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Being "slow to see" is a dynamic visual function consequence of infantile nystagmus syndrome: Model predictions and patient data identify stimulus timing as its cause $\stackrel{\text{tr}}{\approx}$

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Abstract

The objective of this study was to investigate the dynamic properties of infantile nystagmus syndrome (INS) that affect visual function; i.e., which factors influence latency of the initial reflexive saccade (Ls) and latency to target acquisition (Lt). We used our behavioral ocular motor system (OMS) model to simulate saccadic responses (in the presence of INS) to target jumps at different times within a single INS cycle and at random times during multiple cycles. We then studied the responses of 4 INS subjects with different waveforms to test the model's predictions. Infrared reflection was used for 1 INS subject, high-speed digital video for 3. We recorded and analyzed human responses to large and small target-step stimuli. We evaluated the following factors: stimulus time within the cycle (Tc), normalized Tc (Tc%), initial orbital position (Po), saccade amplitude, initial retinal error (e_i) , and final retinal error (ef). The ocular motor simulations were performed in MATLAB Simulink environment and the analysis was performed in MATLAB environment using OMLAB software. Both the OMS model and OMtools software are available from http:// http://www.omlab.org. Our data analysis showed that for each subject, Ls was a fixed value that is typically higher than the normal saccadic latency. Although saccadic latency appears somewhat lengthened in INS, the amount is insufficient to cause the "slow-tosee" impression. For Lt, Tc% was the most influential factor for each waveform type. The main refixation strategies employed by INS subjects made use of slow and fast phases and catch-up saccades, or combinations of them. These strategies helped the subjects to foveate effectively after target movement, sometimes at the cost of increased target acquisition time. Foveating or braking saccades intrinsic to the nystagmus waveforms seemed to disrupt the OMS' ability to accurately calculate reflexive saccades' amplitude and refoveate. Our OMS model simulations demonstrated this emergent behavior and predicted the lengthy target acquisition times found in the patient data.

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Keywords: Infantile nystagmus; Saccades; Target acquisition; Ocular motor system; Model

1. Introduction

Infantile nystagmus syndrome (INS (CEMAS_Working_Group, 2001), previously known as congenital nystagmus, or CN), is characterized by involuntary oscillations of the eyes and degrades visual acuity with varying degrees (Dell'Osso, 1973; Dell'Osso & Daroff, 1975). Foveation quality in each nystagmus cycle and the ability to repeat accurate foveation from cycle to cycle determine the visual-

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acuity reduction (Abadi & Worfolk, 1989; Bedell & Loshin, 1991; Dell'Osso & Flynn, 1979; Dell'Osso & Jacobs, 2002; Dell'Osso, Flynn, & Daroff, 1974; Sheth, Dell'Osso, Leigh, Van Doren, & Peckham, 1995). INS frequently accompanies additional afferent defects of the visual sensory system, which may cause the primary deficit in visual function (Dell'Osso & Daroff, 1997).

Primary-position visual acuity has been measured clinically for decades; however, it is questionable if this single, *static* measurement is sufficient to assess real-life visual function. A previous study in our laboratory showed the necessity of waveform quality measurements taken in lateral gaze for evaluating the tenotomy procedure's "null" broadening effect (Wang, Dell'Osso, Zhang, Leigh, & Jacobs, 2006). These measurements mimic the real-life situation of keeping the head still and looking around with just the eyes, a visual function highly desirable for driving and other daily routines. Assessing this clinically requires measuring visual acuity at different gaze angles (Yang, Hertle, Hill, & Stevens, 2005).

The waveform quality and visual acuity measurements mentioned above, both in primary position and in lateral gaze, are static measures of visual function. In those tests, subjects may be required to fixate on a small light-emittingdiode stimulus against a dark background or look at eye charts and identify letters. However, the real world contains a highly complex combination of object positions and velocities, requiring a mixture of saccadic and pursuit responses. How does the ocular motor system (OMS) perform in this environment, especially in the presence of INS? What factors determine the actual time needed to refoveate a target after it moves? Why do we hear complaints from INS patients that they are "slow to see"? Measurements of the dynamic characteristics of INS foveation are needed to answer these questions. A previous study on INS patients' recognition time of a fixed optotype target at their threshold visual acuity was performed, showing a decrease in recognition time after four-muscle recession. However, that study just used "slow to see" as a patient-reported fact, it did not explore the reasons (Sprunger, Fahad, & Helveston, 1997).

For normal subjects, saccadic latency is 200-250 ms and pursuit latency is ~125 ms (Abel, Schmidt, Dell'Osso, & Daroff, 1978; Leigh & Zee, 2006). It is not known if INS subjects have normal saccadic latency. Normal individuals apply strategies like corrective saccades to quickly foveate step stimuli that have large amplitudes. Those with INS do that as well, and have other "tools" that can be utilized, e.g., the fast and slow phases of their waveforms. It would be informative to investigate INS foveating strategies and determine how they contribute to target acquisition.

This study focuses on the responses of INS subjects to step stimuli with a variety of amplitudes and aims to answer some of the questions asked above. Specifically, this initial study of the dynamic properties of INS foveation will examine possible influencing factors, such as waveform type, stimulus time within the cycle, saccade amplitude, and initial and final retinal error. We will use predictions from our OMS model (Jacobs & Dell'Osso, 2004) to guide and reinforce our data analysis. The OMS model for INS simulated the responses of individuals with several pendular waveforms (pendular with foveating saccades, Pfs, and pseudopendular with foveating saccades, PPfs) based on a hypothesized exacerbation of the normal pursuit-subsystem instability and its interaction with other OMS components. The OMS model consists of smooth pursuit (SP) and saccadic subsystems, and an "Internal Monitor" (IM) that receives afferent information from the retina plus position and velocity efference copy to determine the control signals that drive these motor subsystems. We will demonstrate in this study another emergent behavior of this model and how it guided our data analysis to find out the relationship between stimulus timing and target acquisition.

2. Methods

2.1. Subjects

We studied four INS subjects with different waveforms at primary position: jerk, pseudocycloid (PC), and pseudopendular with foveating saccades (PPfs) (Table 1). Note that Subject 1 had a pendular with foveating saccades (Pfs) waveform in right gaze and that Subject 3 also had Asymmetric, (a)Periodic Alternating Nystagmus (APAN), i.e., his nystagmus amplitude and null position changed with time.

2.2. Recording

Infrared reflection (IR) was used for 1 subject, high-speed digital video for 3. The IR system (Applied Scientific Laboratories, Waltham, MA) was linear to 20° in the horizontal plane and monotonic to 25-30° with a sensitivity of 0.25°. The total system bandwidth (position and velocity) was 0-100 Hz. The digital video system (EyeLink II, SR Research, Mississauga, ON, Canada) had a linear range of $\pm 30^{\circ}$ horizontally and $\pm 20^{\circ}$ vertically. System sampling frequency was 500 Hz, and gaze position accuracy error was 0.5-1° on average. The data from both systems were digitized at 500 Hz with 16-bit resolution. The IR or EyeLink signal from each eye was calibrated with the other eye behind cover to obtain accurate position information; the foveation periods were used for calibration. Eye positions and velocities (obtained by analog differentiation of the position channels) were displayed on a strip chart recording system (Beckman Type R612 Dynograph). Monocular primary-position adjustments for all methods allowed accurate position information and documentation of small tropias and phorias hidden by the nystagmus.

2.3. Protocol

This study was approved by the local IRB and written consent was obtained from each subject before the testing. All test procedures were carefully explained to the subject before the experiment began, and were

Table 1							
Subjects'	waveform	types in	primary	position	and	lateral	gaze

-		-
Subject #	Waveform type in primary position	Waveform type in lateral gaze
1	PPfs	Pfs in right gaze PC in left gaze
2	J	J and PPfs in the "null" region $(-10^{\circ} \text{ to } -15^{\circ})$
3	J*	_
4	PC and occasionally, Pfs	_

* This subject's jerk nystagmus has a time-varying component, i.e. he has Asymmetric, (a)Periodic Alternating Nystagmus (APAN).

reinforced with verbal commands during the trials. Subjects were seated in a chair with headrest and a chin stabilizer, far enough from the stimulus screen to prevent convergence effects (>5 feet). At this distance the LED subtended less than 0.1° of visual angle. The room light could be adjusted from dim down to blackout to minimize extraneous visual stimuli. An experiment consisted of from 8 to 10 trials (including large and small target steps), each lasting \sim 2 minutes with time allowed between trials for the subject to rest. Trials were kept this short to guard against boredom because INS intensity is known to decrease with inattention. Step stimuli were presented to the patients with a variety of amplitudes (5°, small steps; 15°, 20°, 25°, 30°, 35°, 40°, 45°, 50°, 55°, 60°, large steps), to the left and right (all subjects have predominantly horizontal INS). Targets were fixed at the new position for at least 5s, allowing subjects enough time for steady fixation. We repeated these presentations to collect a pool of target jumps at different times in the nystagmus cycle, so that we could obtain enough data points for the curve fitting. Target fixation was monitored throughout the recording through the real-time display of the strip-chart recorder and verbally reinforced. The monocular calibration routine and post-recording data calibration allowed us to determine the fixating eye from the deviated eye and made accurate analysis of the target acquisition possible. Details of accurate eve-movement recording and calibration can be found on http://www.omlab.org/OMLAB_page/Teaching/teaching. html.

2.4. Analysis

All the analysis was performed in MATLAB environment (The MathWorks, Natick, MA) using OMLAB software (OMtools, available from http://www.omlab.org). Only eye position was sampled directly; velocity was derived from the position data by a 4th-order central-point differentiator. Position data were pre-filtered with a low-pass filter with the cutoff frequency of 50 Hz to reduce the noise while minimally affecting the saccadic data. Analysis was always done on the fixating eye. Segments with inattention or blinking were discarded.

We evaluated the following factors that might influence the saccadic latency (Ls) and the time to target acquisition (Lt) after the target jump: stimulus time within the cycle (Tc), normalized Tc (Tc% = Tc/the length of that nystagmus cycle), initial orbital position (Po), saccade amplitude, initial retinal error (e_i), and final retinal error (e_f). We also recorded: waveform types; number of saccades to achieve target acquisition (including reflexive saccades and fast phases that are modified in amplitude—this number may or may not be equal to the number of cycles taken to reach the target); and direction of target jump vs. foveating saccade.

The measurement of Tc was always made from the beginning of the nystagmus cycle, i.e., the beginning of the foveation period. Fig. 1 illustrates the four (most common) types of INS waveforms that we examined in this study; subjects may have combinations of different waveforms as the gaze angle varies. Note that the beginning of each cycle immediately follows the termination of the foveating saccade, except in the case of PC waveforms (foveation occurs after a braking saccade followed by a slow movement of the eye onto the target). Jerk waveforms, which have a less "flat" foveation period than Jef waveforms, were measured with the same criteria as Jef, and therefore, are not shown.

Because of the continuous eye movements of individuals with nystagmus, saccadic characteristic definitions must take into account the baseline velocity and eye position at the time the saccade is made. Saccade amplitude was defined as the distance the eye traveled between the velocityderived and position-derived saccade onset/offset times added to the position-derived amplitude. This modification was shown to be appropriate and necessary for the analysis of saccades made by nystagmus subjects (Jacobs, Dell'Osso, & Leigh, 2003; Wang et al., 2006).

As illustrated in Fig. 2, Ls, the latency to the initial reflexive saccade, is measured from the target-jump time to the beginning of the reflexive saccade (determined by the turning point of the velocity trace, arrow "a"). Lt, the latency to the target arrival time, is measured from the target-jump time to the beginning of the first foveation period on the target (also indicated by the turning point of the velocity trace, arrow "b"). Due to the variation of foveation quality, we defined "the first foveation period on the



Fig. 1. Illustrations of the nystagmus waveforms examined in this study. In this and the following figures, Pfs, pendular with foveating saccades; PPfs, pseudopendular with foveating saccades; PC, pseudocycloid; Jef, jerk with extended foveation. Arrows indicate the beginning of the cycle. PC and Jef waveforms are shown in both directions.

target" to be the first foveation period in the subject's foveation window that was followed by subsequent foveation periods within that window. In this particular section (Fig. 2), the window was quite narrow (the $\pm 0.5^{\circ}$ of the fovea). Using the criteria described in the previous paragraphs, Tc is shown as the time from the beginning of the current nystagmus cycle to the target jump. Po (arrow "c"), initial orbital position, is the eye position when the target step occurred. $e_i = Po$ -initial target position; $e_f = Po$ -final target position. The data were fitted with either linear or higher order polynomial curves.

If the subject switched fixating eye after the saccade, the saccade amplitude was not measured, and only the other characteristics were examined. We categorized the data by the waveform type before the target jump, which may not be the same after the target acquisition; we noted such situations to help identify outliers.

2.5. Simulation

All ocular motor simulations were performed in MATLAB Simulink (Waltham, MA) environment. The OMS model is available from http://www.omlab.org.

3. Results

In the following sections we present the predictive model outputs, followed by the human response data under two different conditions, large target steps and small target



Fig. 2. Position and velocity traces of a typical response to a 15° rightward target step from primary position (Subject 1). Measurements are indicated on the figure. Arrow "c" points to the eye position when the target step occurred. In this and the following figures, Ls, latency to the initial reflexive saccade (measured from arrow "c" to arrow "a"). Lt, latency to the target arrival time (measured from arrow "c" to arrow "b"). Tc, time within the cycle.

steps. Additionally, we summarize typical foveation strategies employed by INS subjects.

3.1. Model simulations for Pfs and PPfs

We performed model simulations of saccadic responses using two different paradigms. Ls was set to 250 ms in our model; we measured Lt for different stimulus-onset times. Firstly, stimuli were presented at variable times within the same nystagmus cycle (single-cycle paradigm) and secondly, we presented the stimuli to several different nystagmus cycles, also at variable times within each cycle (multiple-cycle paradigm). The single-cycle paradigm was an over-simplified version of the multiple-cycle paradigm; it was used to clearly show the trend in the data. The multiple-cycle paradigm was more realistic and simulated what the INS subjects experienced. Fig. 3(a) shows the results of Pfs simulations in the single-cycle paradigm (fitted with two-point moving average) and 3(b) shows results from the multiple-cycle paradigm (fitted with second-order polynomial). Figs. 3(c and d) show PPfs simulations in these same two paradigms. Fig. 3(e and f) are model outputs of eye positions when the stimuli jump in different parts of the cycle. Note that for the rightward saccade in (f), the system "misses a cycle", which results in the elongation of target acquisition time (compare 510 ms in (e) to 620 ms in (f)). The single-cycle and multiple-cycle curves had the same trend, although the latter had more variation. These model outputs predict that: (1) for both Pfs and PPfs waveforms, the latency will be larger when target jumps at the beginning or end of the cycle (near the foveating saccade); (2) for the PPfs waveform, the latency will also be larger when target jumps near the middle of the cycle (near the braking saccade). These model predictions will be reinforced in the following sections.

3.2. Large target steps

Fig. 4 shows a typical set of Lt data, from Subject 1 who had Pfs waveforms. Except for Tc%, data points were scattered, and little ($R^2 = 0.0479$) or no trend could be found. Attempts to fit linear or polynomial curves to the other data resulted in either a low R^2 value (<0.1), or a low slope (<0.001). Note that, as the model predicted (Fig. 3(a and b)), Lt tends to be longer towards the beginning and end of the cycle (Fig. 4, Lt vs. Tc%), which is where the foveating saccade occurs.

Fig. 5 shows the results for each waveform type. Note that for all waveforms, Lt tends to be larger if the target step occurs near the embedded foveating saccades. In the case of the PPfs waveform, the system is also prone to error near the braking saccade in the middle of the INS cycle, making Lt larger. Note the similarities between the multiple-cycle model output (Fig. 3(b and d)) and the human data (Fig. 5(a and b)). In the case of the PC waveform, the curve appears to differ because a braking saccade occurs in the middle of the cycle (defining the beginning of a nystagmus cycle as target foveation) and there is no foveating saccade per se. Transforming the reference starting time to the end of the braking saccade results in a curve that resembles



Fig. 3. Model simulations in multiple-cycle and single-cycle paradigms, both Pfs and PPfs waveforms. (e and f) Show model response difference with respect to the target timing.

the others, as shown in Fig. 5(a,c,d, and f). Subject 3 had a time-varying component in his INS (APAN). We noted the amplitude with each data point on his curve, which is an indication of the time variation in his INS. No influence of the APAN time variation on Lt was found (Fig. 5(d)). For some subjects, Lt vs. Tc showed trends with higher R^2 values than Subject 1 in Fig. 4(a).

Examination of the data (for all waveforms) revealed that none of the factors seemed to influence Ls. Attempts to fit linear or polynomial curves to any of the data sets resulted in either a low R^2 value (<0.01), or a low slope (<0.001). There was no evidence of influence (even Tc%), nor did the APAN subject show any time variance. Since it was not influenced markedly by any of the factors we examined, we averaged Ls for each category, as shown in Fig. 6. For each category, the averaged value for the initial reflexive saccade fell on the higher end of the normal Ls range of 200–250 ms (indicated by the dashed zone). Idiosyncratic variations among the subjects occurred. Note that waveforms Pfs and PPfs share similar averaged values and variation, since the data came from the same subject (Subject 1), but for different waveforms.

3.3. Small target steps

INS subjects used additional foveating strategies for smaller steps (5° steps in our recordings). There were often no reflexive saccades associated (no Ls data were available). Details of these foveating strategies are discussed below. Fig. 7 is a typical set of Lt data illustrating responses under this circumstance. All subjects exhibited the same trend as for the large target-step data, i.e., Tc% was the most influential factor. However, occasionally other factors seemed to have an influence (e.g., Subject 1, Pfs, initial orbital position). The values of Lt were typically smaller than those in the large target-step case. Also, we did not find the direction



Fig. 4. A typical set of Lt data (Subject 1, Pfs waveform), in response to large target steps. In this and the following figures, Po, initial orbital position; e_i , final retinal error; e_i , initial retinal error.

of target jump vs. foveating saccade influenced Lt or Ls, in either large or small target jumps.

3.4. Foveating strategies

3.4.1. Small target steps

INS subjects vary the fast and slow phases of their nystagmus waveform to achieve target foveation. Fig. 8(a and b) shows subjects' responses to a 5° leftward target jump. In (a), after a programmed fast phase, another fast phase with a greater amplitude acquired the target at \sim 300 ms (at arrow). The nystagmus waveform was affected, interfering with the ability to maintain target foveation. In (b) a different strategy was used. After a small saccade, the subject "rode" the slow phase to the target; the eye reversed direction with no associated saccades. The target was acquired \sim 1 s after the target jump (at arrow). Fig. 8(c) shows *anticipation* of a 5° rightward target jump. No reflexive saccades were made; instead, the OMS varied the slow-phase amplitude from cycle to cycle and the eye gradually migrated to the new target position (at arrow); there is no Lt per se. In this and the following section, Figs. 8 and 9 are accompanied by videos showing two schematic eyeballs driven by the fixating eye's position data (right eye (cyan) and left eye (yellow)).

3.4.2. Large target steps

Responses to large target steps showed greater variation. The response in Fig. 2 was the most common. The response to a 15° rightward target jump occurred after a braking saccade. The foveating saccade was already programmed and was followed by a large reflexive saccade. The eye went past the target and turned around, followed by a foveating saccade that had a larger peak velocity than those after target acquisition, as shown in the velocity trace. Steady target foveation did not occur until ~900 ms after the target jump.



Fig. 5. Lt vs. Tc% curve for each waveform type, in response to large target steps. In this and the following figures: J, Jerk; APAN, Asymmetric, (a)Periodic Alternating Nystagmus. The subject with a J waveform who also had APAN is labeled as J*, the peak-to-peak amplitude (in °) at each data point is noted.

Fig. 9(a) shows a response to a 15° rightward target jump occurring shortly after a foveating saccade. The next fast phase was already programmed and executed; however, the amplitude of the reflexive saccade was hypometric, possibly due to interference from the internal mechanism that was already programming a fast phase. The second reflexive saccade brought the fixating eye closer to the target, enabling the following foveation period to be within the foveation window. Steady target foveation occurred ~600 ms after the target jump (at arrow).

Response to a 55° rightward target jump is illustrated in Fig. 9(b). The waveform changed from PC to Pfs after the refixation. The first reflexive saccade fell short of the target and was followed by a second saccade (that went slightly past the target), \sim 280 ms from the beginning of the first saccade. Since the saccades brought the eyes close to the target,

good foveation began in the following cycle, ~ 1.1 s after the target jump (at arrow).

Fig. 9(c) shows combined strategies (reflexive saccade plus slow-phase riding) that the subject used in response to a 30° leftward target jump. Because the next fast phase was already programmed, a reflexive saccade was not generated until \sim 400 ms after the target jump. The eyes then continued to ride the slow phase until a fast phase was made. Target acquisition did not occur until the next cycle, fully 1 s after the target jump (at arrow).

In Fig. 9(d), response to a 30° leftward target jump is demonstrated. At 30° , the subject's ability to hold gaze was impaired, and his fast-phase terminations kept drifting back from the target for a few cycles before one refoveated the target. To acquire the new target at 0° , the OMS relied solely on the centripetally accelerating slow phase; *no*



Fig. 6. Average value for each waveform type, with their respective standard deviations. The subject with a J waveform who also had APAN is labeled as J*.

reflexive saccade was made. The target was initially acquired \sim 400 ms after the target jump but it took a few cycles for the subject to reliably maintain and extend foveation (at arrow); Lt was \sim 900 ms.

Fig. 9(e) shows a pulse-step mismatch that occurred after the initial saccade, in response to a 45° rightward target jump. The pulse-step mismatch resulted in a leftward glissade of \sim 5°. Target acquisition occurred with the next fast phase, \sim 700 ms after the target jump (at arrow).

4. Discussion

Our OMS model predicted, and subject data demonstrated, that target timing, vis-à-vis its occurrence within the INS cycle, is one variable that may explain the difficulties experienced by those with INS when attempting to fixate a suddenly displaced target or when searching a visual scene by making voluntary saccades. Small changes



Fig. 7. A typical set of Lt data, in response to small target steps (Subject 3). The subject had a J waveform (with APAN); the peak-to-peak amplitude (in °) at each data point is noted.



Fig. 8. Foveating strategies employed by INS subjects in response to small target steps. Subject 2 (a), Subject 1 (b), and Subject 4 (c).

in target timing can result in large increases in target acquisition time for the same sized target displacements. Saccades disrupt the OMS' ability to accurately calculate saccade amplitude and refoveate; the degree of this disruption can be idiosyncratic.

We used our OMS model to simulate the behavioral responses of INS individuals. As shown in Section 3, the model outputs accurately predict/simulate human responses. This behavior was not built in; it emerged from the interactions among the required functional blocks in the total OMS model. The fact that this emergent property, along with many others published previously (Jacobs & Dell'Osso, 2004), is consistent with recorded human data, provided support for the basic ocular motor mechanisms and their interconnections embedded in the model. For the first time, we are using the model as a tool to make behavioral predictions and explore underlying ocular motor mechanisms. In this study, the model simulations were reinforced by the subsequent patient data, demonstrating its value in predicting behavior.

Further studies using this model, will allow exploration of which functioning block/blocks in the OMS contribute to the "missing" of a cycle, or the impaired ability to fixate. We will also use it to study the dynamic properties of INS subjects in response to other stimuli, e.g., ramp stimuli. Based on the finding of increased Ls in INS patients, we can set the latency of the initial reflexive saccade to be an idiosyncratic value greater than 250 ms (reflecting an individual with INS), instead of the 250 ms value in the current model that was based on data from normals.

The curves in Fig. 5 show a common characteristic: Lt is larger when the target jump occurs closer to a fast phase/ saccade contained in the INS waveform. Any existing timevarying components of the waveforms (e.g., in APAN) do not disturb this trend. In most INS waveforms (except for PC), a foveating saccade occurs right before foveation begins. Therefore, the fast phase at the beginning (and end) of the cycle influences the acquisition of a new target. The lengthening of target acquisition time for target steps occurring at these particular intervals in each waveform, suggests that new-target foveation capability is disrupted by the intrinsic saccades. For the PC waveform, whose saccade occurs in the middle of the cycle, this trend is also preserved. Although the data for each waveform came from different subjects (except for Pfs and PPfs which came from Subject 1), they all share the same dynamic characteristic. Tc% showed a greater influence on Lt than Tc in most subjects, probably due to variation in the absolute length of each nystagmus cycle.

Interestingly, in the PPfs waveform, we also observed an increase in Lt in the middle of the cycle, where the stereotyped, small, braking saccade occurred (Dell'Osso & Daroff, 1976). This demonstrated that it is not only *foveating* saccades that lengthen the target acquisition time, but also saccades in general. This disruption might come from the saccadic refractory period or the interaction between the saccadic and fixation subsystems, impairing the system's ability to accurately calculate the size of the next foveating saccade required to refixate the target. The OMS model accurately makes these calculations during



Fig. 9. Foveating strategies employed by INS subjects in response to large target steps. Subject 3 (a and d), Subject 1 (b), Subject 2 (c), and Subject 2 (e).

fixation (both normal and with INS or other types of nystagmus) but they are impaired by the interaction between intrinsic and reflexive saccades. Note that, some INS subjects may have varying (both intra- and inter-subject) gaze-holding and fixating capabilities. Based on their baseline level, these capabilities are modulated by the timing of the target jump. This is in accord with anecdotal reports from an individual with INS that the time needed to catch up with a fast moving object (e.g., when aiming at a flushing bird) varies from one instance to another; sometimes acquisition takes more than a second while, at other times it is normal; needless to say, the former results in a miss while the latter, a hit.

Although the initial reflexive saccade is not necessarily the one that foveates the target, Ls is the foundation for prompt target acquisition. Our data in Fig. 6 show that, on average, INS subjects also take a longer time to generate the first refixation saccade. The highest Ls in our study was 380 ms, from Subject 4 (PC waveform); that is 130 ms longer than the upper bound of normal saccadic latency (250 ms). This prolonged Ls adds to Lt, the time it takes to foveate the target after its movement. However, this amount is insufficient to cause the "slow-to-see" impression.

The main refixation strategies employed by INS subjects are slow- or fast-phase changes and refixation saccades, or combinations of them. Note that, the pre-programmed fast phase seems to be modified in Fig. 9(a) in an attempt to foveate the target, with the amplitude inaccurately calculated. In Fig. 8(a), however, the alteration of the fast-phase amplitude was good enough for acquiring the target, in this case a 5° target jump. These strategies are tools that individuals with INS can make use of (probably acquired as their OMS adapted to their INS oscillation) in order to achieve foveation in an effective fashion. It would be interesting to examine the presence and development of this adaptation in infants/children with INS, whose waveform foveation quality is also being refined.

We also found that for the same subject, Lt values for large target steps are generally larger than those for small target steps, mimicking normal subjects, who also take a longer amount of time to acquire large target steps. However, within each stimulus category (large/small steps), saccade size does not determine the value of Lt. This implies that the relationship between target amplitude and Lt could be a step function, although we think not. As shown in Fig. 8(a and b), when small target steps (5°) stimuli are presented, subjects often opt to not use reflexive saccades, but let their nystagmus slow phase take over, e.g., modifying their slow and fast phases to achieve foveation at the new target position. This strategy is totally different from the case in large target steps, in which subjects rely more on reflexive saccades. Therefore the influence of intrinsic saccades is more obvious in large target steps.

Foveating and braking saccades are adaptations of the OMS in the presence of the underlying pendular oscillation. Not only do the saccades bring the eye position back to the target allowing refoveation, but also, the foveation periods following foveating saccades enable individuals with INS to discern details in the target, i.e., foveation periods determine "how well they see". However, based on findings in this study, these intrinsic saccades seem to have an adverse effect on "how quickly they see". Throughout its development, the OMS may have made a trade-off between these two important aspects of visual function. In the case of INS, the former may have been chosen over the latter; alternatively, the observed data may be the best the OMS can do in the presence of an ongoing nystagmus containing intrinsic saccades. Target acquisition time emerges as an additional, dynamic factor determining visual function in individuals with INS. Along with visual acuity at lateral gaze angles (Wang, Dell'Osso, Jacobs, Burnstine, & Tomsak, 2006), it should be part of both their initial clinical evaluation and the determination of therapeutic effectiveness.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.vis-res.2007.01.008.

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