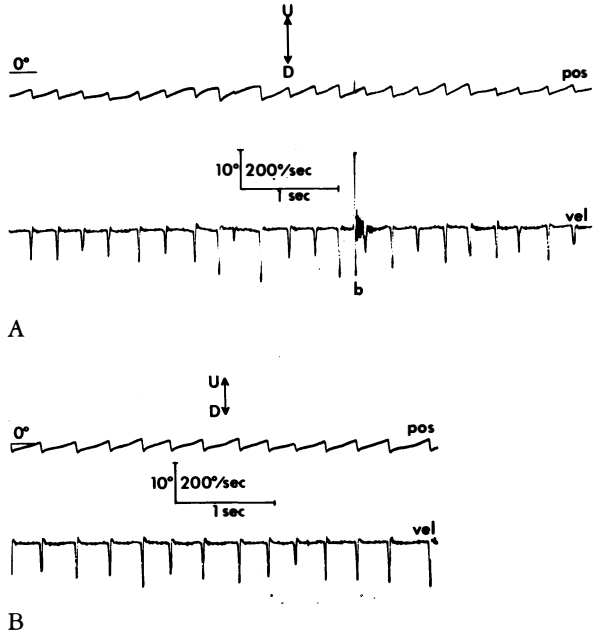


*Fig 4. Variability of the patient's nystagmus, seen on both (A) beat-to-beat and (B) intrabeat bases. (Abbreviations as in Figures 2 and 3.)*

nystagmus, the most striking being a great increase in variability of the slow-phase waveforms. Purely linear slow phases were rare, whereas increasing-velocity exponentials were seen much more often. In addition, decreasing-velocity exponentials were recorded. Figure 3 illustrates the various waveforms. Abrupt and sporadic changes in waveforms, with shifts from one type to another on a beat-to-beat basis (Fig 4A) or even during a beat (Fig 4B), were also documented. The nystagmus amplitude also became much more variable, with amplitudes in upgaze ranging from 1.5 to 10°.

In total darkness, eye movement recordings of nystagmus showed a tendency for the eyes to drift gradually upward and for the nystagmus to become coarser but to retain its basic nature (i.e., frequency, direction, and variability).

In the model, steady fixation could be maintained with appropriate positive feedback. By varying this feedback, and in some cases the leak, the various forms of downbeat nystagmus seen in Figure 5 were generated. These forms correspond to those seen in our patient (see Fig 3). Similarly, if an ongoing nystagmus was generated and the value of the leak varied during a single beat, waveforms could be produced that went from increasing- to decreasing-velocity exponentials during a single beat, and vice versa. These re-

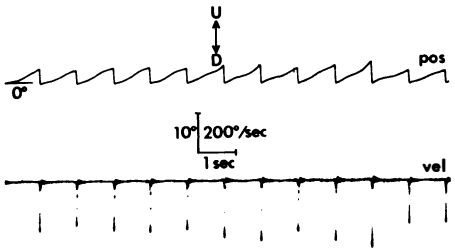


*Fig 6. Model simulation of nystagmus showing intrabeat variability produced by manually varying the inherent "leakiness" of the up integrator while an ongoing increasing-velocity exponential nystagmus was present. (Feedback parameters: $K_d$ "normal," $K_u$ twice "normal"; leak varied between one-sixth and twice "normal." Abbreviations as in Figure 2.)*

sponses, shown in Figure 6, parallel the patient's eye movements as seen in Figure 4B.

## Discussion

For all forms of true nystagmus, the slow eye movement is responsible for the genesis and continuation of the oscillation [6]. The cause of the slow eye movement is one of the variables that differentiate the various types of nystagmus. High-gain instability of the slow eye movement subsystem has been considered responsible for all varieties of CN [8]. The most common CN waveforms are jerk, with the slow phase consisting of an increasing-velocity exponential (runaway), and pendular. Downbeat nystagmus had previously been described with a linear slow phase and its origin ascribed to an imbalance in pursuit tone [15] or central vestibular tone [3]. Zee and co-workers [16] postulated that the increasing-velocity slow phases in their patient's nystagmus arose from a brainstem neural integrator that was made unstable by cerebellar dysfunction. Previously, Robinson [13] had attributed the inability of cerebellectomized cats to maintain eccentric gaze to a disorder of the tonic neurons. He held that the cerebellum improves the performance of an inherently leaky brainstem neural integrator by increasing its time constant.

An animal model for downbeat nystagmus was developed by Zee and co-workers [17]. They produced downbeat nystagmus in monkeys by creating lesions in the flocculus and paraflocculus, and found that the slow-phase waveform was in some cases an increasing- and in others a decreasing-velocity exponential. They presented a possible model for this nystagmus, involving cerebellar control of a positive feedback loop around the inherently leaky brainstem neural integrator.

The precise nature of the defect in our patient remains uncertain, because the exact location and the extent of his lesion are yet to be determined. Evidence that his pursuit system was functioning comes from the observation that attempted pursuit caused changes in the slopes of the slow phases of his nystagmus. These changes in slow-phase slopes may indicate the presence of a pursuit response added to the ongoing nystagmus. His first recording showed a nystagmus with a generally linear slow phase; this could be the result of either a tonic drift or an exponential waveform with a long time constant. Conceivably, his second recording might indicate some progression of the disease process making the defects in the up and down integrators more erratic, perhaps because of an increasingly compromised circulation. The waveform of the nystagmus then depended on the exact characteristics of the integrators at a given time. A sudden change in their condition could produce slow phases that changed from acceleration to deceleration (or vice versa) in midbeat, as were frequently seen in the record.

Our computer implementation of the model of Zee and co-workers [17] has yielded several insights into possible mechanisms for the generation of downbeat nystagmus. One difference between our version and theirs is caused by the much shorter time constants and, hence, faster runaways seen in our patient's nystagmus than seen in the flocculectomized monkeys. To achieve these, much greater amounts of positive feedback (i.e., a higher gain) were required. Indeed, our model was unable to quite match our patient values because of voltage saturation of the amplifiers (note the different time bases in the actual and model tracings). This difficulty is easily overcome by rescaling the model and is in no way a fundamental limitation. Another finding was that the intrabeat variability was best reproduced by varying the inherent leakiness (gain) of the neural integrator instead of the gain of the positive feedback loop.

Figure 5B suggests a possible origin for downbeat (or upbeat) nystagmus with a linear slow phase. Previously, these have been ascribed to tonic imbalances in either the pursuit [15] or the vestibular system [3]. The recording shown here, however, was generated by producing an increasing-velocity exponential downbeat nystagmus with a very long time constant—one that looks linear when only a few hundred milliseconds of the curve are visible. This possibility had previously been suggested for gaze evoked nystagmus with a very slowly leaking integrator [1]. In patients like the one reported here, with a high degree of variability evident in the nystagmus waveforms, it is possible that the waveforms all stem from one basic defect: short-term gain changes in the neural integrator. This hypothesis has the attractiveness of not requiring separate explanations for the exponential and linear waveforms. It remains possible that some cases of downbeat nystagmus, particularly those with consistently linear slow phases, are caused by tonic imbalance, perhaps in the vestibular system [3].

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