17

Expanding the Original Behavioral Infantile Nystagmus Syndrome Model to Jerk Waveforms and Gaze-angle Variations

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ABSTRACT

Our objective was to expand the behavioral ocular motor system (OMS) model for infantile nystagmus syndrome (INS) by (a) incorporating jerk and jerk with extended foveation waveforms using a unifying mechanism for both pendular and jerk waveforms and (b) incorporating idiosyncratic variation of INS amplitude with gaze angles. Ocular motor recordings of humans, using infrared reflection, high-speed digital video, and magnetic search coil systems, were used as templates for the computer simulations. All simulations and analyses were performed in MATLAB Simulink environment. Examinations of eye movement data during different states of attention suggested that pendular and jerk INS waveforms came from the same underlying smooth-pursuit-system oscillation. Simulation of unidirectional jerk waveforms required a resettable neural integrator in the pursuit premotor circuitry. Alexander's law relationships were used to produce desired INS "null" positions and sharpness. At various gaze angles, these Alexander's law relationships influenced the INS slow-phase amplitudes differently, thus mimicking the same gaze-angle effects observed in INS patients. The simulations of a robust behavioral OMS model demonstrated that both pendular and jerk waveforms can be generated by the same pursuit-system instability. Alexander's law output effectively modulates the nystagmus variation at different gaze angles.

The ocular motor system (OMS) model for infantile nystagmus syndrome (INS) simulates the responses of individuals with several pendular waveforms (pendular with foveating saccades [Pfs] and pseudopendular with foveating saccades [PPfs]) based on a loss of damping of the normal pursuit-subsystem instability and its interaction with other OMS components. Accurate model simulations during fixation, saccades to known targets (steps, pulses, and pulse-steps), and smooth pursuit (ramps and step-ramps), as well as many emergent properties and unexpected predictions of the model, duplicate the recorded responses of humans with INS, providing strong support for the hypothetical mechanisms in the model.[1,2]

There are, however, a number of INS features that were not included in the original OMS model. To expand this behavioral model, we intend to incorporate jerk and jerk with extended foveation waveforms by employing a unifying mechanism for both pendular and jerk waveforms. Alexander's law variation of slow-phase velocity was included in an interim version of the model; its output will be utilized to simulate slow-phase amplitude changes affecting the eXpanded Nystagmus Acuity Function (NAFX) peak,[3] or the INS "null."

METHODS

The ocular motor recordings and observations used for the computer simulation came from approximately 1,000 subjects with INS, who were recorded

in our laboratory over 37 years. Eye movements were measured using either an infrared reflection (Eye-Trac 210, Applied Science Laboratories, Bedford, MA), a magnetic scleral search coil (CNC Engineering, Seattle, WA), or a high-speed digital video (EyeLink II, SR Research Ltd., Mississauga, Ontario, Canada) system. Specifications of the recording systems can be found elsewhere.[4] All simulations were performed in the MATLAB Simulink (MathWorks, Natick, MA) environment.

RESULTS

Eye movement data with inattention from INS individuals revealed large pendular oscillations underneath the jerk waveforms (Fig. 17.1A). In Figure 17.1B, the foveating fast phase was delayed, and the accelerating slow phase actually decelerated (with a point of inflection) before the fast phase reset the fovea on target. As soon as attention to the target was reestablished (either spontaneously or after verbal prompting by the experimenter), a foveating fast phase was generated and jerk waveforms reoccurred.

Examination of these data demonstrated that the underlying pendular oscillation had to be reset when each foveating saccade was made. A resettable neural integrator in the pursuit premotor circuitry (PMC+) was necessary to accomplish the resetting. This neural integrator has the same structure as that found in pulse generators,[5-7] and is different from the common neural integrator in the final motor pathway. Using the foveating-saccade motor command, the oscillation was reset so that the underlying pendular waveform could be restarted. The time delays in both the feedback and feed-forward loops in PMC+ were also reset (i.e., the stored energy had to be dumped). Figures 17.1C–F show simulations of the model under various visual inputs. Jerk waveforms in both directions consistently arrived at the new target positions; despite slight differences in the sizes of each saccade, foveation always occurred (within ±0.5° of the target). The model also responded correctly to step inputs with different directions, onset times, and durations.

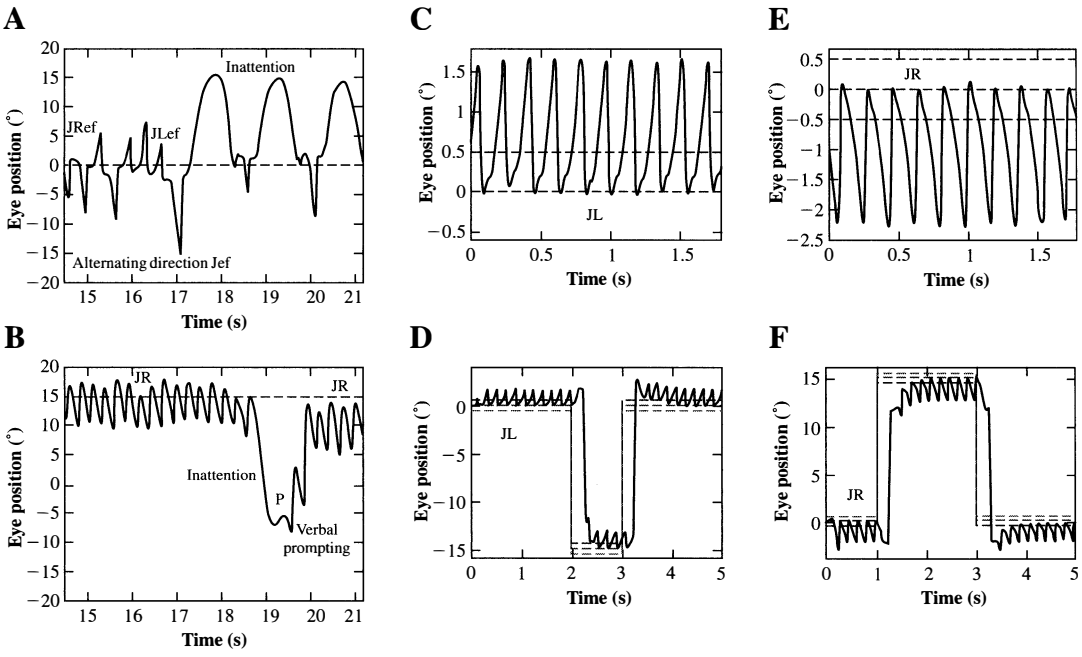

Figure 17.1 (A) Fixation data from a patient with alternating-direction jerk with extended foveation (Jef) waveforms showing a large underlying pendular oscillation when inattention suppresses the fast phases. (B) Fixation data from a patient with jerk right (JR) waveforms showing a delayed foveating fast phase and a decelerating slow phase before the fast phase resets the oscillation (by verbal prompting). (C) Model output of jerk left (JL) fixation. (D) Model responses with −15° step input. (E) Model output of jerk right (JR) fixation. (F) Model responses with 15° step input. In (D) and (F), dashed lines indicate fovea (±0.5° around the target position).

Alexander's law describes the increase in the amplitude of nystagmus as the eye is moved in the direction of the fast phase in vestibular nystagmus and fusion maldevelopment nystagmus syndrome (FMNS). The Alexander's law functional block in the internal monitor of the OMS model is based on a tonic imbalance signal modulated by efference copy of the eye position signal. In a previous simulation, gaze-angle effects in FMNS (i.e., foveating and defoveating fast-phase alternation) waveforms were guided by Alexander's law input.[8] For FMNS patients, the two Alexander's law lines (one for fixation by each eye) operate independently of each other, with only one (depending on the fixating eye) determining the gaze-angle variation. In INS, we hypothesize that both Alexander's law relationships operate together. This same imbalance, produced by improper calibration of the vestibular system, may also be the underlying reason for INS gaze-angle variation. Figure 17.2A demonstrates the gaze-angle variation model position output, corresponding to the "null" in Figure 17.2B (the NAFX peak in 17.2C) at 10°. Figure 17.2B shows how the two linear functions act simultaneously, with their intersection establishing the "null" position and the slopes of the curves controlling the broadness of the "null." The modulation was produced by a variable gain in the PMC+ block.

DISCUSSION

When the first version of the OMS model was completed in 2003,[2] it simulated the most complex INS waveforms (Pfs, PP, and PPfs) and the behavioral responses consistent with INS data. It demonstrated that our hypothesis for the generation of P, Pfs, PP, and PPfs could be realized by a functionally normal OMS. We have now demonstrated that, without adding a separate mechanism for jerk waveforms to the prior OMS model, and in agreement with observations and accurate eye movement recordings on inattention and waveform transition, the model can simulate pendular and jerk waveforms and behavioral responses from the same underlying mechanism. This supports the hypothesis that most pendular and jerk INS waveforms are due to a loss of pursuit-system damping.

The behavioral output of the OMS model at different gaze angles demonstrated the effectiveness of using Alexander's law input to simulate the variation of IN waveforms across the whole visual field. The Alexander's law imbalance (possibly asymmetrical) produced by improper calibration of the vestibular system may have caused the INS gaze-angle variation. The Alexander's law effects on INS amplitude will be used in future versions of the model to control the

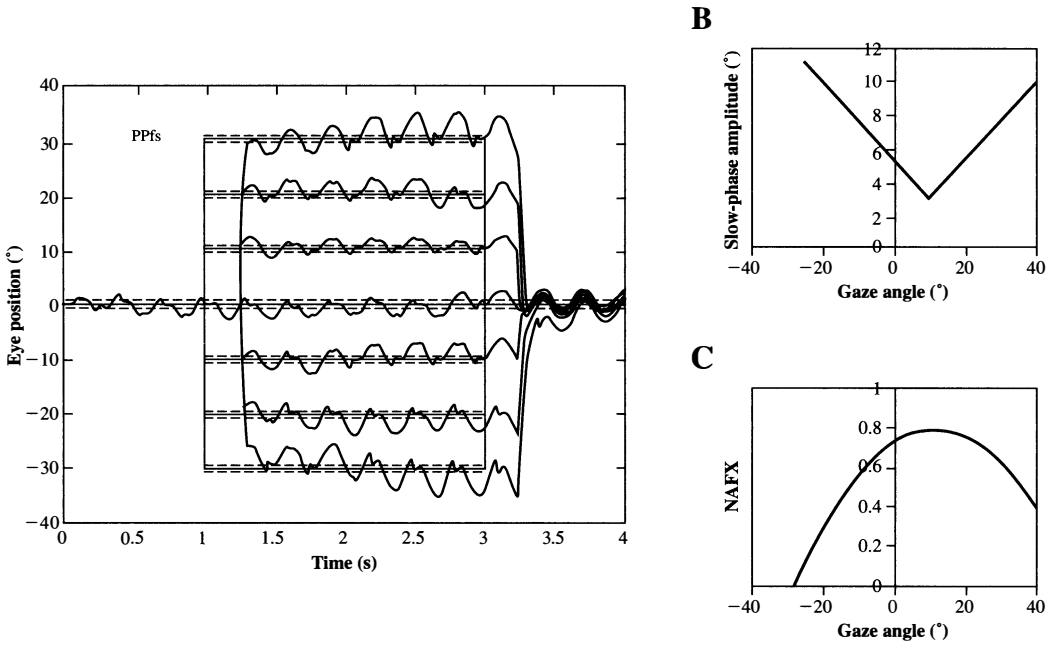

Figure 17.2 Model output of PPfs waveform (A) with a "null" at 10° and increased slow-phase amplitude to either side of the null. The intersection and slopes of the two Alexander's law lines (B) correspond to the position and sharpness of the null, as seen in (A). The peak position and sharpness of the eXpanded Nystagmus Acuity Function (NAFX) curve (C) correspond to those of the null as shown in (A) and (B).

idiosyncratic transitions between pendular and jerk waveforms. The effects of inattention on INS waveforms will also be incorporated into the model, through the same modulating gain in the PMC+ circuit.

These improvements in the OMS model add another step to the implementation of a complete and idiosyncratic OMS model that can simulate normal as well as pathological (e.g., INS) behaviors.

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References

1. Jacobs JB. An Ocular Motor System Model that Simulates Congenital Nystagmus, Including Braking and Foveating Saccades [dissertation]. Cleveland: Case Western Reserve University; 2001.
2. Jacobs JB, Dell'Osso LF. Congenital nystagmus: hypothesis for its genesis and complex waveforms within a behavioral ocular motor system model. *JOV*. 2004;4(7):604–625.
3. Dell'Osso LF, Jacobs JB. An expanded nystagmus acuity function: intra- and intersubject prediction of best-corrected visual acuity. *Doc Ophthalmol.* 2002;104:249–276.
4. Wang Z, Dell'Osso LF, Zhang Z, Leigh RJ, Jacobs JB. Tenotomy does not affect saccadic velocities: support for the "small-signal" gain hypothesis. *Vision Res*. 2006;46:2259–2267.
5. Abel LA, Dell'Osso LF, Daroff RB. Analog model for gaze-evoked nystagmus. *IEEE Trans Biomed Engng*. 1978;BME(25):71–75.
6. Abel LA, Dell'Osso LF, Schmidt D, Daroff RB. Myasthenia gravis: analogue computer model. *Exp Neurol*. 1980;68:378–389.
7. Kustov AA, Robinson DL. Modified saccades evoked by stimulation of the Macaque superior colliculus account for properties of the resettable integrator. *J Neurophysiol*. 1995;73:1724–1728.
8. Dell'Osso LF, Jacobs JB. A normal ocular motor system model that simulates the dual-mode fast phases of latent/manifest latent nystagmus. *Biological Cybernetics*. 2001;85:459–471.

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