A Robust, Normal Ocular Motor System Model with Latent/Manifest Latent Nystagmus (LMLN) and Dual-Mode Fast Phases

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Summary

The fast phases of LMLN may either cause the target image to fall within (foveating) or outside (defoveating) the foveal area. We verified that both types are generated by the same mechanism as voluntary saccades and propose a hypothetical, dual-mode mechanism (computer model) for LMLN that utilizes normal ocular motor control functions. Fixation data were recorded from subjects with LMLN using both infrared and magnetic search coil oculography and used as templates for our simulations. Fast-phase amplitude vs. both peak velocity and duration of simulated saccades were equivalent to those of saccades in normal subjects. Based on our LMLN data, we constructed a hypothetical model in which the slow-phase velocity acted to trigger the change between foveating and defoveating LMLN fast phases. Foveating fast phases were generated during lower slow-phase velocities whereas, defoveating fast phases occurred during higher slow-phase velocities. The bidirectional model simulated Alexander's law behavior under all viewing and fixation conditions. Our ocular-motor model accurately simulates LMLN-patient ocular motility data and provides a hypothetical explanation for the conditions that result in both foveating and defoveating fast phases. As is the case for normal physiological saccades, position error determined saccadic amplitudes for foveating fast phases. However, final slow-phase velocity determined amplitudes of defoveating fast phases. In addition, we sug-

gest that individuals with LMLN use their fixation subsystem to further decrease the slow-phase velocity as the target image approaches the foveal center.

Introduction

Latent/manifest latent nystagmus (LMLN) is a specific type of infantile nystagmus that occurs subsequent to strabismus in some patients.[1, 2] The amplitude of LMLN usually follows Alexander's law (i.e., it increases as the fixating eye moves into abduction and decreases in adduction (see Figures 9 and 10 [1]). The slow phases of LMLN may be either linear or of decreasing velocity in the same patient.[3] Depending on the slow-phase velocity, LMLN fast phases could be programmed to cause the target image to fall either within (foveating) or outside (defoveating) the foveal area.[3] Higher slow-phase velocities were found to precipitate defoveating fast phases.[4] Also, as presaccadic slow-phase velocities grow, fast-phase amplitudes follow.

We present a dual-mode, control-system model that is capable of producing normal saccades and both foveating and defoveating fast phases in LMLN. Additionally, the model contains a mechanism by which linear slow phases undergo the transition to decreasing velocity slow phases. The model includes programmable Alexander's law behavior (zero to maximal) and fixation conditions (e.g., either eye fixating under either monocular or binocular viewing conditions and is, therefore, capable of simulating the idiosyncratic characteristics of a broad spectrum of individuals with LMLN.[5]

Materials and Methods

The computer simulation of the control-system model was accomplished using the Simulink component of MATLAB. The model is of modular design, consisting of functional building blocks thought to be required for accurate ocular motor control. The modular design facilitates expansion of the model to include additional subsystems and preserves the separation of functions required to produce the wide variety of ocular motor responses exhibited by humans, both normals and those with specific dysfunction. In addition to modularity, the model contains distributed delays that duplicate those known to exist from neurophysiological studies.

THE SACCADIC SUBSYSTEM: The saccadic system responds to abrupt changes in target position and is capable of making short-latency (130 msec) corrective saccades, based on efference copy of position motor commands.

THE INTERNAL MONITOR: The internal monitor is essential for this model, as the functions it performs have been required by all of our past models of ocular motor dysfunction.[6-13] It makes use of afferent signals from the retina and efferent signals from the brainstem to enable the model to detect target changes, to accurately reconstruct target position and velocity, and to differentiate them from eye position and velocity in the presence of motor instabilities. It calculates saccadic motor commands for voluntary and corrective saccades and for fast phases, perceived target position and velocity, and a signal to control the percentage of every saccadic pulse that should be integrated. Provision is also made for Alexander's law variation of nystagmus slow phases.[10, 13] Without such abilities, we contend that the human ocular motor system could not function (as we know it does function) in the presence of either nystagmus or saccadic instabilities. The internal monitor makes use of a combination of afferent and efferent signals to achieve its goal of providing needed signals to its own internal structures or to external functional blocks. Working together, these subsystems allow the ocular motor system to properly differentiate target position/velocity from eye position/velocity and make appropriate decisions to generate responsive eye movements.

FAST-PHASE GENERATION: For generation of a *foveating* fast phase, the output of the neural integrator is compared with a desired eye-position signal and the difference between them is subjected to a position-signal error threshold. If this error exceeds the threshold, a saccade proportional to the error is generated. When the slow-phase velocity exceeds the velocity threshold (4°/sec), a *defoveating* fast phase is generated instead. The transition from foveating to defoveating saccades in the model is based on phase-plane data from LMLN subjects. Such phase planes show a significant difference in the pre-saccadic velocities for the foveating and defoveating cases. Some phase planes however, show a region of overlapping slow-phase velocities where either foveating or defoveating fast phases can occur. This could be simulated in the model by a change in the position-error threshold.

DECREASING VELOCITY SLOW PHASES: Previous studies showed correlation of fast-phase size with pre- and post-saccadic velocity.[4, 14, 15] The linear relationship of the size and post-saccadic velocity suggested that an unintegrated pulse (i.e., a saccadic pulse or "stepless" saccade) was being used by the system. The post-saccadic velocities indicated that the pulse was not totally unintegrated and the data suggested that the fast-phase generator produces a pulse width and height for a saccade of a relatively small size. In order to generate the decreasing velocity profiles of LMLN slow phases, additional mechanisms were

required in the model. Increasing the pulse to values that produce saccades greater than that required to foveate the target leads to a larger unintegrated pulse, which is summed with the output from the neural integrator and produces a decreasing velocity slow phase.

Results

Manifest Latent Nystagmus (MLN):The nystagmus of individuals with MLN (both eyes open) contains linear slow phases and foveating fast phases throughout most gaze angles. When a small gaze-angle Alexander's law effect is simulated, even though slow–phase velocity increases as the fixating right eye abducts the fast phases remain foveating. With a larger gaze-angle effect, slow-phase velocity increases more rapidly as fixation moves in the abducting direction of the fixating right eye. When it exceeds 4°/sec, the fast phases become larger and defoveating and the slow phases exhibit a decreasing velocity. Importantly, neither type of MLN interferes with the ability of the saccadic subsystem to accurately foveate the target, including making corrective saccades when necessary.

Latent Nystagmus (LN): The nystagmus of individuals with LN (one eye occluded) contains linear slow phases and foveating fast phases throughout most gaze angles; When a small gaze-angle Alexander's law effect is simulated, even though slow–phase velocity decreases as the fixating right eye adducts, the fast phases remain defoveating except in far adduction.

With a larger gaze-angle effect, the slow-phase velocity decreases more rapidly as the fixating right eye adducts. As a result, the slow phases drop below 4°/sec at a more central gaze angle, causing smaller foveating fast phases and linear slow phases. Neither type of LN interferes with the ability of the saccadic subsystem to accurately foveate the target, including making corrective saccades when necessary.

Conclusions

We constructed a computer model of the normal ocular motor system that also has the ability to simulate LMLN. We demonstrated that an internal monitor could make use of afferent retinal and efferent motor information to detect changes in target position and to accurately differentiate target position and velocity from internally generated eye position and velocity (e.g., resulting from LMLN). In addition, we demonstrated that when slow-phase velocity exceeded 4°/sec, the foveating fast phases of the LMLN would switch to defoveating fast phases and the resulting slow phases become decreasing velocity due to unintegrated portions of the fast-phase pulses. Finally, we demonstrated that if slow-phase veloc-

ity increased as gaze was directed in the abducting direction of the fixating eye (due to Alexander's law), that would ultimately cause the switch from foveating to defoveating fast phases.

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