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Between-subject variability and within-subject reliability of the human eye-movement response to bilateral galvanic (DC) vestibular stimulation

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Abstract Recent studies have shown that responses to surface galvanic vestibular stimulation (GVS) show substantial interindividual variation. Between-subject variability may be due to individual differences between subjects, or to the poor reliability of the test, or to differences in test details, or to host factors. The aim of the present study was to compare variability between and within subjects in binocular 3-D eye-movement responses to long-duration, maintained, large-amplitude, bilateral, bipolar, surface GVS. Subjects were seated and restrained, and in one condition fixated a small, centrally located visual target; in the other condition, testing was carried out in complete darkness. Surface GVS of 5 mA, with a rectangular waveform was delivered bilaterally for 5 min while eye movements were measured using computerised video-oculography (VTM). In the first experiment, ten subjects participated in both conditions in one session, and in the second experiment, two subjects participated in both conditions for a total of five repeated sessions. The stimulation was well tolerated by all subjects and produced a change in torsional position with the upper pole of both eyes rolling towards the anode and away from the cathode in all subjects in both conditions. Although little vertical nystagmus was evident in either condition, most subjects showed relatively strong horizontal nystagmus (slow phases towards the anode) in darkness. This study confirms previous observations that the torsional response to GVS is highly variable between subjects, whilst also showing for the first time that eye-movement responses to GVS show good within-subject repeatability. This study also demonstrates considerable between-subject variability in the relative ratios of response components (torsional and horizontal nystagmus, torsional position), whereas the relatively small within-subject variability can be characterised more by changes

in the overall amplitude of the eye-movement response. Subjects show idiosyncratic oculomotor response patterns to GVS, varying slightly in absolute magnitude between sessions. Thus, GVS may be a more reliable stimulus than may have been anticipated from the literature.

Keywords Galvanic vestibular stimulation (GVS) · Ocular torsion · Labyrinth · Eye movement · Individual differences

Introduction

For over 200 years it has been known that delivering current across the head produces sensations of dizziness (Kayam et al. 1974). Whether this surface galvanic stimulation acts peripherally or centrally has been a matter of considerable debate (Goldberg et al. 1982, 1984), however, it is widely accepted that surface galvanic stimulation delivered to the mastoids activates at least some part of the vestibular system. For this reason, galvanic vestibular stimulation (GVS) has been the focus of continued studies seeking to determine its usefulness in a clinical diagnostic setting (Pfaltz 1969; Coats 1972; Watanabe et al. 1985).

Early studies focused on the eye-movement response to GVS using nystagmography, however, the results were highly variable (Straub and Thoden 1992). Investigation in this area turned more and more to the effects of GVS on postural responses, such as GVS-induced body sway (see, for example, Coats 1973; Magnusson et al. 1991), and EMG responses to GVS in normals and in people with vestibular deficits (see, for example, Britton et al. 1993; Watson et al. 1998b). Again, the overall high variability of the results of GVS initially led some researchers to discount the utility of GVS as a test of peripheral vestibular function at all (Blonder and Davis 1936; Pfaltz and Richter 1965). In addition, the delivery of GVS has sometimes been too noxious for subjects to tolerate without considerable discomfort, resulting in many researchers questioning whether GVS could ever

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be an appropriate clinical tool for the assessment of vestibular function (Blonder and Davis 1936).

Recent refinements in the delivery of GVS have, however, greatly reduced the level of discomfort produced. The use of large surface electrodes and generous quantities of conductive medium (such as electrode paste or gel) greatly reduces the likelihood of GVS causing discomfort or resulting in burns to the skin. In addition, the characteristics of the stimulus appear to play an important role in whether the stimulus produces noxious subjective responses, such as overpowering sensations of spinning or falling, nausea or metallic tastes in the mouth. These subjective responses to GVS mostly appear to accompany onset or rapid changes in the amplitude of current delivered (Hlavacka and Njiokiktjien 1985; Magnusson et al. 1990; Johansson and Magnusson 1991; Watson et al. 1998a) as well as being mediated by the absolute magnitude of the stimulus (Zink et al. 1997, 1998). Thus, high-velocity impulses at large current amplitudes delivered through electrodes with small surface area may be quite noxious to a subject, whereas slowly increasing the current from approximately zero to the same large amplitude and maintaining that level of stimulation over a long duration (>30 s) is tolerated well by most subjects (Watson et al. 1998a). Using these refinements, Watson et al. (1998a) showed that long-duration GVS could be delivered comfortably and that it caused a maintained change in ocular torsional position (OTP) with the upper pole of both eyes rotating away from the cathode and/or towards the anode, regardless of whether the stimulus was delivered bilaterally or unilaterally.

However, uncertainty still exists regarding the reliability of the GVS-induced responses. Studies have shown that GVS causes substantial individual variations in regional cerebral blood flow to vestibular cortical areas (Lobel et al. 1998) and in torsional eye-movement responses (Kleine et al. 1999; Schneider et al. 2000). This variability appears to limit the potential of surface GVS as a diagnostic tool. However, studies have rarely attempted to identify the source of between-subject variability. This may be because experiments using GVS can be demanding for subjects, as the stimulus can be noxious enough to deter subjects from participating in multiple sessions.

When response differences are found between subjects, one of the first sources of variability that must be suspected is that arising between tests. In other words, between-subject variability may be due to individual differences between subjects, or to differences in test details between sessions, such as electrode placement and resistance, current delivery, or even host factors such as arousal or changes in response bias in resolving ambiguous sensory input (Lobel et al. 1998). The aim of the present study was to examine the 3-D eye-movement responses to long-duration, maintained, large-amplitude, bilateral, surface GVS. In particular, this study sought to compare between- and within-subject variability in oculomotor responses to surface GVS.

Measurement of torsional eye movements using techniques such as scleral search coils is problematic due to coil slippage (especially during blinks; Bockisch and Haslwanter 2001). To overcome such potential artefacts, the present study used a robust and sensitive method of computerised video-oculography (VTM; Moore et al. 1991, 1996) to measure binocular eye movements during unobstructed vision. This avoids the inherent confounds when one or both eyes are occluded (Howard and Templeton 1966), for example, by video cameras.

The presence of a fixation light is known to drastically affect the eye movements of normal subjects. In addition to largely suppressing horizontal and vertical nystagmus, the presence of a fixation light has been shown to slightly reduce torsional eye movements (Enright 1990). In addition, Smith et al. (1995) have shown that, during on-centre rotation without fixation, the unsuppressed horizontal nystagmus tends to reduce or 'dump out' the centred OTP response. The present study investigated the response to GVS in both complete darkness and fixation conditions. Results obtained in darkness permit an analysis of the complex, 3-D eye-movement response to GVS, whereas the results obtained with a fixation light allow the isolation of predominantly stable, torsional components. Lastly, the present study uses long-duration (5 min) maintained galvanic stimulation in order to investigate the variability of the long-term decay and adaptation seen in previous studies (Watson et al. 1998a).

Materials and methods

Subjects

Ten subjects (four males and six females; mean age 28.7 years, SD 11.5 years) volunteered to participate in this study. All ten subjects participated in experiment 1: variability. Two of these subjects (one male, aged 32 years, and one female, aged 20 years) also participated in experiment 2: repeatability. No subject reported any history of vestibular dysfunction. All procedures were approved by the appropriate institutional ethics committees and all subjects gave informed written consent.

Galvanic stimulation

Galvanic stimulation was delivered via surface electrodes of approximately 1,000 mm², individually cut from electrosurgical plating (3 M) generously coated with electrode gel and placed over each mastoid process (see, for example, Watson et al. 1998a). Stimulation electrode placement was bilateral (cathode applied to one mastoid and anode to the other). This kind of bilateral delivery is preferable where there is no reason to expect asymmetry of response from each side (unlike patient testing, which would require unilateral comparisons). Further, bilateral stimulation was chosen because it is, in effect, twice as strong as unilateral stimulation, thereby generating larger eye-movement responses which allow more effective analysis (improved signal:noise ratio). A custom-designed isolated current stimulator was used to deliver the desired current from a battery source over a prolonged period. Prior to the test commencement, the stimulator was manually preset to deliver a current level of 5 mA (this was monitored continuously), then left at this level and switched off (see procedures). When ready to test, the stimulator was switched on, thereby delivering a 5-mA square-wave galvanic stimulus.

Procedure

Prior to the commencement of the test session proper, the electrodes were attached to the mastoids of the subjects. Once subjects were seated comfortably, they were given a practice session to ensure comfortable toleration of the stimulus. The stimulator was connected, switched on (at 0.6 mA) and then gradually increased to 5 mA (over approximately 10 s), left at 5 mA (approximately 15 s) and then switched off. During this practice session, subject tolerance of the stimulus was verbally verified. In this way we ensured that all subjects were able to tolerate both the maximal level of stimulation (5 mA) and a square-wave change of 5 mA in stimulation (offset at end of practice). In addition, we asked subjects to describe any illusory sensations of movement in order to satisfy ourselves that the stimulus was effective. Drops of pilocarpine (used to constrict the pupil for video-oculography) were then administered to subjects' left and right eyes. A rest period of 20 min between the practice session and the commencement of the test allowed the pilocarpine to take effect, and ensured that subjects recovered fully from the practice stimulus.

Following the rest period, subjects donned the video headset required for continuous eye movement recording (see below). Subjects were seated such that Reid's line (the line joining the inferior margin of the orbit and the upper margin of the external auditory meatus) was held about 7° nose up relative to earth horizontal. This is a standard position that is both comfortable and allows for comparable orientation of the otoliths across subjects. Head and shoulders were held firmly by padded supports.

Stimulus polarity was cathode left-anode right (CLAR) in all trials. In the first condition (FIX ON) subjects fixated a light that was positioned 80 cm straight ahead (i.e. centred both vertically and horizontally). Eye-movement recording commenced 2 min prior to the onset of GVS. The constant-current stimulator was then switched on, delivering 5 mA CLAR with square-wave onset. The stimulus was left at this level for 5 min and was then switched off (square-wave offset). Eye-movement recording continued for another 5 min. Subjects were allowed at least 15 min rest before commencing the second condition (FIX OFF), in which the sequence was repeated, except that the fixation light was extinguished at the commencement of the eye-movement recording and subjects were asked to maintain their direction of gaze as if the fixation light were still present.

These procedures were used for both experiment 1 and experiment 2. For experiment 2, subjects returned to participate in four additional repeat test sessions each (in addition to their original session, which formed part of experiment 1). Repeat sessions were separated by at least 1 day and no more than 3 months.

Eye movement measurement and analysis

Eye movements were recorded using video recording techniques described previously (Moore et al. 1991, 1996). The resolution of this method is 0.1° of ocular torsion and the sampling rate was 30 Hz (NTSC frame rate). The pupils of both eyes were constricted by 2% pilocarpine hydrochloride (Chauvin Pharmaceuticals, UK), and the eyes were illuminated with infrared light sources. Half-silvered ("hot") mirrors (Coolbeam; OCLI, Santa Rosa) reflected a close-up image of the iral pattern onto a lipstick-sized CCD camera (Panasonic WV-CD1E) while permitting the subject unobstructed vision. The cameras, mirrors and infrared light sources were mounted on thermoplastic masks (SanSplint; Smith and Nephew) individually moulded to the subject's face and held in place by Velcro straps. This tight-fitting but comfortable "wrap-around" mask minimised camera slippage relative to the eye, and our measures of eye position at the start and end of the test show that there was no detectable camera slippage.

All data were recorded onto VHS videotape using two VCRs and analysed after the test session. Eye position and velocity were processed for three dimensions, giving a total of six possible measures (horizontal, vertical and torsional eye position, and horizontal, vertical and torsional slow-phase eye velocity), however, re-

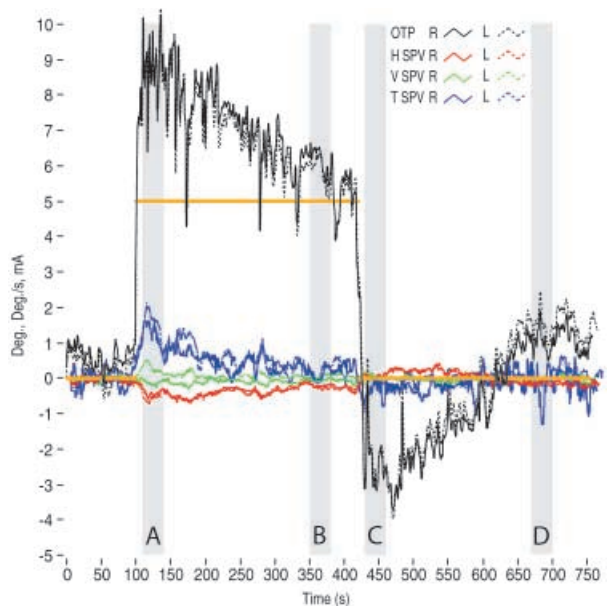


Fig. 1 The 3-D eye-movement traces for a subject during 5-mA cathode left-anode right (CLAR) surface galvanic vestibular stimulation (GVS) in the FIX ON condition. The results of both eyes are shown (right eye: *solid traces*, left eye: *dashed traces*), showing a high degree of binocular conjugacy in the response to GVS. The *vertical grey bars* indicate the regions of interest (A "onset", B "maintained", C "overshoot" and D "final"). The *orange horizontal bars* represent the presence and strength of the galvanic stimulus. *OTP* Ocular torsional position, *HSPV* horizontal slow phase velocity (SPV), *VSPV* vertical SPV, *TSPV* torsional SPV

sults for horizontal and vertical eye position were not included in all analyses, as these responses are under the voluntary control of subjects. The right-hand rule was used so that clockwise ocular torsion (where the upper pole of the eye rotated towards the subject's right shoulder) is positive and counterclockwise ocular torsion is negative. At the start of each condition, reference images of both eyes were recorded while the subject gazed at the fixation point. The average value of the response measured during this period was taken as the baseline measure for each dimension for a particular subject and arbitrarily given the value of 0° (position measures) or 0°/s (velocity measures).

Results

Experiment 1: variability

General findings

The long-duration, 5-mA stimulus was well tolerated by all subjects. Surface GVS produced eye-movement responses in all subjects. In response to the onset of GVS, the OTP of all subjects rotated in the positive direction (i.e. upper pole of the eye rotated towards the anode and away from the cathode). The change in eye position generally reached a maximum magnitude soon after stimulus onset (Fig. 1 *region A*), and then tended to decay, eventually reaching a tonic OTP (Fig. 1 *region B*). With the offset of GVS, the OTP of all subjects reversed direction (i.e. the upper pole of the eye rotated away from

Table 1 Average (and standard error of the mean *in parentheses*) of the time constant (seconds) for the decay of the eye-movement response to the onset and offset of galvanic vestibular stimulation (GVS) in darkness (FIX OFF) and with fixation (FIX ON). Results are shown for those measures showing a statistically significant decay of response to GVS, i.e. ocular torsional position (OTP), and horizontal and torsional slow phase eye velocity (HSPV and TSPV, respectively). The time constant for OTP in darkness is not shown, as there was no statistically significant decay in this condition (see Fig. 2). The number of subjects whose data were included in the calculation is indicated beneath each result. (NA Not applicable)

	FIX OFF		FIX ON	
	Galvanic onset	Galvanic offset	Galvanic onset	Galvanic offset
OTP	NA	NA	66 (± 10) <i>n</i> =7	113 (± 24) <i>n</i> =8
HSPV	98 (± 10) <i>n</i> =8	159 (± 32) <i>n</i> =10	84 (± 15) <i>n</i> =8	109 (± 29) <i>n</i> =10
TSPV	114 (± 36) <i>n</i> =9	113 (± 25) <i>n</i> =9	41 (± 17) <i>n</i> =7	58 (± 13) <i>n</i> =8

the anode and toward the cathode), reaching a peak offset response (Fig. 1 *region C*) before returning to baseline levels by the end of the trial (Fig. 1 *region D*). The amplitude of OTP change to GVS offset was similar in magnitude to that for GVS onset, that is, the magnitude of a subject's decay of OTP is similar to that of their adapted overshoot of OTP (see Fig. 1). Surface GVS also produced torsional nystagmus, with slow phases directed towards the anode and away from the cathode.

Four measures were used to summarise all subjects' 3-D oculomotor responses. The average of 30 s of data 10 s after the onset of GVS was calculated ("onset", corresponding to *region A* in Fig. 1). Similarly, 30 s of data 10 s after the offset of GVS was averaged ("offset", corresponding to *region C* in Fig. 1). The "maintained" response was calculated as the average of 30 s of data commencing 250 s after the onset of GVS (corresponding to *region B* in Fig. 1), and the "final" response was calculated as the average of 30 s of data commencing 250 s after the offset of GVS (corresponding to *region D* in Fig. 1). Figure 2 shows the average response and associated 95% confidence intervals for horizontal, vertical and torsional slow phase velocity (SPV) and OTP, for all subjects in experiment 1. Averages and 95% confidence intervals for the four time periods of interest, as described above, are also shown in Fig. 2.

In the FIX OFF condition (Fig. 2 *left half*) there was a substantial change in OTP and torsional SPV in response to GVS, as described above. In addition, GVS produced horizontal nystagmus, with the SPV directed towards the anode and away from the cathode (Fig. 2). In this condition there was very little vertical velocity response obtained to GVS. There was no significant change in vertical eye position, but there was a deviation in horizontal eye position, towards the anode and away from the cathode (i.e. to the right in this instance) in response to GVS

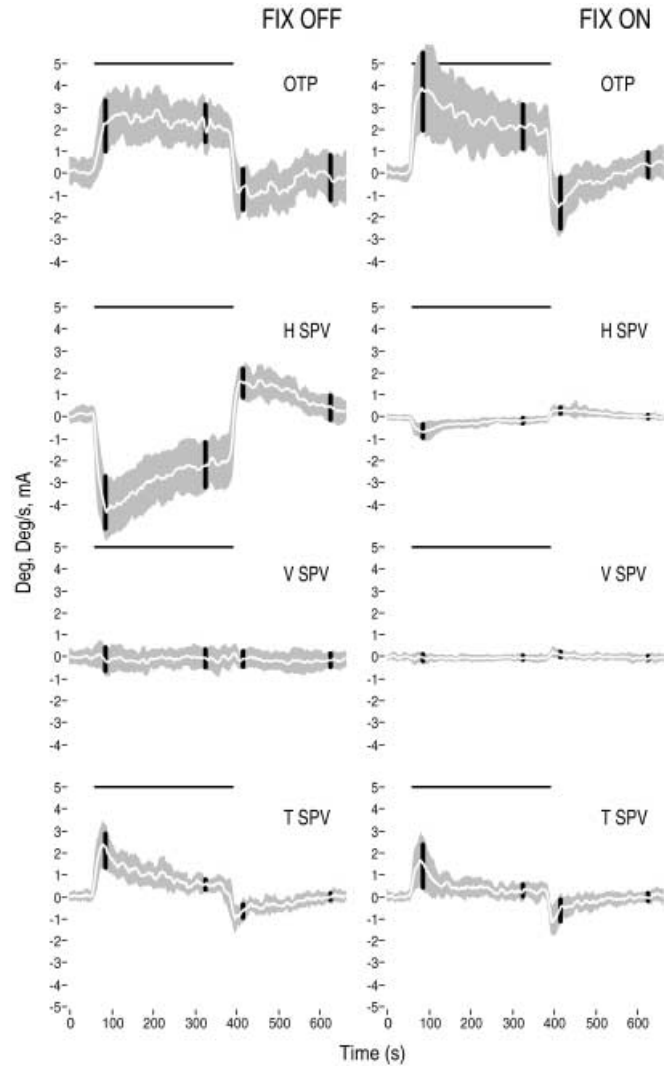


Fig. 2 Average eye-movement responses and associated 95% confidence intervals for (rows) OTP, horizontal SPV, vertical SPV and torsional SPV for all ten subjects in the FIX OFF (*left half*) and FIX ON (*right half*) conditions (*columns*). The averages for the time periods of interest ("onset", "maintained", "overshoot" and "final", in chronological order) are superimposed as vertical black lines. The horizontal bars indicate the presence and the strength of the galvanic stimulus. Note that, since confidence intervals are calculated using *n*=10 (subjects) in this figure, the range indicated by the confidence intervals is not directly comparable to that shown in Fig. 4

onset in darkness, with a corresponding overshoot in horizontal position at stimulus offset. Horizontal and vertical eye position responses are not analysed any further, due to subjects being directed by the experimenter to return their gaze to a central position when there was no fixation light present.

In the FIX ON condition (Fig. 2 *right half*), the fixation light suppressed horizontal and vertical eye movements to negligible levels, thus making it possible to isolate the torsional position and velocity components of the eye-movement response evident in all subjects. Although the magnitude of the OTP response tended to be

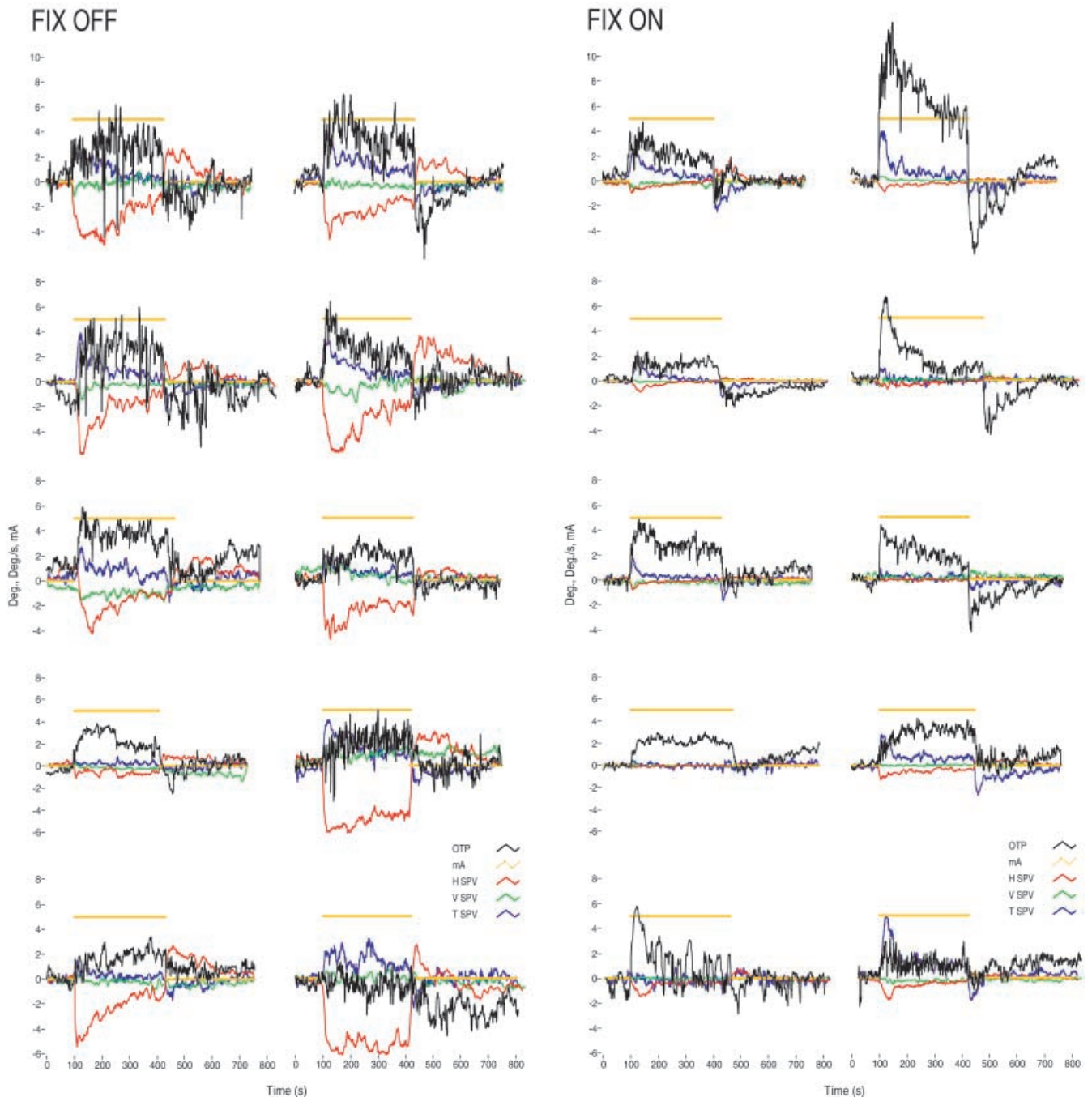


Fig. 3 Individual 3-D eye-movement traces for all ten subjects during 5 mA CLAR surface GVS in darkness (FIX OFF, left half) and during fixation (FIX ON, right half). Subjects 1 through 10 are arranged in numerical order, top to bottom then left to right. Due to the high degree of conjugacy of the oculomotor response to GVS (Fig. 1), traces here show the left-eye response only, for clarity. The orange horizontal bars represent the presence and the strength of the galvanic stimulus

larger with fixation than in darkness, this difference was not statistically significant ($P > 0.05$), due to the high degree of variability between subjects. With fixation, GVS also produced a change in ocular torsional velocity, with the slow phase directed towards the anode and away from the cathode. Again, although the magnitude of tor-

sional SPV tended to be smaller with fixation than in darkness, the difference was not statistically significant ($P > 0.05$) due to the considerable variability in responses.

A modified Prony method (Osborne and Smyth 1995) was used to fit exponentials in order to determine time constants for the decay of response to the onset and offset of the galvanic stimulus (Table 1). Our algorithm assumed that, at the end of a sustained period of stimulation (or long after stimulus offset), the response had decayed to an asymptotic value (the “maintained” or “final” response), but there were no constraints on these values. Horizontal and vertical eye position were not included in this analysis, nor were time constants calculated for OTP (in darkness) or for vertical SPV (in either

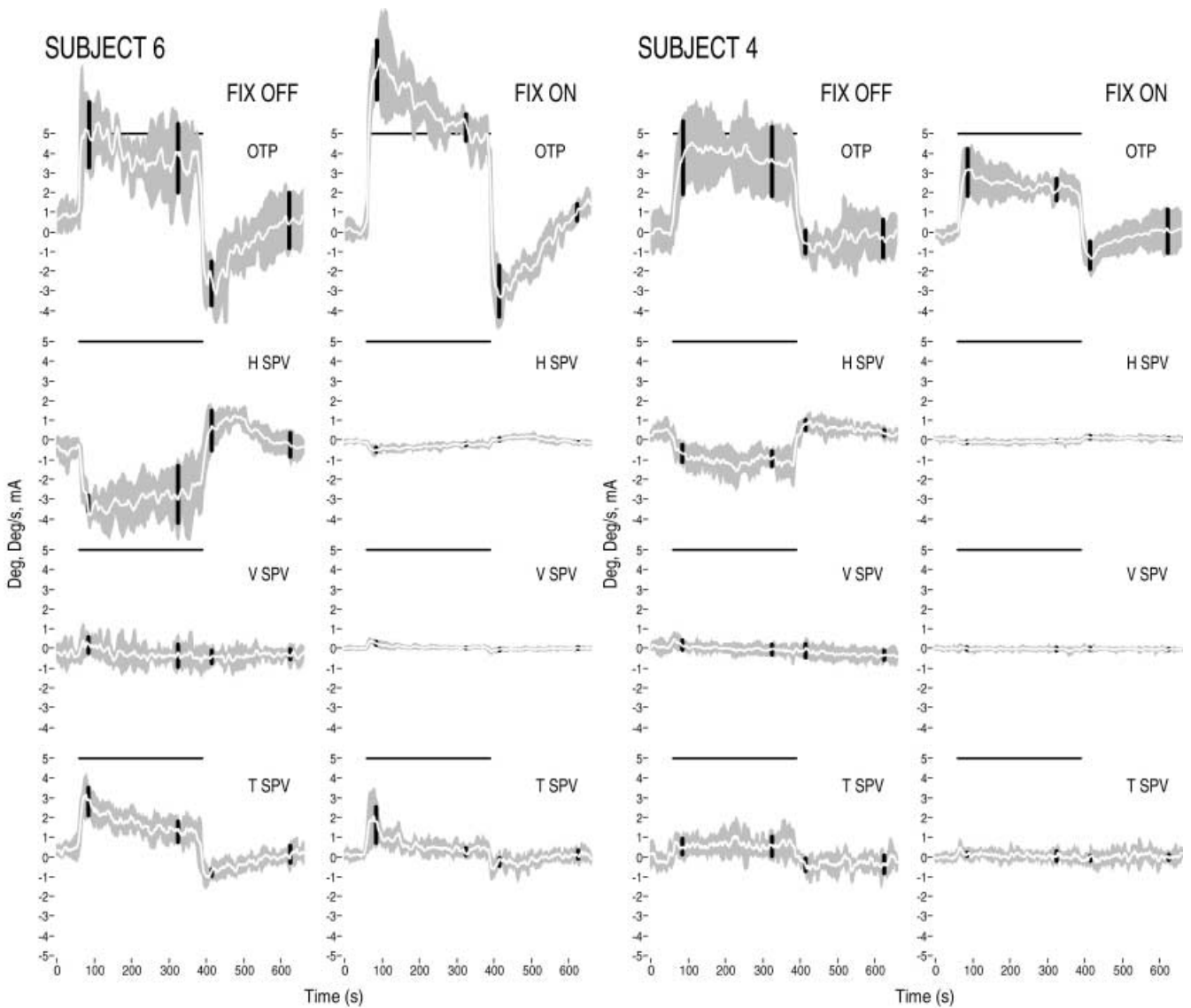


Fig. 4 Average eye-movement responses and associated 95% confidence intervals for OTP, horizontal SPV, vertical SPV and torsional SPV for two subjects over five repeats each (rows), in the FIX OFF (left) and FIX ON (right) conditions (columns). The averages for the time periods of interest (“onset”, “maintained”, “overshoot” and “final”, in chronological order) are superimposed as vertical black lines. The horizontal bars indicate the presence and the strength of the galvanic stimulus. Note that, since confidence intervals are calculated using $n=5$ (repeats per subject) in this figure, the range indicated by the confidence intervals is not directly comparable to that shown in Fig. 2

condition), as these responses showed no significant decay. In addition, individual subjects were excluded from these calculations if their response did not show substantial decay. Time constants for those responses which showed a significant decay were of the order of 1.5 min. Calculating the time constant of decay in data of this kind can be problematic. The relationship between the galvanic vestibular stimulus and complex eye-movement responses is not as straightforward as observed in electronic or thermal systems. A number of factors influence

the adequacy of the fit, including the fact that eye-movements come from multiple sources and different components interact in complex ways. Time constants derived from this kind of data can be no more than approximations and little can be concluded from comparisons between the various eye-movement components, between the conditions of fixation or between stimulus onset and offset.

Between-subject comparisons

Notwithstanding the similarities just described, the eye-movement response to GVS tended to vary markedly across subjects. The peak values of OTP and horizontal and torsional SPV varied greatly across subjects. In addition, the proportions of these eye-movement components show no consistent relationship between subjects (Fig. 3). In addition, although subjects tended to demonstrate similar rates of decay and adaptation of torsional eye movements to GVS, the magnitudes of the decay and

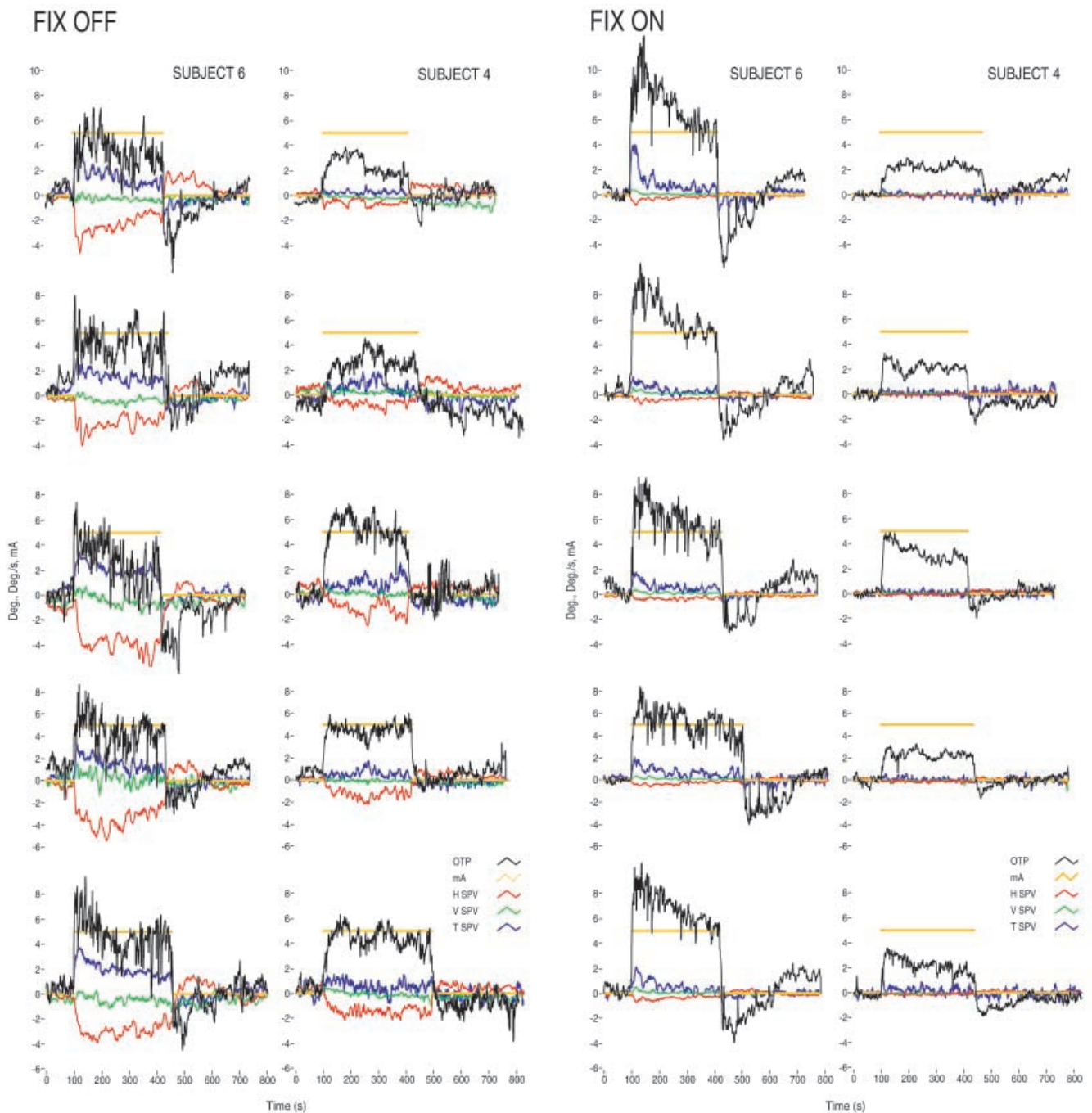


Fig. 5 The 3-D eye-movement response traces for two subjects (*columns*) in five repeated sessions (*rows*) during 5 mA CLAR surface GVS in darkness (FIX OFF, *left half*) and during fixation (FIX ON, *right half*). As the responses were highly conjugate, only the left-eye traces are shown here, for clarity. The *orange horizontal bars* represent the presence and the strength of the galvanic stimulus

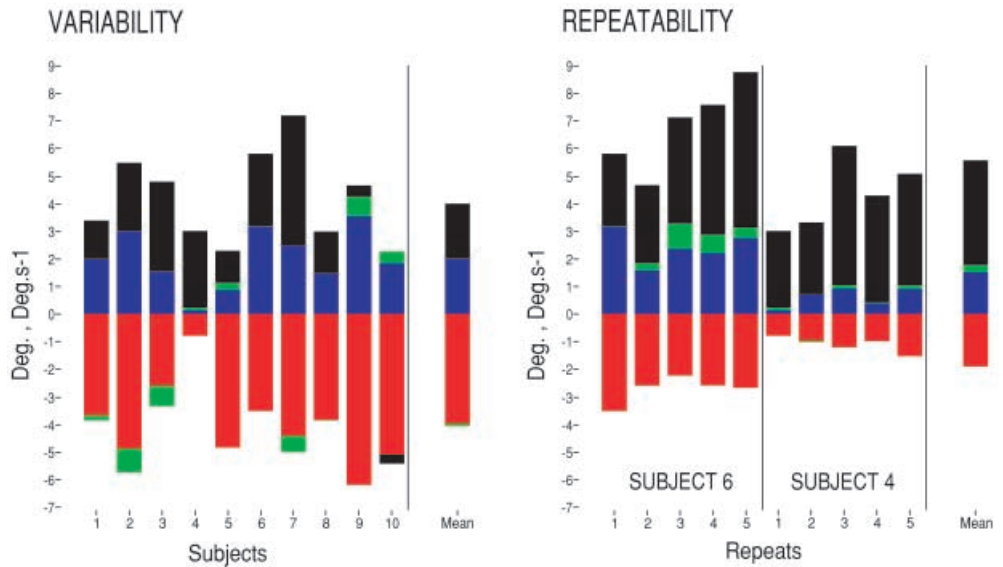
adaptation varied substantially across subjects. Furthermore, there seems to be no simple relationship between the magnitude of decay/adaptation and the magnitude of the peak amplitudes of the eye-movement components, even within subjects (Fig. 3).

Experiment 2: repeatability

As in experiment 1, four measures (“onset”, “maintained”, “offset” and “final”) were used to summarise subjects’ 3-D oculomotor responses. Averages and 95% confidence intervals for these measures are shown in Fig. 4, superimposed on the continual averages and 95% confidence intervals for horizontal, torsional and vertical SPV, and OTP.

Once again, responses to GVS varied between subjects. There was substantial difference between the two subjects in the peak values of OTP and horizontal and torsional SPV. In addition, there was considerable differ-

Fig. 6 Amplitude of the 3-D eye-movement response components (indicated by different colours: *black* OTP, *red* horizontal SPV, *green* vertical SPV, *blue* torsional SPV) to surface GVS in ten subjects ('variability') and two subjects over five repeated trials ('repeatability') at a representative moment ('onset' response in darkness). A comparison of eye-movement response components within subjects (*right half*) shows repeatability of the relative ratios of these components and little within-subject variability in magnitude between trials. However, greater variability can be seen between subjects (*left half*), both in terms of overall magnitude and in terms of the relative ratios of response components



ence between the two subjects in the ratios of the magnitudes of these eye-movement components.

Within-subject comparisons

There was some variability in oculomotor responses to GVS within subjects. Each subject's peak values of OTP and horizontal and torsional SPV varied somewhat between trials. There was also some within-subject variability in the relative proportions of these eye-movement components. The variability observed within subjects was, however, much less marked than the variability observed between subjects. The relatively large between-subject variability and relatively small within-subject variability can be seen in the raw data in both the FIX OFF and FIX ON conditions (Fig. 5), and is summarised in Fig. 6.

Between- vs within-subject variability

Analysis of variance was carried out for experiment 1 (the factor being "Subject") and individually for each subject in experiment 2 (the factor being "Repeats"). A comparison of the results of these analyses showed that the *F* ratios of the results of experiment 1 were, on average, 2.6 times greater than the *F* ratios for experiment 2. This indicates that the magnitude of response alone varies more than twice as much between subjects as it does within subjects over repeated trials. We have been unable to quantify satisfactorily the difference in variability in the relative ratios of response components between subjects to within subjects, however, Fig. 6 shows the reliability of within-subject responses over repeated trials when compared to between-subjects responses. For example, subject 4 shows a large OTP change in response to GVS (in darkness) in all repeats, and this response is

accompanied in all repeats by a relatively minimal amount of nystagmus in all three dimensions. In comparison, subject 6 shows a larger overall response to GVS onset (in darkness), with a large OTP response accompanied by substantial horizontal and torsional SPV but with negligible vertical nystagmus. The ten normal subjects in experiment 1 show a wide variety of patterns of responses to GVS onset (in darkness), from those with systematic changes predominantly in SPV (for example, subjects 5 and 9), from those with systematic changes predominantly in eye position (for example, subject 4), to a combination of these (for example, subjects 3 and 7). Further, subject 4 shows both little decay and little overshoot of the response to onset of GVS, either in darkness or with fixation (Fig. 5), in all repeats, whereas subject 6 shows both significant decay and overshoot in eye-movement response to GVS in both conditions (Fig. 5) in all repeats. Again, the ten normal subjects in experiment 1 show variability in the amount of decay and overshoot of their eye-movement response (Fig. 3), from those who show almost no decay at all and minimal overshoot (for example, subjects 3 and 4), to those who show a relatively moderate amount of decay and overshoot (for example, subjects 1 and 8), to those whose response decays almost to zero during GVS followed by a relatively large overshoot on offset of GVS (for example, subject 7).

Discussion

The present study has confirmed previous findings that there is substantial between-subject variability in responses to GVS. The results of the present study also show that oculomotor responses are more reliable within subjects than might have been anticipated and that, therefore, GVS may be more reliable than previously thought. This was able to be shown because of the im-

improvements in GVS delivery techniques, eye-movement recording system and stimulus parameters employed in this study. Other research has tended to highlight only the large between-subject variability in responses to GVS, and this is probably because, in general, studies have tested different subjects at each session, rather than testing the same subjects over repeated sessions.

The variability that can be seen within subjects seems to be characterised by changes in the overall amplitude of the eye-movement response. That is, the magnitudes of OTP, torsional SPV and horizontal SPV may all increase or decrease together from trial to trial, but do not, within any subject, seem to vary independently of one another. In other words, the pattern of responses, or ratio of eye-movement response components, is consistent within a subject. The variability which does occur on repeated presentations is most likely a result of subject arousal or fatigue, or inconsistencies in test administration such as the placement of electrodes, irregularities in current level, etc.

Since there is this within-subject variability in the gain of the response, at least as much variability in gain must be present between subjects. However, variability in gain is expected to be greater overall between subjects than within subjects. This is because between-subjects comparisons also include another potential source of overall gain variability between subjects (*viz.* subject sensitivity to GVS). Our results show that the variability is greater between subjects than within. However, the difference in variability between Between-Subject and Within-Subject comparisons is much greater than has typically been seen in response to natural stimuli. Responses to natural stimuli (such as head rotation) tend to have smaller variability due to individual differences because subjects do not tend to differ greatly in factors affecting the response, such as the orientations of their canals (Schneider et al. 2000).

The variability between subjects is not only larger than that within subjects, but also of a different kind. Between-subject variability comprises the small changes in gain, which result from such factors as subject sensitivity, but also large differences in the ratio of eye-movement response components. This leads to the conclusion that there is some factor that varies across individuals but is unchanging within individuals and contributes significantly to the variability in GVS responses. Since responses to natural stimuli show little between-subject variability, then these responses cannot be affected by the source of large intersubject variability seen here.

These results lend weight to the suggestion that large between-subject variability in response to GVS is affected by some factor that varies across individuals. The present results show that the response to GVS is reliable within subjects. Therefore, the factor influencing variability between subjects in GVS is relatively unchanging within subjects. That is, eye-movement responses to GVS are affected by individual differences to a greater degree than other influences (such as differences between test sessions or subject sensitivity).

Individual differences in responses to GVS are reminiscent of individual differences in responses to caloric vestibular stimulation. For example, Proctor and Glackin (1985) found greater variability across subjects than day-to-day variability within subjects for caloric and postrotatory test scores. Responses to stimuli like calorics and GVS may be more variable across individuals because there has been no advantage to evolving a useful response to them. This is in contrast to natural stimuli, such as tilts and rotations, to which normal humans show a similar, beneficial compensatory response. In addition, calorics and GVS are quite different to natural stimuli because they can stimulate endorgans in unusual ways, producing patterns of activity in various endorgans which would be impossible to match with natural stimuli. Individuals can be expected to interpret the resulting ambiguous or contradictory patterns of sensations in different ways. Another source of variability may arise from the fact that subjects have had no experience with these novel stimuli.

Responses to caloric stimulation are also thought to be influenced by individual differences in morphology of the vestibular system. The structure and orientation of the organs in the temporal bone, and characteristics such as density/pneumatisation of the temporal bone, are believed to influence thermal conductivity, which is crucial to differences in the pattern of eye-movement response in the caloric vestibular test. One study estimated that 23% of variability in responses to calorics in a normal population could be attributed to a combination of anatomical characteristics (pneumatisation of the petrous and buttress areas of the temporal bone and dimensions of the auditory canal) affecting heat flow in the vestibular system (Proctor 1982). Similarly, individual differences in the morphology of the vestibular system entail individual differences in impedance throughout the vestibular system, thus affecting how the current delivered at the surface influences each endorgan, and the resulting pattern of eye-movement responses.

The present study showed that 3-D eye-movement responses to long-duration, maintained, large-amplitude, bilateral, surface GVS show good within-subject repeatability, while confirming that there is substantial between-subject variability, both in the size of the response and in the ratio of response components. This is perhaps due to individual differences in morphology, resulting in idiosyncratic patterns of stimulation of the endorgans and concomitant eye-movement responses. Thus, GVS may be a more reliable stimulus than has been anticipated from the literature.

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