Enhanced smooth pursuit eye movements in patients with bilateral vestibular deficits

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Patients with bilateral vestibular deficits experience unsteady gait and oscillopsia that can reduce the quality of life, though many patients adapt remarkably well and lead mostly normal lives. One source of adaptation could be the ability of sensory-motor systems to compensate for the vestibular loss by adaptive enhancement of their performance. We studied smooth-pursuit eye movements in five patients and six healthy control subjects using a step-ramp paradigm. Eye movements were measured with scleral search coils. Patients showed open- and closed-loop pursuit gains that were about 9% higher than controls. We suggest that the challenge of living with a deficient vestibular system caused an enhancement in the pursuit system, which contributes to the patient's overall compensation. *NeuroReport* 15:2617–2620 © 2004 Lippincott Williams & Wilkins.

Key words: Adaptation; Smooth pursuit eye movements; Vestibular ocular reflex

INTRODUCTION

Patients with bilateral vestibular deficits experience impaired vision during head movements, as vividly portrayed by J.C. [1]. While initially such patients are quite disabled, they compensate over time and on casual observation may appear normal. This improvement probably relies on behavioral strategies (restriction of problematic movements [1]; pre-programming of eye movements [2]), as well as adaptive changes of sensorimotor systems (e.g., increased gain of cervico-ocular reflexes [2–4]). Here we report on improvements in smooth pursuit eye movements in patients who have adapted to their bilateral vestibular loss.

Smooth pursuit (SP) eye movements are slow eye movements used to track moving targets and keep the visual image of the target on the high acuity fovea. SP eye movements typically assist the vestibular ocular-reflex (VOR), because the vestibular canals have high-pass frequency characteristics [5] and, as a result, the VOR gain for low frequencies is not perfect.

SP is composed of two functionally different periods: an initial 'open-loop' period, lasting roughly 100 ms, where SP operates without the benefit of corrective visual signals because of delays transferring visual information from the retina to the ocular motor system; and a later 'closed-loop' period where such corrective feedback can improve SP. The open-loop portion of SP is known to be under adaptive control [6–8], which allows the SP system to maintain long-term calibration and rapidly acquire targets to support clear vision.

We measured the open- and closed-loop performance of SP in normal controls and patients who have adapted to a bilateral vestibular deficit. All of our patients had lived with their deficits for 1–12 years, and so they and their SP systems had ample opportunity to re-calibrate to the challenge of living with a bilateral vestibular deficit. Portions of this work have been presented previously in abstract form [9].

MATERIALS AND METHODS

The experimental protocols were approved by the local ethics committee at Zürich University Hospital, and adhered to the Declaration of Helsinki for research involving human subjects. All subjects gave their informed consent to participate.

Subjects: We studied five consecutive patients diagnosed with a peripheral, bilateral vestibular loss without other known neurological disorders. Among the patients there were two suspected cases of ototoxicity and one auto-immune disorder. The average age of patients was 41 (range 24–62) years, and the first symptoms occurred on average 6 years prior to testing (range 1–12 years). All of the patients were very well adapted to their vestibular deficit by the time of testing, though all reported some vestibular-related problems. No subject showed spontaneous nystagmus in the dark.

Six normal control subjects, who were free of any known ocular motor or vestibular dysfunction, completed the SP studies. Twenty healthy subjects provided normative data for the high frequency tests of the VOR.

Eye and head movement measurement: Eye and head movements were measured in three dimensions with dual

search coils (Skalar, Delft, The Netherlands). One search coil annulus was worn in one eye, and another was tightly affixed to the forehead. Subjects sat inside a 1.4 m diameter coil frame, which generated three orthogonal magnetic fields with frequencies of 42.6, 55.5, and 83.3 KHz. Voltages induced on the coils were digitized at 1000 Hz and 16-bit resolution. Either the right or left eye was measured, but for all analysis, we converted the data so that the measured eyes appear as right eyes. Head movements were restricted with an individually adjusted chin rest, and subjects wore a patch on the non-measured eye.

We represent eye positions as 3D rotation vectors in a head-fixed coordinate system. Angular velocity was computed as described previously [10,11]. Slow phase velocity was found with an interactive computer program that first automatically detected saccades based on velocity and noise criteria, and then allowed the user to adjust the automatically marked saccades and to remove blink artefacts. Saccades were omitted from all quantitative analysis, and were replaced by linear interpolation to produce graphs of average traces.

VOR testing: All patients underwent VOR testing on the same day as we measured SP. Our primary method of diagnosis was the head impulse test [12], which tests the high frequency VOR. Subjects fixed a straight-ahead target, and the experimenter rapidly rotated the head in different directions. Head movements could be generated with speeds of at least 170°/s in all directions tested: yaw (horizontal), pitch (vertical), roll (torsional), and in the planes of the vertical canals: left-anterior, right-posterior (LARP) and right-anterior, left-posterior (RALP). The VOR-gain was defined by $VOR = 1 - \frac{\Delta gaze}{\Delta head|_{(3°-7°)}}$ where gaze (eye-in-space) and head were evaluated when the head had turned from 3° to 7°. A gain of +1.0 indicates perfect compensation.

The patients showed VOR deficits of varying degrees (Fig. 1). All patients showed substantial horizontal deficits. One patient, P2, showed clearly better vertical, RALP, and LARP responses than the other subjects. For this patient we also measured the low (0.05) and medium (0.7 Hz) frequency vertical VOR by rotating the patient about the head-fixed pitch axis while upright, and the gain was <0.2.

We also tested caloric responses with hot (44°) and cold (30°) water. None of the patients showed any response.

Smooth pursuit: The pursuit target was a pattern of five spots (each ~0.1° diameter), in the shape of a 2° diameter Greek cross. The subject was instructed to fixate the central spot. A mirror-galvanometer and laser under computer control presented targets by pulsing the laser at each position for 10 ms. The pulsing of the laser was not visible.

Targets moved with a step-ramp [13] profile, where targets first stepped in the opposite direction of the subsequent constant velocity movement. This stimulus facilitates the analysis of the open-loop period of SP because the initial eye movement response is often devoid of saccades. The initial target position was 10° right and 10° down from straight ahead. After 1–2 s fixation, the target stepped either right or down, and then moved in the opposite direction (left or up) at speeds of 10, 20, or 40°/s. (When we measured the left eye, the initial target position was left and down, and targets moved either right or up.)
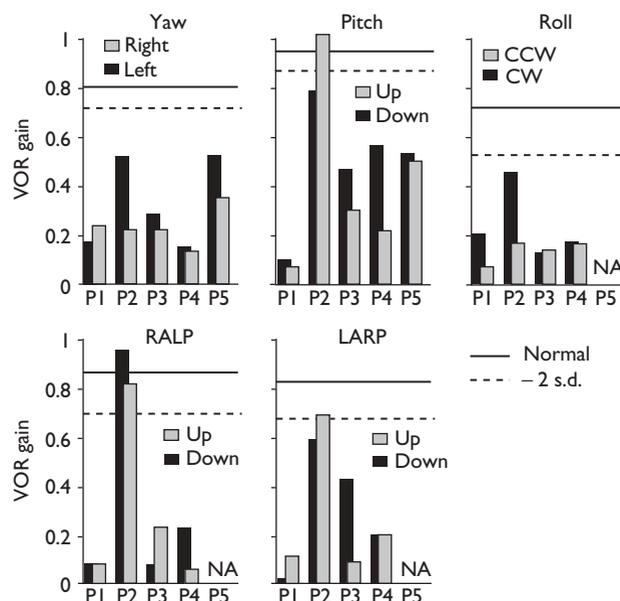

Fig. 1. The high frequency VOR measured in patients with bilateral vestibular deficits. Solid lines indicate the average, across directions, of 20 normal subjects, and the dashed lines are 2 standard deviations below the mean. Each panel refers to an axis of head rotation (RALP=right-anterior, left-posterior; LARP=left-anterior, right-posterior). CW=clockwise. CCW=counterclockwise. NA=not available.

The size of the back-step increased with target speed so that after 150 ms of movement the target crossed the initial fixation point, which reliably produced trials where subjects began tracking the target with SP rather than a saccade. Target direction and speed were chosen randomly on each trial. All subjects had 5–10 practice trials before the experiment, and between 10 and 20 trials were completed for each combination of target speed and direction.

Pursuit latency was determined by the intersection of two regression lines (based on [14]): the first was fit to eye velocity from 50 ms before to 100 ms after the start of target movement; and the second was from the point when acceleration was 10% of peak acceleration to 100 ms later. Each trial was inspected individually to verify reasonable fits. Trials with saccades within 100 ms of pursuit onset were eliminated from further analysis.

Open-loop velocity was calculated as the median eye velocity 80–100 ms after pursuit onset. We defined close-loop gain as the median velocity from 200 ms after pursuit onset to the end of the trial, divided by target speed. The 200 ms delay was chosen because it occurs after the early period of acceleration and after initial 'catch-up' saccades. Since subjects can make predictive SP movements [15,16], we also computed median velocity 80–100 ms after the onset of target movement to determine if patients and controls differed in their predictive strategies.

Statistical tests were performed by first computing means within individual subjects, and then subjecting the means to ANOVA with subject type (patient, control), target speed (10, 20, 40°/s) and direction (horizontal, vertical) as factors. ANOVAs were computed with the statistical software program MINITAB using the general linear model command.

RESULTS

Both patients and control subjects could track the slow targets well, but performance declined at high speeds. Figure 2 shows example vertical movements for a typical control and a patient for slow ($10°/s$) and fast ($40°/s$) targets. For slow trials, eye velocity increases and slightly exceeds target velocity as the eye acquires the target, before matching the target speed. For fast trials (bottom row), the initial movement is SP, followed by a saccade, and interleaved SP and saccades characterize tracking. Stable SP velocity was achieved immediately after the first saccade, though for fast targets it was not sufficient to track the target. The patient tracked the fast target more accurately with a higher velocity SP.

On average, patients and controls performed similarly for slow targets, but for fast targets ($40°/s$) patients reached higher SP velocities (Fig. 3). The decline in eye velocity at the end of fast trials might be caused by SP gain decreases

Fig. 4. Top: eye velocity at the end of the open-loop period, with horizontal velocity on the left, and vertical velocity on the right. Bottom: closed loop smooth pursuit gain, with horizontal velocity on the left, and vertical velocity on the right. Points have been offset slightly for clarity.

with eccentricity (known to be true for SP initiation [17]), or by subjects anticipating the end of trials.

Patients achieved higher SP velocities than controls during the open-loop period (Fig. 4, top). An ANOVA found a main effect of subject type on velocity at the end of the open-loop period ($F(1,54)=9.47$, $p<0.005$). Velocity also significantly increased with target speed ($F(2,54)=12.98$, $p<0.001$). No other factors or interactions were statistically significant.

Closed-loop SP gain declined with target velocity for both subject groups (Fig. 4, bottom). Patients showed an average SP gain that was 0.09 higher than controls, and this difference was confirmed by a significant main effect in an ANOVA ($F(1,54)=18.65$; $p<0.001$). The main effect of SP direction did not reach statistical significance ($F(1,54)=1.7$, $p<0.2$), but the decline in gain with target speed was significant ($F(2,54)=24.10$, $p<0.001$).

Patients, on average, had longer reaction times than normal subjects (166 vs 153 ms; significant main effect in ANOVA). However, this appears due to one patient who had unusually long average reaction times of 194 ms; if we remove this patient's data then no significant difference in latency was observed.

For all subjects, eyes tended to drift up ($0.15°/s$ on average) and to the left ($0.32°/s$) prior to SP onset (recall that target direction was either up or left, so subjects were anticipating the movement). Single factor ANOVAs found no significant difference between patients and controls in these predictive eye movements.
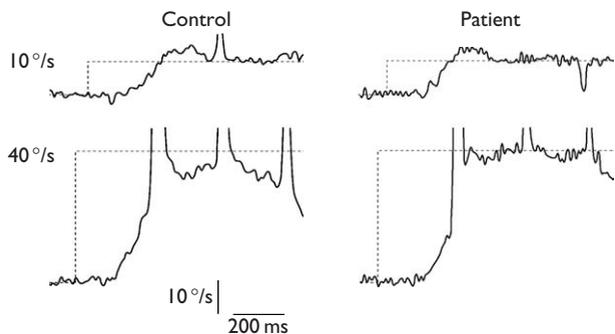

Fig. 2. Example trials show eye (solid line) and target (dotted) velocity for slow (top row) and fast (bottom row) trials with a healthy control subject (left) and a patient with a bilateral vestibular deficit (right).
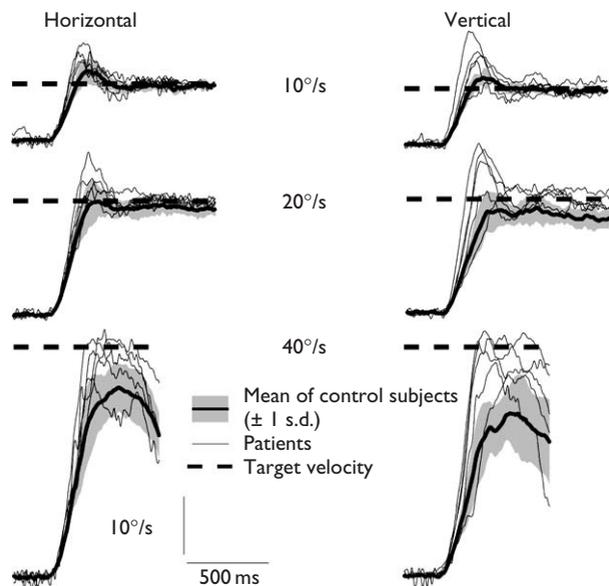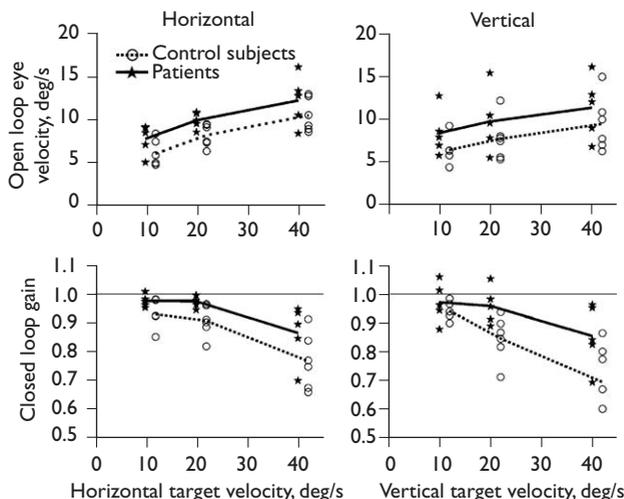

Fig. 3. Average eye velocity for horizontal (left column) and vertical (right column) trials, aligned on pursuit onset. Target velocities (dashed lines) are 10, 20, and $40°/s$. Average traces of each individual patient are shown with thin lines, and the average of control subjects is shown with a thick line (gray band=± 1 s.d.).

DISCUSSION

Patients with bilateral vestibular deficits have improved SP, probably because their SP systems adaptively changed in response to the challenge presented by their vestibular disorder. Patients' SP show higher acceleration to acquire targets, as evidenced by the higher velocity at the end of the open-loop period (Fig. 4, top), and they could better pursue fast moving targets when visual feedback of accuracy was available (closed-loop gain, Fig. 4, bottom). We did not find

any difference between patients and controls in predictive movements or latencies (except for one patient), so the improvements in SP are not strategic. The increased open-loop velocity shows that the internal gain of the SP system was higher in patients. Our results may be related to reports of increased optokinetic responses in labyrinthine-defective patients [18].

We found the biggest difference in closed-loop gain between controls and patients at the highest speed we tested (40°/s). Other studies that did not find improved SP in patients may have used too low a peak velocity (e.g., 16°/s [19]) or too predictable target movements [2]. Anecdotal evidence of patients who showed enhanced SP has been reported [2,20], supporting our findings. We believe ours is the first study of the open-loop SP in patients with bilateral vestibular loss.

CONCLUSION
Living with a deficient vestibular system challenges sensorimotor systems to adapt their performance in order to improve vision and mobility. We found that patients with bilateral vestibular deficits who have compensated for their disorder have improved smooth pursuit eye movements, which could improve their vision during head movements. Bilateral vestibular deficits are rare, and they present a particularly demanding strain on patients, though all our patients showed remarkable compensation for their disorders. If adaptive improvement of SP is one component of compensating for vestibular problems, we speculate that specific SP training might assist all patients with vestibular problems in shortening recovery periods. Further, as VOR re-training is typical for patients, we suggest that some of the improvement maybe due to changes in SP.

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