Oscillopsia and the Influence of Stress and Motivation in Fusion Maldevelopment Nystagmus Syndrome

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PURPOSE. We examined factors influencing perceptual stability in observers with fusion maldevelopment nystagmus syndrome (FMNS). In addition, we also investigated the effect of visual demand, task-related physiologic stress, and motivation on the nystagmus waveform.

METHODS. Perception of oscillopsia during daily activities was assessed via a questionnaire. Perception of oscillopsia in the laboratory was assessed using central and peripheral (10°) light emitting diodes (LEDs) in front of a background display of random, fixed-contrast shapes. Task-induced stress was achieved via a time restricted acuity task with or without concurrent mental arithmetic challenge, and motivation varied using a reward-penalty paradigm. The experiments have been previously described elsewhere.

RESULTS. Six out of nine subjects reported experiencing oscillopsia in certain daily activities. In the laboratory, the percentages of trials with perceptions of motion of the LED and background were as follows: neither, 60% to 70%; background only, 20% to 50%; both, 5% to 15%, and LED only, 5% to 15%. Over all trials, six of nine experienced oscillopsia for both the low- and high-contrast image respectively (i.e., three subjects never experienced oscillopsia). The background was frequently seen moving for both images regardless of contrast and/or condition. Trials with and without oscillopsia did not differ when comparing foveation. In the second experiment, task-related physiologic stress and motivation were reflected in an increase in heart rate; nystagmus waveform intensity increased and foveation decreased. The magnitude of changes in heart rate was uncorrelated with changes in waveform parameters for all experiments, however.

CONCLUSIONS. Preliminary results suggest that the FMNS group does perceive spatially inhomogeneous oscillopsia, similar to infantile nystagmus syndrome (INS), in certain visual environments. In investigating the effect of stress and motivation on FMNS, a new, if tentative, finding suggests that task-induced physiologic stress and/or motivation may have a negative impact on the nystagmus waveform. In the current study, we investigated two aspects of FMNS. Firstly, we investigated the relationship between the nature of the visual stimulus and occurrence of oscillopsia in daily activities via a questionnaire, and also the relationship between waveform parameters, and the onset of oscillopsia in the laboratory. Our study was designed to assess the consistency of perceptual stability reports by repeatedly exposing subjects to the same stimulus multiple times. Secondly, we also assessed the influence of task-induced physiologic stress and motivation on the FMNS waveform.

METHODS

Our study conformed to the declaration of Helsinki and was approved by the Human Research Ethics Committee of the University of Melbourne, and all subjects gave written informed consent before participating. Eye movement recordings were performed in nine FMNS subjects (three males and six females, mean age 25.8 ± 15.9). Mean distance visual acuity (logMAR) was 0.30 ± 0.25 and near 0.31 ± 0.27. The diagnosis of FMNS was primarily made by the referring ophthalmologist and later verified on the basis of clinical examination and eye movement recording analysis performed by the investigators. One subject had albinism, with no evidence of INS on waveform recordings; the others had no sensory abnormalities. All subjects had either an exotropia (n = 4) or esotropia (n = 5). The waveforms exhibited were jerk (n = 9). Baseline (i.e., subjects fixating an light emitting diode [LED] target in primary gaze) means and SDs of the waveform parameters for all subjects were: foveation periods (percent
Table 2. Foveation, Amplitude, Frequency, and Intensity of Trials with and without Oscillopsia for Both the Low- and High-Contrast Images

<table>
<thead>
<tr>
<th>Waveform Parameters</th>
<th>Oscillopsia, Low-Contrast Image</th>
<th>Oscillopsia, High-Contrast Image</th>
<th>No Oscillopsia, Low-Contrast Image</th>
<th>No Oscillopsia, High-Contrast Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foveation, percent</td>
<td>45.25 ± 30.43</td>
<td>28.44 ± 19.75</td>
<td>45.61 ± 30.94</td>
<td>35.58 ± 23.44</td>
</tr>
<tr>
<td>Amplitude, deg</td>
<td>2.14 ± 1.59</td>
<td>2.70 ± 2.23</td>
<td>2.42 ± 1.52</td>
<td>2.89 ± 2.00</td>
</tr>
<tr>
<td>Frequency, Hz</td>
<td>3.65 ± 1.07</td>
<td>3.96 ± 1.43</td>
<td>5.52 ± 1.18</td>
<td>4.03 ± 1.32</td>
</tr>
<tr>
<td>Intensity, deg × Hz</td>
<td>8.85 ± 7.05</td>
<td>10.84 ± 8.56</td>
<td>8.96 ± 6.61</td>
<td>12.34 ± 9.12</td>
</tr>
</tbody>
</table>

Only changes in frequency were significant in the low contrast setting (shown in bold), as assessed by using paired t-tests.
Of the trials when oscillopsia was perceived, three subjects consistently reported that the same part of the stimulus moved (i.e., LED, background, or both) regardless of the condition and/or contrast presented. The responses of the remaining subjects varied depending on the condition. Age did not correlate with oscillopsia at either contrast level (Spearman rank correlation: low contrast, $r = -0.11; P = 0.78$; high contrast, $r = 0.24; P = 0.52$). No change in waveform type was observed when compared with baseline.

**Stress and Motivation**

We compared the waveform parameters and heart rate in the baseline, unrestricted viewing, and restricted viewing tasks using a one-way ANOVA with repeated measures. Unlike visual acuity, significant alterations were seen in all waveform parameters (Fig. 3). Heart rate was also significantly increased (Fig. 3), indicating our restricted viewing condition evoked a significant amount of physiologic stress.

For the reward manipulation task, paired $t$-tests illustrated significant changes only in heart rate and foveation when compared with baseline (Fig. 4). When examining the heart rates and waveform parameters during minimum (largest optotype read) and maximum (smallest optotype read) visual demand, significant differences were found using paired $t$-tests only for foveation in the unrestricted viewing and for heart rate in the restricted viewing tasks (Table 3). No significant differences were found for any other parameters in the three tasks.

When comparing the restricted viewing and reward manipulation tasks, heart rate increased significantly more (paired $t$-test: $t = 4.46, P = 0.003$) and foveation decreased significantly more ($t = 4.02, P = 0.01$) in the restricted viewing task. Table 4 shows the effects of increased visual demand on FMNS parameters (i.e., decreased, that is, deteriorated, foveation) during the unrestricted viewing and of increased heart rate during the restricted viewing tasks. Considerable intersubject variability can be seen.

A Pearson correlation was performed to investigate the relationship between changes (restricted viewing minus unrestricted viewing) in heart rate and changes in waveform parameters between the unrestricted and restricted viewing tasks. The correlation was done separately for each subject. Changes in heart rate were uncorrelated with changes in waveform parameters (amplitude, $r^2 = 0.25, P = 0.23$; frequency, $r^2 = 0.05, P = 0.6$; intensity, $r^2 = 0.18, P = 0.5$; and foveation, $r^2 = 0.15, P = 0.3$).
assessed by using paired t-tests. Results for the paired t-test were as follows: heart rate: $t = 2.84, P = 0.02$, amplitude: $t = 0.59, P = 0.58$, frequency: $t = 0.5, P = 0.77$; intensity: $t = 1.3, P = 0.22$; foveation: $t = 2.57, P = 0.04$; and visual acuity: $t = 0.82, P = 0.44$. Error bars = standard error of mean.

When evaluating task performance (change from baseline heart rate versus number of correct responses in the mental arithmetic task or the number of skipped optotypes), Pearson correlation was significant for the mental arithmetic ($r^2 = 0.47, P = 0.04$) in the restricted viewing task, but not for the skipped optotypes ($r^2 = 0.013, P = 0.77$). No significant correlation was found for the reward manipulation task (skipped optotypes, $r^2 = 0, P = 1.0$). No change in waveform type was observed when compared with baseline. The subjects were not asked explicitly about the experience of oscillopsia, but no one reported any movement during all experimental components in experiment (2).

**Table 3.** Amplitude, Frequency, Intensity, Foveation, and Heart Rate during Minimum and Maximum Visual Demand for All Three Tasks

<table>
<thead>
<tr>
<th>Task</th>
<th>Visual</th>
<th>Amplitude, deg</th>
<th>Frequency, Hz</th>
<th>Intensity, deg × Hz</th>
<th>Foveation, Percent ± 2° and ± 4 deg/s</th>
<th>Heart Rate, beats/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrestricted</td>
<td>Min</td>
<td>1.8 ± 0.7</td>
<td>2.9 ± 1.4</td>
<td>5.9 ± 5.2</td>
<td>55.1 ± 52.0</td>
<td>82.8 ± 13.5</td>
</tr>
<tr>
<td>viewing</td>
<td>Max</td>
<td>1.8 ± 1.0</td>
<td>3.2 ± 1.5</td>
<td>5.5 ± 5.4</td>
<td>41.4 ± 52.0</td>
<td>85.7 ± 13.8</td>
</tr>
<tr>
<td>Restricted</td>
<td>Min</td>
<td>5.1 ± 1.8</td>
<td>2.9 ± 1.7</td>
<td>9.0 ± 6.9</td>
<td>46.9 ± 51.9</td>
<td>80.5 ± 15.9</td>
</tr>
<tr>
<td>viewing</td>
<td>Max</td>
<td>2.5 ± 1.6</td>
<td>2.8 ± 1.1</td>
<td>7.3 ± 5.2</td>
<td>45.0 ± 27.1</td>
<td>88.9 ± 11.0</td>
</tr>
<tr>
<td>Reward</td>
<td>Min</td>
<td>2.6 ± 1.8</td>
<td>3.4 ± 1.5</td>
<td>10.4 ± 10.1</td>
<td>55.1 ± 50.5</td>
<td>85.4 ± 12.7</td>
</tr>
<tr>
<td>manipulation</td>
<td>Max</td>
<td>2.0 ± 1.6</td>
<td>3.2 ± 1.8</td>
<td>7.2 ± 6.8</td>
<td>50.6 ± 25.9</td>
<td>85.2 ± 10.6</td>
</tr>
</tbody>
</table>

Only changes in foveation during the unrestricted viewing and heart rate in the restricted viewing tasks (shown in bold) were significant, as assessed by using paired t-tests.

**DISCUSSION**

**Oscillopsia during Daily Activities**

Six out of nine subjects (67%) perceived motion in their daily life, with the majority reporting this to occur under dim lighting; however, oscillopsia was occasional and usually lasted only seconds. Four subjects reported the viewed background moved. We have previously reported that 89% of subjects with INS perceived either uniform or nonuniform oscillopsia either under dim lighting or unrelated to any particular viewing condition. This proportion is not significantly different from that found in the current study for FMNS (Fisher’s Exact test, $P = 0.30$). Fatigue was commonly associated with oscillopsia in FMNS, while stress was more often identified as an additional factor in INS.8 Looking away from the fixation point or turning/tilting the head could prevent or minimize oscillopsia in a small number of INS subjects,8 and a similar proportion of FMNS subjects in the current study could minimize oscillopsia by turning away. Since FMNS generally obeys Alexander’s law,12 one might expect a gaze shift, which reduced nystagmus intensity to work similarly to adoption of a null position in INS.

The experience of oscillopsia in FMNS subjects was uncorrelated with age, although the limited range and the number of subjects in this study would make finding such a correlation difficult.

**Oscillopsia under Laboratory Conditions**

In the current study, neither the LED nor the background was reported to move (i.e., oscillopsia was absent) in the majority of the trials. In trials where motion was reported, spatially inhomogeneous oscillopsia was observed, with the background often seen moving. The LED was rarely seen as oscillating. Two subjects consistently reported the same stimulus elements moved regardless of contrast and condition. In their questionnaire results, they frequently perceived oscillopsia.

No changes in the waveform parameters were observed when oscillopsia occurred in the high-contrast condition. However, when viewing the low-contrast image, nystagmus frequency increased when oscillopsia occurred. In FMNS, there are no explicit foveation periods; slow phases are either decreasing velocity exponentials or linear. Most often, the fast phases place the image of the point of regard on the fovea, immediately followed by the highest velocity portion of the slow phase. At times, however, the fast phase may carry the fovea past the target; as the slow phase velocity decays, the target image drifts onto the fovea.14 There is no part of the waveform where the eye is stationary for a brief period while...
Table 4. Mean Foveation during the Unrestricted Viewing and Heart Rates during the Restricted Viewing Tasks at Times of Minimum and Maximum Visual Demand

<table>
<thead>
<tr>
<th>Subject</th>
<th>Foveation, Percent ± 2° and ≤ 4 deg/s – Unrestricted Viewing</th>
<th>Heart Rate, beats/min – Restricted Viewing</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Min 74.50 Max 51.00 SD 33.11</td>
<td>Min 95.78 Max 96.39 SD 11.22</td>
</tr>
<tr>
<td>C</td>
<td>Min 17.32 Max 16.50 SD 6.16</td>
<td>Min 95.14 Max 94.13 SD 1.01</td>
</tr>
<tr>
<td>D</td>
<td>Min 83.34 Max 73.00 SD 3.18</td>
<td>Min 83.57 Max 94.76 SD 11.18</td>
</tr>
<tr>
<td>E</td>
<td>Min 98.00 Max 97.80 SD 0.02</td>
<td>Min 95.44 Max 104.67 SD 11.22</td>
</tr>
<tr>
<td>F</td>
<td>Min 48.30 Max 33.00 SD 5.11</td>
<td>Min 64.56 Max 70.63 SD 5.11</td>
</tr>
<tr>
<td>G</td>
<td>Min 60.13 Max 45.00 SD 5.11</td>
<td>Min 66.67 Max 79.41 SD 5.11</td>
</tr>
<tr>
<td>H</td>
<td>Min 6.85 Max 6.40 SD 0.01</td>
<td>Min 81.18 Max 90.00 SD 11.22</td>
</tr>
<tr>
<td>I</td>
<td>Min 56.42 Max 10.10 SD 5.11</td>
<td>Min 63.85 Max 81.30 SD 11.22</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>55.11 ± 51.98 Max 41.55 ± 52.00</td>
<td>Mean 80.52 ± 13.88 Max 88.91 ± 11.01</td>
</tr>
</tbody>
</table>

Group means and SD are also shown for each measure.

the target image falls onto the fovea, as is the case in many INS waveforms. Hence, foveation in the present context is that percentage of the slow phase, which meets specific position and velocity criteria.

It seems that good foveation did not prevent the breakdown of perceptual stability at either contrast level. It appears there is not a simple relationship between perceptual stability and foveation, and so the role of waveform parameters in influencing FMNS subjects’ perceptions requires further investigations. Some relationship must exist, however, as it is known that occlusion therapy for amblyopia in an FMNS patient can provoke oscillopsia as it elicits a greater nystagmus12, something analogous occurs in congenital periodic (or aperiodic) alternating nystagmus, where oscillopsia is common during the most intense portions of the cycle.17

Influence of Stress and Motivation

This study is the first to provide evidence for the negative impact of stress and/or motivation upon the characteristics of the FMNS waveform. Task-induced physiologic stress, as evident by an increase in heart rate when performing the restricted viewing task, led to an increase in the intensity of the nystagmus waveform, and decreased foveation in FMNS. This suggests that FMNS increases with psychologic factors (such as stress and anxiety) that affect visual performance, similar to INS.15 It is curious that such internal influences have not been previously commented upon for FMNS, unlike INS. Perhaps most FMNS patients have sufficiently minimal nystagmus with binocular viewing that a statistically significant deterioration of foveation still does not noticeably compromise acuity to the extent that it does in INS; that is, there may be a greater “safety margin.” We do not fully understand the mechanisms that underlie foveals and INS, although this influence of internal state may reflect the role of inputs from stress and motivation-modulated brain regions on a common component of the smooth eye movement pathway. Such brain regions may include the amygdala and the anterior cingulate cortex, which are known to influence emotion and affective behavior.18

Various brain regions have also been implicated in motivation. The brain–reward circuit involves the mesocorticolimbic dopaminergic network that regulates motivation, spanning the frontal cortex, amygdala, mesencephalon, nucleus accumbens, striatum, thalamus, and cerebellum.19–21

Maximum visual demand decreased foveation in the unrestricted viewing and increased heart rate in the restricted viewing tasks. It is rather surprising that foveation decreased at maximum visual demand during the unrestricted viewing and not in the restricted viewing task, since the latter is more stressful (evident by elevated heart rate) than the former. Since foveation was lower in the restricted viewing task even for minimal visual demand, it may be that there was less scope for further change in this task.

Even though foveation decreased significantly during the visual tasks, visual acuity remained relatively unchanged. As mentioned previously in our study on INS,13 our methods were not primarily designed to measure visual acuity, but rather to produce a stressful visual environment by briefly presenting optotypes. This unconventional visual acuity task might account for the increased variability (and hence, nonsignificant) in visual acuity among the visual tasks. The infrared limbus eye tracker also precluded the use of patients’ spectacles for refractive errors correction, thus, further limiting our ability to evaluate best-corrected visual acuity.

In the reward manipulation paradigm, foveation decreased significantly when compared with baseline. Concurrently, heart rate increased, but not as much as it did in the restricted viewing task. This reflects a greater motivational role compared with stress in the current task.

Although heart rate, nystagmus amplitude, and foveation were significantly associated in our ANOVA, we failed to find any significant correlation between the magnitude of these changes when subjects performed different visual tasks, possibly due to reasons as mentioned previously regarding INS.13 It is possible that although both observed changes covary with stress, they do not covary with each other. It is also possible that the variability of the data in our study results in insufficient power to illustrate the correlation, or the nature of how both changes vary cannot be demonstrated by correlation, or both. The underlying functional relationship between stress, changes in heart rate, and changes in nystagmus parameters is unknown. Furthermore, recording heart rate over a short period of time is a coarse measure. Being an episodic rather than a continuous measure, heart rate is less robust and less sensitive than other measures such as galvanic skin response or pupil size to detect subtle changes when monitoring the psychologic state of the subjects in this study. Again, the use of additional, more continuous measures such as galvanic skin response or pupil diameter might better quantify the psychologic state of an individual compared with heart rate. Monitoring pupil diameter in oscillating eyes, of course, presents its own difficulties.

Conclusions

Limited research on perception in FMNS exists. In the current study, preliminary results suggest that people with FMNS do
References


Appendix: Responses to the Oscillopsia Questionnaire

Do you ever see things moving, which are not supposed to move? □ Yes □ No

FMNS – Yes: 6/9; No: 3/9

If yes, can you describe by giving an example(s)?

FMNS – LEDs, backlights of cars, clock radio display, taillights (2)

Light on the computer screen

LEDs in the experiment

Shapes on the computer

Lights

Writing on the whiteboard at school

When was your first experience?

FMNS – years ago: 4/6; today: 2/6

How often do you encounter it? □ Rarely □ Sometimes

FMNS – Frequently: 3/6; Sometimes: 2/6; Frequently: 1/6

How long does it usually last? □ Seconds □ Minutes

FMNS – Seconds: 6/6

How do you think it has affected your life? □ No □ Minimal

FMNS – Moderate □ Major

FMNS – No: 6/6

Were there any other symptoms when you see things moving (e.g., blurred vision, double vision)?

FMNS – No: 4/6; Blurred vision: 1/6; Blur & Double vision: 1/6

What is the speed of the movement? □ Slow □ Moderate

FMNS – Slow: 1/6; Moderate: 1/6; Fast: 4/6

What is the direction of the movement? □ Horizontal

FMNS – Vertical □ Both

FMNS – Horizontal: 1/6; Vertical: 1/6; Both: 4/6

Can you try to stop it? If yes, how?

FMNS – No, can’t stop it (3)

When the lights go off

Focusing

Look away

What triggers the movement (e.g., fatigue, illness, etc.)?°

FMNS – Tired (5)

Lights

When the movement occurred, what moved? □ Viewed object □ Background □ Both
Does it occur when looking □ straight ahead □ off to one side or □ both?
FMNS - Straight ahead: 3/6; Both: 3/6
Does it happen in a particular lighting condition? □ Dim □ Bright □ Any condition
FMNS - Dim: 5/6; Any condition: 1/6

Who else in the family has nystagmus? Do they complain of seeing things moving?
FMNS - No one: 6/6
Have you undergone any form to treatment to decrease the movement of things? If so, was it effective?
FMNS
No (6)
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