The influence of visual vertigo and vestibulopathy on oculomotor responses

Oz Zur\textsuperscript{a,}*\textsuperscript{,} Ruth Dickstein\textsuperscript{b}, Elizabeth Dannenbaum\textsuperscript{c}, Eli Carmeli\textsuperscript{d} and Joyce Fung\textsuperscript{c,e}

\textsuperscript{a}Department of Physical Therapy, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel
\textsuperscript{b}Physical Therapy Services, Flieman Geriatric Rehabilitation Hospital, Haifa, Israel
\textsuperscript{c}Feil and Oberfeld Research Centre, Jewish Rehabilitation Hospital, Research Site of the Montreal Center for Interdisciplinary Research in Rehabilitation (CRIR), Laval, QC, Canada
\textsuperscript{d}Physical Therapy Department, Haifa University, Social Welfare and Health Sciences, Haifa, Israel
\textsuperscript{e}School of Physical and Occupational Therapy, McGill University, Montreal, QC, Canada

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Abstract.

\textbf{OBJECTIVE:} Dynamic visual inputs can cause visual vertigo (VV) in patients with vestibulopathy, leading to dizziness and falls. This study investigated the influence of VV on oculomotor responses.

\textbf{METHODS:} In this cross-sectional, single-blind study, with experimental and control groups, 8 individuals with vestibulopathy and VV, 10 with vestibulopathy and no VV, and 10 healthy controls participated. Oculomotor responses were examined with 2-dimensional video-oculography. Participants were exposed to dynamic visual inputs of vertical stripes sweeping across a screen at 20 deg/sec, while seated or in Romberg stance, with and without a fixed target. Responses were quantified by optokinetic nystagmus frequency (OKNf) and gain (OKNg).

\textbf{RESULTS:} Seated with no target, VV participants had higher OKNf than controls (37 ± 9 vs. 24 ± 9 peaks/sec; \(P<0.05\)). In Romberg stance with no target, they had higher OKNf than controls (41 ± 9 vs. 28 ± 10 peaks/sec; \(P<0.05\)). With a target, OKNf was higher in VV participants compared to controls (7 ± 7 vs. 1 ± 2 peaks/sec; \(P<0.05\)). In Romberg with no target, OKNg was higher in the VV group (0.8 ± 0.1) compared to controls (0.6 ± 0.2; \(P=0.024\)). OKNf and OKNg did not differ according to VV status.

\textbf{CONCLUSIONS:} VV participants had increased OKNf and OKNg compared to healthy participants. Visual dependency should be considered in vestibular rehabilitation.

Keywords: Oculomotor, visual vertigo, vestibulopathy

1. Introduction

Patients diagnosed with vestibulopathy have a high incidence of visual vertigo (VV) [2,11]. Patients with VV experience dizziness and often have difficulty moving in shopping malls and busy streets when they are exposed to dynamic visual inputs. VV has been variously termed as ‘supermarket syndrome’ [24], ‘visual vestibular mismatch’ [1], a syndrome ‘generated by incongruence between visual and vestibular signals’ [20–22], and ‘space and motion discomfort’ [10].

The oculomotor system controls eye movements based on dynamic visual inputs. Gaze stability is achieved by optokinetic nystagmus (OKN), which operates together with the smooth pursuit mechanism and the vestibular ocular reflex (VOR) to maintain or replace moving objects on the fovea [6,15]. Patients with VV suffer from hypersensitivity to visual information;...
yet, the relationship between optokinetic nystagmus stimulation (OKNS) and VV in environments with a lot of motion is not well described. The OKN system includes a fast phase that is characterized by saccadic eye movements and a slow phase that indicates pursuit eye movement. These phases help determine OKN frequency and OKN gain, respectively [9,14].

Staring at vertical stripes, as in OKNS, involves movement of a visual image across the retina [14]. OKNS is generally tested under two conditions, ‘stare’ nystagmus and ‘look’ nystagmus as first described by Ter Braak [27] and more recently by Knapp et al. [18]. Stare nystagmus is a passive test in which the subject is asked to gaze at a screen with no instruction to follow the moving stripes. In this condition, the nystagmus usually has a lower gain with smaller amplitude. Whereas look nystagmus is a test in which a subject is asked to follow each moving stripe. Here, the nystagmus usually has a high gain and large OKN amplitude [12,22]. The motion of the visual image across the retina is called retinal slip. Retinal slip is the sliding of an image across the retina, which stimulates OKN, pursuit and saccades [7,15].

Even after vestibular rehabilitation, some patients continue to complain of dizziness in visually demanding environments. This study investigated the difference in eye movements among vestibulopathy participants with and without VV compared to healthy individuals. The goal was to identify whether patients with VV have higher OKNf and OKNg compared to vestibulopathy subjects without VV and healthy controls.

2. Patients and methods

2.1. Participants

Sixty-five potential patients with vestibulopathy, presenting with or without VV, were referred by an otolaryngologist from a vestibular rehabilitation clinic in Laval, Canada. Inclusion criteria were healthy, independent males and females over the age of 18 years, with unilateral vestibular deficits. Exclusion criteria were neurological disorders, acute labyrinthectomy (chemical or surgical); Meniere’s disease; bilateral vestibular pathology; ocular pathologies; and/or significant orthopedic conditions.

2.2. Participant allocation

Of the 65 participants referred to the study, 24 either refused or were ineligible to participate; therefore, 41 participants were recruited. Five of the 41 participants did not meet the inclusion criteria, and five participants did not meet the exclusion criteria, leaving 31 participants eligible to participate. Two participants from the VV group and one participant from the Vest group dropped out before completing the tests. Thus, the results reported pertain only to the 28 of 31 participants who completed all test procedures.

The study was approved by the ethics committee of the Montreal Centre for Interdisciplinary Research in Rehabilitation (CRIR). All eligible consenting patients provided written informed consent.

2.3. Outcome measures

The Dizziness Questionnaire (DQ) [21] was administered to differentiate between vestibulopathy participants with and without VV. The DQ included nine questions. Subjects with 2 or more positive answers were assigned to the VV group. Those with a score of 0 were assigned to the vestibulopathy without VV (VEST) group or the healthy control group (CONT). VV and Vest were diagnosed according to ICD-9-CM, Vol. 1, code 386.12 criteria as having unilateral vestibulopathy caused due to idiopathic inflammation of the vestibular nerve, characterized clinically by the acute or subacute onset of vertigo, nausea, and imbalance, with no symptoms of hearing loss or tinnitus [17].

Two-dimensional video-oculography (2D-VOG), version 4 (SensoMotoric Instruments GmbH, Teltow, Germany) was used to test oculomotor responses. Participants were exposed to dynamic visual inputs consisting of vertical stripes sweeping across a screen (towards the affected ear or to the opposite ear) at a speed of 20 deg/sec. Eye movements were collected every 17 ms during the 23 seconds of each OKN stimulation test. The data analysis included 15 seconds of the test, from 5 seconds through 19 seconds. Each participant was assessed in a quiet room and all tests were performed in a single day. Three tests of OKNS were done randomly in sitting or Romberg position (standing straight with feet together), under five consecutive conditions (described below). Each test was repeated three times. However, only the last repetition was included in the data analysis because two participants from the VV group and one participant from the Vest group dropped out before completing the third repetition. Participants gazed forward at a screen (3 m wide \( \times \) 2 m high) from a distance of 3 m. The projector was aimed slightly above eye level.

For Test 1, participants gazed forward at the screen with the vertical stripes motionless and with the target,
a red Ping-Pong ball, approximately 3 cm in diameter, fixed in the middle of the screen at eye level. The stable stripes and target constituted the baseline test, which is Condition 1. For Test 2, participants gazed forward at a screen with no target, with optokinetic stimulation, vertical stripes move to the left (Condition 2) and after a short rest (approximately 90 sec) to the right (Condition 3). Test 3 consisted of gazing forward at a screen with optokinetic stimulation while the target (a red Ping-Pong ball) was fixed in the middle of the screen and the vertical stripes moved to the left (Condition 4) and after short rest, to the right (Condition 5). Participants were given about 90 seconds to relax from the visual stimulus.

Oculomotor responses were quantified as optokinetic nystagmus frequency (OKNf), where OKNf is the frequency (f) of eye movements, measured in peaks/second. It is measured by taking the inverse value of the combined times of the slow component duration (sd) and the fast component duration (fd) of eye movements, according to the equation

\[ f = \frac{1}{sd + fd} \]

The optokinetic nystagmus gain (OKNg) was calculated as a ratio obtained by dividing the eye velocity by the velocity of the stimulus (here, the moving stripes) according to the following equation

\[ \text{OKNg} = \frac{\text{SPVeye}}{\text{SPVstripes}} \]

2.4. Study design

This was a cross-sectional, single blind study, with experimental and control groups.

Participants were classified into 3 groups: Visual vertigo group (VV) (n = 8; 5 females and 3 males); vestibulopathy group without VV (VEST) (n = 10; 2 females and 8 males); and healthy control group (CONT) (n = 10; 4 females and 6 males).

2.5. Data analysis

Descriptive statistics for continuous variables included mean, standard deviation, median, range (minimum and maximum), and frequencies for nominal data. As the data were not normally distributed (Shapiro-Wilks test), differences among groups were analyzed using nonparametric statistics.

Nonparametric Poisson regression was used in two levels: measurement and participant. A multilevel, mixed-effects Poisson regression and mixed-effects restricted maximum likelihood (REML) regression were used to study group differences while considering the effect of testing positions (seated and Romberg stance). The Kruskal-Wallis test was used when comparing the OKNf and OKNg between the study groups. Bonferroni multiple comparisons were used to compare between each pair of groups. The Wilcoxon rank test was used for paired comparisons of continuous data. A P-value of \( \leq 0.05 \) was considered statistically significant.

G*Power software [8] was used for sample size calculation. STATA/IC 11.1 software (StataCorp, College Station, TX, USA) and SPSS-17 (Chicago, IL, USA) were used for statistical analysis.

3. Results

The 28 study participants ranged in age from 35 to 82 years (mean ± 59.5±12.1, median 62 years). There were no significant differences in age or sex among the groups. There were no significant differences between OKNf and OKNg measured in the different repetitions.

3.1. Responses to optokinetic nystagmus (OKN) stimulation

Figure 1 shows OKNf for one healthy participant and one participant with VV; neither participant had nystagmus. The OKNf is presented for the three tests (that included the five conditions described above: 1) Baseline with a fixed target and no OKNS; 2) Right and left OKNS with no target; and 3) Right and left OKNS with a fixed target.

3.2. Effects of optokinetic stimulation

Results are presented by two outcome measurements: OKNf followed by OKNg. Each outcome is presented according to group and posture (sitting or Romberg stance).

3.3. Optokinetic nystagmus frequency (OKNf): Between groups

For Test 1, there were no significant differences in the baseline tests between groups (Table 1). For Test 2, OKNf was significantly higher in participants with VV compared to healthy controls (38.8 ± 8.3 [median=38] vs. 25.9±7.2 [median = 23.9] peaks/sec, respectively, \( P < 0.05 \)) (Fig. 2). There was no significant difference in OKNf between the VV group (38.8 ± 8.3 [median = 38] peaks/sec) and the VEST group (32.2 ± 8.8 [median = 34.3] peaks/sec) (\( P = 0.09 \)) (Fig. 2). OKNf was measured in beats per 15 seconds; y-axis. In Figs 2 and
Table 1
Optokinetic nystagmus (OKN) between sitting and Romberg stance in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Test</th>
<th>Mean ± SD</th>
<th>(Min–Max)</th>
<th>Median</th>
<th>Wilcoxon Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VV</td>
<td>Test 2 Sitting</td>
<td>0.77 ± 0.12</td>
<td>(0.6–1.02)</td>
<td>0.73</td>
<td>−2.100</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.84 ± 0.17</td>
<td>(0.64–1.16)</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VV</td>
<td>Test 3 Sitting</td>
<td>0.07 ± 0.11</td>
<td>(0–0.25)</td>
<td>0.02</td>
<td>−0.405</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.05 ± 0.05</td>
<td>(0–0.15)</td>
<td>0.04</td>
<td></td>
<td>0.686</td>
</tr>
<tr>
<td>Vest</td>
<td>Test 2 Sitting</td>
<td>0.60 ± 0.27</td>
<td>(0.19–0.9)</td>
<td>0.67</td>
<td>−2.803</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.70 ± 0.20</td>
<td>(0.36–0.97)</td>
<td>0.73</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Vest</td>
<td>Test 3 Sitting</td>
<td>0.08 ± 0.10</td>
<td>(0–0.31)</td>
<td>0.04</td>
<td>−1.260</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.09 ± 0.11</td>
<td>(0–0.34)</td>
<td>0.06</td>
<td></td>
<td>0.208</td>
</tr>
<tr>
<td>Cont</td>
<td>Test 2 Sitting</td>
<td>0.59 ± 0.24</td>
<td>(0.19–1.05)</td>
<td>0.59</td>
<td>−1.172</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.55 ± 0.18</td>
<td>(0.22–1.16)</td>
<td>0.68</td>
<td></td>
<td>0.241</td>
</tr>
<tr>
<td>Cont</td>
<td>Test 3 Sitting</td>
<td>0.03 ± 0.07</td>
<td>(0–0.31)</td>
<td>0.02</td>
<td>−0.943</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Romberg</td>
<td>0.04 ± 0.05</td>
<td>(0–0.34)</td>
<td>0.04</td>
<td></td>
<td>0.345</td>
</tr>
</tbody>
</table>

VV = vestibulopathy and visual vertigo, Vest = vestibulopathy and no VV, Cont = healthy controls.

Fig. 1. Optokinetic nystagmus stimulation (OKNS) in a healthy subject and a subject with right vestibulopathy and VV, responding to five conditions of visual stimulation. Condition 1 – Baseline, (upper trace). Conditions 2 and 3 show optokinetic nystagmus frequency (OKNf) with no fixed target. Conditions 4 and 5 show OKNf with fixed target. The data analyzed included the 15 seconds between the two dotted lines. OKNf was measured in beats per 15 seconds.

3.4. Differences in OKNf according to posture and group

OKNf was significantly higher in Romberg stance compared to the sitting position. Results of the Poisson regression analysis are shown in Figs 2 and 3. VV participants had significantly higher OKNf in Test 2 in the sitting position (36.7 ± 9.3 [median = 33.5]) vs. 23.5 ± 8.6 [median = 24.8] peaks/sec and in Romberg stance (40.8 ± 8.6 [median = 33.5] vs. 28.4 ± 9.7 [median = 27.5] peaks/sec, respectively; \( P < 0.05 \) compared to controls.

In Test 3, significantly higher OKNf was found only in Romberg stance between VV and controls (6.8 ± 7.2 [median = 6] vs. 1.2 ± 1.6 [median = 0.25] peaks/sec; \( P < 0.05 \)). No significant differences were found between sitting position and Romberg stance.

3.5. Optokinetic nystagmus gain (OKNg)

For Test 1, the baseline test, no differences in OKNg were found among the three groups. This finding was not affected by posture. In Test 2, the VV group had significantly higher OKNg compared to the CONT group (0.82 ± 0.13 [median = 0.78] vs. 0.63 ± 0.19 [median = 0.6], respectively, \( P < 0.05 \)) using a multi-level mixed-effects REML regression analysis. OKNg
was higher in Romberg stance than in sitting position ($P < 0.05$). For Test 3, there were no significant differences in OKNg between VV and the other two groups.

3.6. Differences in Optokinetic Nystagmus Gain (OKNg) according to Posture and Group

In Test 2, the VV group had significantly higher OKNg than the CONT group ($0.84 \pm 0.17$ [median = 0.82] vs. $0.55 \pm 0.18$ [median = 0.56]; $P = 0.024$) in Romberg stance only. Also in Test 2, the VV and Vest groups had higher OKNg in Romberg stance than in sitting position ($P = 0.036$; $P = 0.005$, respectively) (Table 1).

4. Discussion

Based on OKNS testing, we found that participants with VV demonstrated increased OKNf compared to healthy control subjects. Participants with VV also had greater difficulty ignoring or inhibiting peripheral visual stimuli even when they were asked to focus on a fixed target.

Currently, physicians and clinicians primarily use the Rod and Frame test, dizziness questionnaires, and OKNg to evaluate subjects with VV [11,13,19,25,26, 28]. Although OKNf is not used routinely to measure

VV, it was employed here in addition to OKNg, because in our understanding, OKNS closely mimics situations that occur in real life such as walking along store isles, seeing moving traffic while standing on a sidewalk, or watching television.

The results of this study demonstrated that participants with VV have increased OKNg compared to healthy controls. This means that the ratio of eye movement to target movement is closer to 1, compared to healthy controls.

We also found that during Test 2 (moving stripes with no target) in Romberg stance, the OKNg in participants with VV and Vest was significantly closer to 1 compared to that of healthy participants (Table 1). These results might indicate that using a strategy of ‘looking’ (instead of staring) at moving stripes helps participants with VV and Vest maintain balance while standing in a demanding environment. It also might indicate that these participants are more visually dependent than control participants who can successfully ignore this visual stimulation. The test results in Romberg stance might indicate that the VV and Vest groups used a similar balance strategy, i.e., trying to convert the moving environment to a static one in an attempt to have two sensory inputs that provide accurate information. Thus, an OKNg close to 1 might indicate an involuntary strategy for postural stability. When retinal slip occurs in individuals with VV, feel-
ings of dizziness (described as a sensation of floating or heaviness in the head) or vertigo increase [4]. Most in-
dividuals tolerate different levels of sensory input mis-
mismatch every day (e.g., visual, vestibular and proprio-
ception inputs). An example is standing on a sidewalk
(i.e. stable from the vestibular and somatosensory sys-
tems) and seeing moving traffic (i.e. movement from
the visual system). OKNg closer to 1 occurs when one
follows the stripes at the same velocity as the target;
thus, it feels like there is no motion from the visual
input. Individuals with VV dislike feeling the back-
ground motion supplied by the visual system when the
other systems are not giving the same information, be-
cause it might trigger vertigo [11]. These individuals
struggle to determine what is actually moving, the en-
vironment or themselves?

Participants with VV had lower OKNf when asked to
fix their eyes on a stationary target with stripes mov-
ing over it, compared to moving stripes with no tar-
get. Nevertheless, OKNf was still significantly higher
than in the control group under the same conditions.
Contrary to previous reports [13,16] that OKNf can
only be totally inhibited by voluntary effort if there is
a stationary object in view or if the eyes converge on a
point outside the plane of the moving display, we found
that participants with VV were unable to totally ignore
OKNS, even when they were asked to stare at a fixed
target. The discrepancy between our findings and that
of others [13,16] could be due to different participant
characteristics (participants with VV were not included
in their study). The fact that participants with VV could
not fully ignore the stripes, whereas healthy partici-
pants were able to gaze at the stripes intermittently,
suggests that participants with VV depend mainly on
the visual system to maintain balance during Romberg
stance [1,5,11].

A limitation of this study was that larger sample
sizes might have revealed greater statistical differences
between the subgroups of vestibulopathic individuals
with and without VV.

5. Conclusions

In summary, this study provides new information
that subjects with VV have more OKNf in demanding
environments compared to healthy individuals. In ad-
inction, challenging positions such as Romberg stance
have some effect on the OKNf and OKNg of vestibu-
lopathy subjects with and without VV. Therefore, we
recommend that OKNg and OKNf testing in both sit-
ting and Romberg positions should be added to the
clinical diagnostic work up.

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