Clinical note

Visual–vestibular interaction in progressive supranuclear palsy

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Abstract

We measured the stability of gaze during horizontal head rotations at 1–3 Hz in four patients with progressive supranuclear palsy (PSP), while they viewed a stationary target. Median gain of compensatory eye movements was 0.94, similar to control subjects. During rotation in darkness, median gain of vestibulo-ocular reflex (VOR) was 0.88, similar to controls. Conversely, the median gain of smooth-pursuit eye movements at 1.0 Hz was 0.23, lower than controls. A simple superposition model of smooth pursuit and the VOR could not account for the observed gaze stability during fixation. Our results are further evidence that a visually mediated mechanism, independent of smooth pursuit, optimizes eye movements to compensate for head rotations. © 2000 Published by Elsevier Science Ltd.

Keywords: Vestibulo-ocular reflex; Visual-vestibular; Smooth pursuit; Progressive supranuclear palsy

1. Introduction

During natural activities, especially locomotion, eye rotations must be generated to compensate for head movements. Such compensatory eye movements may be vestibularly or visually mediated. The vestibulo-ocular reflex (VOR) generates eye movements to compensate for head movements at short latency (< 15 ms) (Maas, Huebner, Seidman & Leigh, 1989; Crane & Demer, 1998). In contrast, visually mediated eye movements, such as smooth pursuit, act at longer latencies (~ 100 ms) (Carl & Gellman 1987). If vestibular function is lost, visually mediated eye movements cannot compensate for the head perturbations that occur during locomotion, which have predominant frequencies of 0.5–5 Hz (Leigh & Brandt, 1993; Das, Zivotofsky, DiScenna & Leigh, 1995b; Crane & Demer, 1997). Although the VOR acts at short latency, its performance is influenced by the ability to view a stationary target. Thus, when subjects attempt to fix upon the remembered location of a target in darkness, VOR gain is less than if they actually view the target (Barr, Schultheis & Robinson, 1976; Keller, 1978; Collewijn, Martins & Steinman, 1983; Correia, Perachio & Eden, 1985; Demer, 1992; Paige, 1994).

In a prior study of human subjects with normal smooth pursuit and VOR, we tested the hypothesis that a linear superposition of visually mediated eye movements and the VOR accounts for gaze stability during head rotation while viewing an earth-fixed target (Das, DiScenna, Feltz, Yaniglos & Leigh, 1998). Subjects viewed targets through an optical device that made increased demands on visually mediated movements. We found that the superposition hypothesis could not account for the observed stability of gaze as subjects viewed an earth-fixed target during high-frequency head rotations, unless the properties of smooth-pursuit eye movements changed according to test conditions. In the...
2. Methods

2.1. Subjects and experimental equipment

We studied four patients with PSP (three male, one female); all gave informed consent in compliance with our institutional guidelines and the tenets of the Declaration of Helsinki. The patients’ ages ranged from 62 to 77 years and duration of illness from 2 to 5 years. One patient was taking levodopa/carbidopa, but otherwise no drugs with effects on the nervous system were being administered at the time of testing. All patients had uncorrected vision adequate to clearly see the visual target (a projected laser spot), and they were all tested without refractive correction. We compared results from these four PSP patients with those from the four normal subjects (age range 25–50 years) studied with similar stimuli in the prior study (Das et al., 1998). Head and gaze rotations were measured using the magnetic search coil technique, with 6-ft field coils (CNC engineering, Seattle, WA) as previously described (Das et al., 1998). Each subject wore a scleral search coil (Skalar Delft, Netherlands) on one eye, and another firmly attached to the forehead to measure angular head position. The search coils were calibrated prior to the experiment using a protractor device. Subjects sat in a 30-ft-lb vestibular chair (Templin Engineering, Laytonville, CA) during all the experimental paradigms. The subjects’ heads were firmly braced against the headrest of the chair throughout the procedure.

2.2. Experimental stimuli

The visual target was a red laser spot that was rear-projected onto a white, semitranslucent tangent screen, located at a distance of 1.2 m from the subject; the room was otherwise dimly illuminated (high mesopic range). To test horizontal smooth-pursuit, the position of the moving target was controlled using a mirror galvanometer (model CCX-660, General Scanning, Watertown, MA), driven by a computer-generated signal. Vestibular stimuli were generated by a laboratory computer and consisted of horizontal chair rotations at various frequencies and peak head velocities.

2.3. Experimental paradigms

1. (VVOR) Subjects were asked to maintain fixation on the stationary visual target while they were rotated passively in the chair at three frequencies (1.0, 2.0 and 3.0 Hz) with a peak head velocity of 30°/s at each frequency.

2. (VOR) Subjects attempted to fix on the remembered location of the stationary target while they were rotated in complete darkness at 2.0 Hz with a peak head velocity of 30°/s. For safety reasons, we limited this testing to one experimental run. We chose this mental set because Barr et al. (1976) reported it to maximize VOR gain in darkness.

3. (SP) Subjects attempted to track a target moving sinusoidally +5° at 0.25 and 1.0 Hz. The rationale behind choosing these stimuli was to measure smooth tracking at a frequency similar to that used during Paradigm 1, but also to confirm that smooth-pursuit performance was impaired even for low-frequency stimuli.

Each experimental run lasted 20 s.

2.4. Data acquisition and analysis

Target, head, and gaze position signals were filtered with analog Butterworth filters (Krohn-Hite, Avon, MA) set at a bandwidth of 0–90 Hz, before digitization at 210 Hz with 16 bit resolution. Details of the analysis are described in prior publications (Das, Leigh, Thomas, Averbuch-Heller, Zivotofsky, DiScenna et al., 1995a; Das et al., 1998) and are briefly summarized here. Data were digitally differentiated with a bandwidth of 0–30 Hz and saccades were removed from the eye and gaze movement records, using an interactive routine. We analyzed segments of at least 1000 points and determined the gain of compensatory eye movements during head rotation for each trial by calculating the ratio of the power spectral density of eye and head velocity at the frequencies of interest. Similarly smooth-pursuit gain during tracking paradigms was measured by calculating the ratio of power spectral density of gaze and target velocities. The phase response was determined by measuring phase differences between these signals in the frequency domain and recording the phase shift at the frequency of interest. We used the data from the PSP patients to test the superposition model for vestibulo-visual interaction in the same way that we did for the normal subjects (Das et al., 1998).

3. Results

Data from all four patients and controls are summarized in Table 1. For Paradigm 1 (VVOR), during head rotations at 1 Hz, all four patients showed gain values close to 1.0 and phase shifts close to 180°; i.e. almost completely compensatory eye rotations. These results...
were similar to the control subjects (Table 1A). Fig. 1 summarizes gain and phase for all patients; the gain of compensatory movements fell as stimulus frequency increased, but phase showed no consistent trend. For Paradigm 2 (VOR in darkness) at 2 Hz, median gain was 0.88 and phase was close to 180° (Table 1B), similar to normal subjects. For Paradigm 3 (smooth pursuit), median gain was 0.67 at 0.25 Hz (Table 1C, first column), and all patients showed gains less than the range of the control subjects. The median smooth pursuit gain of PSP patients at 1.0 Hz was 0.23, much lower than the range for control subjects. Patients 1 and 3 showed substantial phase lags during smooth pursuit at 1.0 Hz. Such severely impaired smooth pursuit might be expected to detract, rather than enhance, the VOR at frequencies at or above 1.0 Hz. To test this possibility, we used the simple superposition model (Das et al., 1998) to predict what smooth pursuit gain and phase would be required to account for the observed VVOR performance (given the measured VOR gains). Table 1C (right four columns) compares the model’s predictions of smooth-pursuit gain and phase and experimentally observed values for visual target motion at 1 Hz with peak velocity of 30°/s. All patients showed lower gains than the model predicted by a factor of more than two.

4. Discussion

We found that, in patients with PSP, gaze stability is normal during head rotations that correspond to the frequency range of natural movements. Further, VOR measured in darkness is similar to normal subjects. These results are consistent with prior studies of the VOR and VVOR in PSP (e.g. Rottach, Riley, Discenna, Zivotofsky & Leigh, 1996), and explain why such patients do not complain of visual disturbance (oscillopsia) during locomotion (Leigh & Zee, 1999). Horizontal smooth pursuit is known to be impaired in PSP (Troost & Daroff, 1977; Rottach et al., 1996), but direct comparison of pursuit and visuo-vestibular responses at higher frequencies were lacking. We found smooth pursuit gain at 1.0 Hz in PSP patients to be less than half of that shown by normal subjects. This large discrepancy of smooth pursuit and the VOR perfor-

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<table>
<thead>
<tr>
<th>Patient/controls</th>
<th>Gain-1 Hz</th>
<th>Phase</th>
<th>Gain-2 Hz</th>
<th>Phase</th>
<th>Gain-3 Hz</th>
<th>Phase</th>
</tr>
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<tbody>
<tr>
<td>A. Paradigm 1 (VVOR) at 30°/s</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>0.97</td>
<td>182.9</td>
<td>0.88</td>
<td>182.1</td>
<td>0.82</td>
<td>182.7</td>
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<td>2</td>
<td>0.95</td>
<td>179.4</td>
<td>0.94</td>
<td>182.4</td>
<td>0.88</td>
<td>179.8</td>
</tr>
<tr>
<td>3</td>
<td>1.03</td>
<td>183.1</td>
<td>0.95</td>
<td>185.4</td>
<td>0.83</td>
<td>185.0</td>
</tr>
<tr>
<td>4</td>
<td>1.01</td>
<td>180.4</td>
<td>0.90</td>
<td>182.6</td>
<td>0.93</td>
<td>182.3</td>
</tr>
<tr>
<td>Controls*</td>
<td>0.96–1.00</td>
<td>180.5–181.5</td>
<td>0.93–0.98</td>
<td>181.1–183.5</td>
<td>0.84–0.99b</td>
<td>182.8–183.9b</td>
</tr>
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<table>
<thead>
<tr>
<th>B. Paradigm 2 (VOR in darkness) at 2 Hz</th>
<th>Gain-2 Hz</th>
<th>Phase-2 Hz</th>
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<tbody>
<tr>
<td>1</td>
<td>0.89</td>
<td>181.3</td>
</tr>
<tr>
<td>2</td>
<td>0.88</td>
<td>177.2</td>
</tr>
<tr>
<td>3</td>
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<td>181.7</td>
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<tr>
<td>4</td>
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<td>178.9</td>
</tr>
<tr>
<td>Controls*</td>
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<td>178.9–180.2</td>
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<thead>
<tr>
<th>C. Comparison of model predictions and observed values of smooth pursuit gain and phase</th>
<th>Experimentally observed SP</th>
<th>Model predicted SP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gain (0.25 Hz)</td>
<td>Phase lag (0.25 Hz)</td>
<td>Gain (1.0 Hz)</td>
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<tr>
<td>1</td>
<td>0.72</td>
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<td>2</td>
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<tr>
<td>Controls*</td>
<td>0.97–1.02c</td>
<td>0.7–1.1c</td>
</tr>
</tbody>
</table>

* Values from Das et al. (1998) are ranges.
* For VVOR, test frequency was 2.8 Hz.
* For smooth pursuit, test frequency was 0.2 Hz.
impaired pursuit (due to PSP) and test whether the discrepancy between VVOR and smooth pursuit performance could be accounted for by a superposition model. The failure of the model to predict the observed responses may reflect a nonlinear effect on the response of smooth pursuit in PSP. It is also possible that another mechanism (presumably dependent on vision) may have acted in concert with the VOR to guarantee gaze stability and allow clear vision of the object of regard. Although it might seem possible that the presence of light itself (without contrast) plays a role, VOR gain is not increased if subjects attempt to view a stationary target through a ganzfeld contact lens (Barr et al., 1976; Das, Yaniglos & Leigh, 1999b). On the other hand, a visually mediated eye movement — such as occurs during VVOR — might increase the VOR gain to levels required for gaze stability. Such a ‘priming’ effect has been recently reported when a visually mediated eye movement precedes a transient head rotation (Das, Dell’Osso & Leigh, 1999a).

In summary, the present study supports the view that the gain of the VOR is modulated in response to visual demands, but that this modulation is not due to a simple superposition of smooth-pursuit eye movements. Preservation of the ability to modulate VOR gain in PSP may provide clues to identifying which pathways, spared in this disorder, are carrying out this function — which guarantees clear vision during natural head movements.

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References


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