

Recruitment properties and significance of short latency reflexes in neck and eye muscles evoked by brief lateral head accelerations

James G. Colebatch · Danielle L. Dennis ·
Sendhil Govender · Peggy Chen · Neil P. McAngus Todd

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Abstract Short lateral head accelerations were applied to investigate the recruitment properties of the reflexes underlying the earliest ocular and cervical electromyographic reflex responses to these disturbances. Components of both reflexes are vestibular dependent and have been termed “ocular vestibular evoked myogenic potentials” and “cervical vestibular evoked myogenic potentials”, respectively. Previous investigations using a unilateral vestibular stimulus have indicated that some but not all these vestibular-dependent reflexes show a simple power law relationship to stimulus intensity. In particular, crossed otolith-ocular reflexes showed evidence of an inflection separating two types of behaviour. The present stimulus acts bilaterally, and only the earliest crossed otolith-ocular reflex, previously shown to have a strictly unilateral origin, showed evidence of an inflection. Reflex changes in ocular torsion could, in principle, correct for the changes associated with translation for an elevated eye, but our findings indicated that the responses were consistent with previous reports

of tilt-type reflexes. For the neck, both vestibular and segmental (muscle spindle) reflexes were evoked and followed power law relationships, without any clear separation in sensitivity. Our findings are consistent with previous evidence of “tilt-like” reflexes evoked by lateral acceleration and suggest that the departure from a power law occurs as a consequence of a unilateral crossed pathway. For the neck, responses to transients are likely to always consist of both vestibular and non-vestibular (segmental) components. Most of the translation-evoked ocular and cervical reflexes appear to follow power law relationship to stimulus amplitude over a physiological range.

Keywords Vestibular reflexes · Translational reflexes · Vestibulo-ocular · Vestibulocollic · Cervicocollic reflexes

Introduction

Lateral head accelerations occur naturally when walking or running and may evoke both vestibular-dependent translational ocular (tVOR: Angelaki 2004) and cervical reflexes (tVCR). Both reflexes potentially have an important role in stabilising the head and thus vision in response to linear accelerations. Short latency vestibular-dependent ocular (Iwasaki et al. 2007; Todd et al. 2009) and cervical (Rosengren et al. 2009) reflexes can be recorded from specific muscles in human subjects in response to brief lateral accelerations and are termed “ocular vestibular evoked myogenic potentials” (oVEMPs) and “cervical vestibular evoked myogenic potentials” (cVEMPs), respectively. In the case of the neck, however, reflexes evoked by impulsive stimuli appear to also include short latency responses arising from muscle afferents, a segmental stretch or cervico-cervical reflex (CCR: Halmagyi et al. 1995). Ocular

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J. G. Colebatch · D. L. Dennis · S. Govender · P. Chen
Prince of Wales Clinical School and Neuroscience Research
Australia, University of New South Wales, Randwick, Sydney,
NSW 2052, Australia

J. G. Colebatch (✉)
Institute of Neurological Sciences, Prince of Wales Hospital,
Randwick, Sydney, NSW 2031, Australia
e-mail: j.colebatch@unsw.edu.au

N. P. M. Todd
Faculty of Life Science, University of Manchester,
Manchester M13 9PL, UK

recordings from monkeys, however, indicate that, while torsional responses are evoked by lateral accelerations, the effects are not compensatory (Telford et al. 1997) although these observations have not been made with the eyes elevated.

In our recent study (Dennis et al. 2014), we investigated vestibular evoked reflexes (VEMPs) evoked using activation with air-conducted (AC) sound, to examine the recruitment properties of unilateral otolith-dependent reflexes for both ocular and neck muscles. We showed that the changes with stimulus intensity were well fitted by an exponential relationship or power law for most of the neck (sternocleidomastoid muscle) responses, but that this did not hold for the extraocular muscle responses recorded contralateral to the stimulus. The latter showed the presence of a threshold above which a steeper gradient for the response curve was present. It was not clear from this study whether this effect was specific to the type of stimulation used and its laterality or a consequence of the reflex pathway itself.

The present study was designed to investigate further these relationships using a short, lateral head acceleration evoked using a bone-conducted (BC) impulsive stimulus. The impulse was applied so as to cause a near-pure lateral acceleration of the head (Rosengren et al. 2009), within the physiological range. The stimulus was chosen to be very different from that used by Dennis et al. (2014) in order to determine to what extent the relationships these authors had shown were a consequence of the afferents excited or were properties of the pathways mediating the reflexes, upstream from the receptors. This form of stimulation is known to be particularly effective for exciting afferents from the utricle (Fernández and Goldberg 1976) and is commonly used to identify utricular afferents (Jamali et al. 2009). Of particular importance to our study was to examine whether the properties we had previously shown using a unilateral vestibular (otolith) stimulus also applied to this contrasting form of stimulation and, in the case of the neck projection, the nature of the interaction between vestibular-dependent and stretch reflex/muscle afferent-dependent reflexes.

Methods

Subjects

Fourteen healthy adults aged 18–57 with no history of vestibular dysfunction participated in this study. Nine subjects were tested at Prince of Wales Hospital, Sydney (5 men, 4 women; mean age 31 ± 15 years) and 5 subjects at University of Manchester (2 men, 3 women; mean age 38 ± 13 years). Twelve subjects were common to this study

and the preceding study investigating the input–output properties of the VEMP with air-conducted stimulation (9 from Sydney: 5 men, 4 women; 3 from Manchester: 1 man, 2 women). Subjects gave written consent according to the Declaration of Helsinki before the experiment, and the study was approved by the local ethics committees in Sydney and Manchester.

Stimuli

The stimulus waveform consisted of a third-order gamma distribution (Ross 2007) with a 4-ms rise time which was delivered at the mastoid using a customised hand-held minishaker (model 4810, Brüel and Kjaer P/L, Denmark) with an attached perspex rod (diameter 2.5 cm, length 9.2 cm). Stimuli were generated using customised software attached to a laboratory interface (1401 micro, Cambridge Electronic Design, Cambridge UK). A reference intensity of 10 V peak (136 dB peak FL) was used.

Cervical and periocular montages

Electromyographic (EMG) activity was recorded simultaneously from the SCMs and below the eyes using self-adhesive Ag/AgCl electrodes (Cleartrace 1700-030, Conmed Corp., NY, USA). For the neck recordings, the active electrodes were placed on the upper third of the SCM belly and the reference electrodes on the sternal end of the clavicles. An earth electrode was placed above the lateral third of the clavicle. Subjects reclined to $\sim 30^\circ$ above horizontal and were required to lift their heads to activate the SCM muscles for the duration of the recording. For the extraocular recordings, electrodes were placed on the orbital margin inferior to both eyes and reference electrodes were positioned approximately 3 cm below them. This montage, with upgaze, has been shown to record activity specifically from the inferior oblique (IO) muscle (Weber et al., 2012). A custom-made headband was used to secure a laser pointer that projected a red spot onto the ceiling (Fig. 1). The pointer was positioned to produce an elevated gaze of $\sim 30^\circ$ for the subject, and this was used as a constant point of reference for eye elevation regardless of slight changes in head position. Amplitudes were measured from the SCMs and extraocular muscles both contralateral and ipsilateral to the stimulated mastoid. EMG was recorded from 20 ms before to 100 ms after stimulus onset and averaged over 200–250 individual trials. Signals were amplified (cervical: $2,500\times$; ocular: $100,000\times$), bandpass filtered (cervical: 8 Hz–1.6 kHz; ocular: 5 Hz–1 kHz), and both were sampled at 5 kHz by means of a second CED Power 1401 using SIGNAL software (version 3, Cambridge Electronic Design, Cambridge UK).

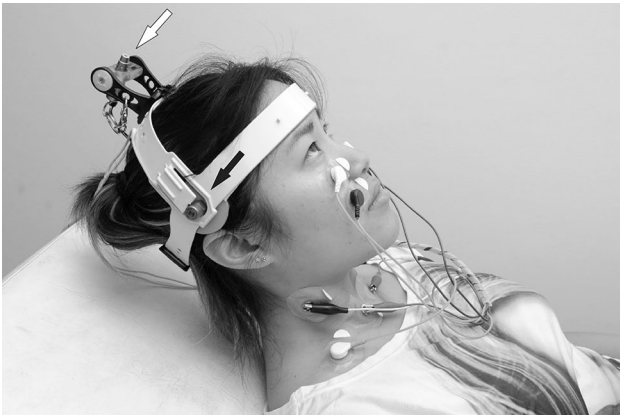


Fig. 1 Typical experimental setup showing vestibular reflexes and head accelerations recorded simultaneously in a single subject. Linear accelerometers were placed above both ears (*black arrow*). A laser light (*white arrow*) was used to direct the subjects gaze to a projected red spot and allowed gaze elevation to be kept constant despite changes in head position during head lifting

Accelerometry

Head acceleration was recorded at the same time as the ocular and neck reflexes and was measured using two uni-axial accelerometers (Endevco 751-100), mounted in the headband (Fig. 1) and positioned to sit on the left and right temporal bones directly superior to the ear. Head acceleration was recorded from 20 ms before to 100 ms after stimulus onset and averaged from 200 to 250 individual trials. This was very closely related to applied force (FL) intensities, and equivalent accelerations are given at some places in the text, based upon the average relationship between FL intensity and the induced acceleration. Accelerations are given with respect to g , the acceleration due to gravity.

Stimulus protocol

Each subject was stimulated on one mastoid (10 on the left and 4 on the right) using a “positive” stimulus, accelerating the head contralaterally, away from the minishaker. The direction of head acceleration has been shown to determine the nature of the evoked responses on the two sides (Todd et al. 2008b; Rosengren et al. 2009). Response peaks were thus termed ipsilateral or contralateral with respect to the stimulated side and abbreviated using their latency and polarity. Electrode impedance was maintained below 10 k Ω before recordings commenced. The initial (maximum) stimulus intensity used was 136 dB peak FL (equivalent to approx. 6.6 N). The stimulus intensity was then decreased in 6 dB increments to 124 dB FL and then in 3 dB increments from thereon with 100 dB FL being the lowest intensity recorded. The order was reversed for one subject (starting at 100 dB FL and then increasing to 136 dB FL).

Recording was stopped at 103 dB FL for 4 subjects due to fatigue, and 5 subjects from the UK laboratory were not tested at 121 dB FL. The neck reflex data for one subject at 130 dB FL were excluded due to a recording error.

For all subjects, the initial and repeat recordings were checked offline for reproducibility of peaks and then averaged. The averaged recording was then used for amplitude and latency measurements. An overall grand average for all subjects was made for both ocular and cervical recordings.

Data analysis

The standard deviation of the prestimulus background activity in the averaged record was used to determine whether a response was present for any given trial. The criterion was an amplitude 2.5 SDs above or below the prestimulus mean level. The latencies of any significant peak also had to be appropriate. Amplitudes were measured when the peaks were above the significant criterion. When they were not, to avoid bias, the amplitude value at the average latency for the peak was used. Latencies were only measured for significant peaks.

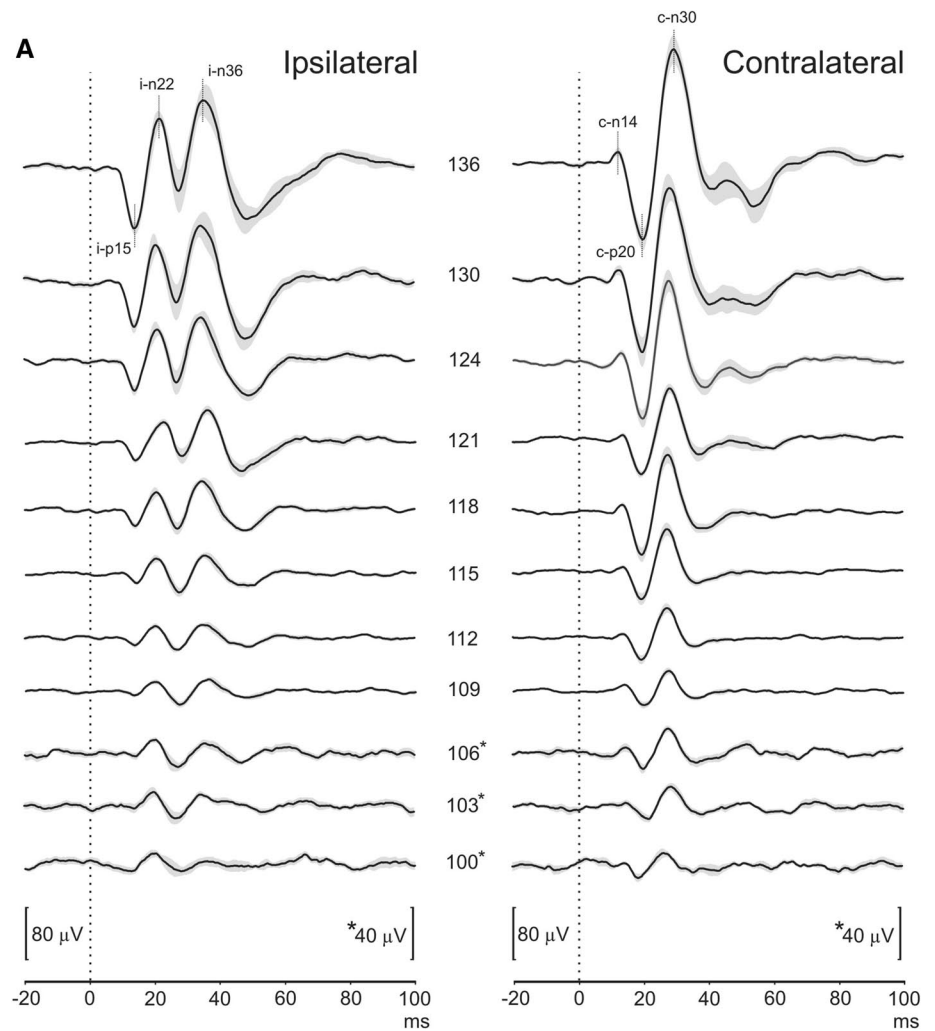
A threshold for each peak was determined for all subjects. We allowed a peak to fail to reach significance in a single intensity trial if it returned for at least the next lowest intensity (either -6 or -3 dB). Subjects with no responses to the most intense and second-most intense stimuli were assumed to have a threshold of 142 dB for the missing peaks. The overall thresholds for each subject were determined based on the i-p15 response for the cervical recording and the c-n11 response for the ocular reflexes (Figs. 2, 3).

Regression analysis was performed using log-transformed data. The data were based upon the model of Todd et al. (2008a), namely:

$$V(s) = ks^{\beta}$$

where k = scaling constant, s = intensity (Pa) and β is the power law parameter. When the data were transformed to dB versus dB plot, β is given as the slope of the linear fit. We used dB as $20 \times \log_{10}(\text{value})$ for both sound intensity and reflex amplitude. Given that the reflexes evoked are determined by the direction of head acceleration (Todd et al. 2008b; Rosengren et al. 2009), the data were therefore recoded as ipsilateral or contralateral to the stimulus. Regression analysis was performed for log-transformed population-averaged values for all subjects' i-p15, n22, n36, c-n14, p20 and n30 (SCM recording), and c-n11, p16, n20 and i-p10, n16, p21 and n26 (IO montage) from 136 to 100 dB FL. Departures from a linear relationship were determined by performing a quadratic regression and testing the significance of the reduction in residual error due to the quadratic component (Snedecor and Cochran 1989).

Fig. 2 Grand mean recordings ($n = 14$) for the impulse evoked cervical reflexes at each stimulus intensity (136–100 dB FL). **a** Shows that the responses from the SCMs ipsilateral and contralateral to the side of stimulation have different waveforms, corresponding to the two different directions of acceleration with respect to the midline, as reported by Rosengren et al. (2009). The ipsilateral (p15 and n22) and contralateral (p20 and n30) can be seen to be present for all stimulus intensities. The grey areas show the SE of the mean (SEM). Note higher gains for three lowest intensities, indicated by the asterisks. **b** Shows the (raw) amplitudes of the different peaks plotted against stimulus intensity

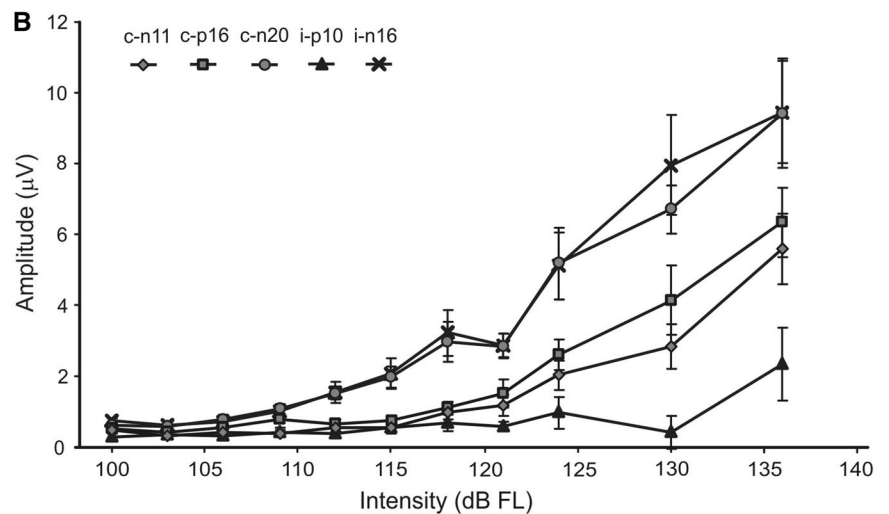
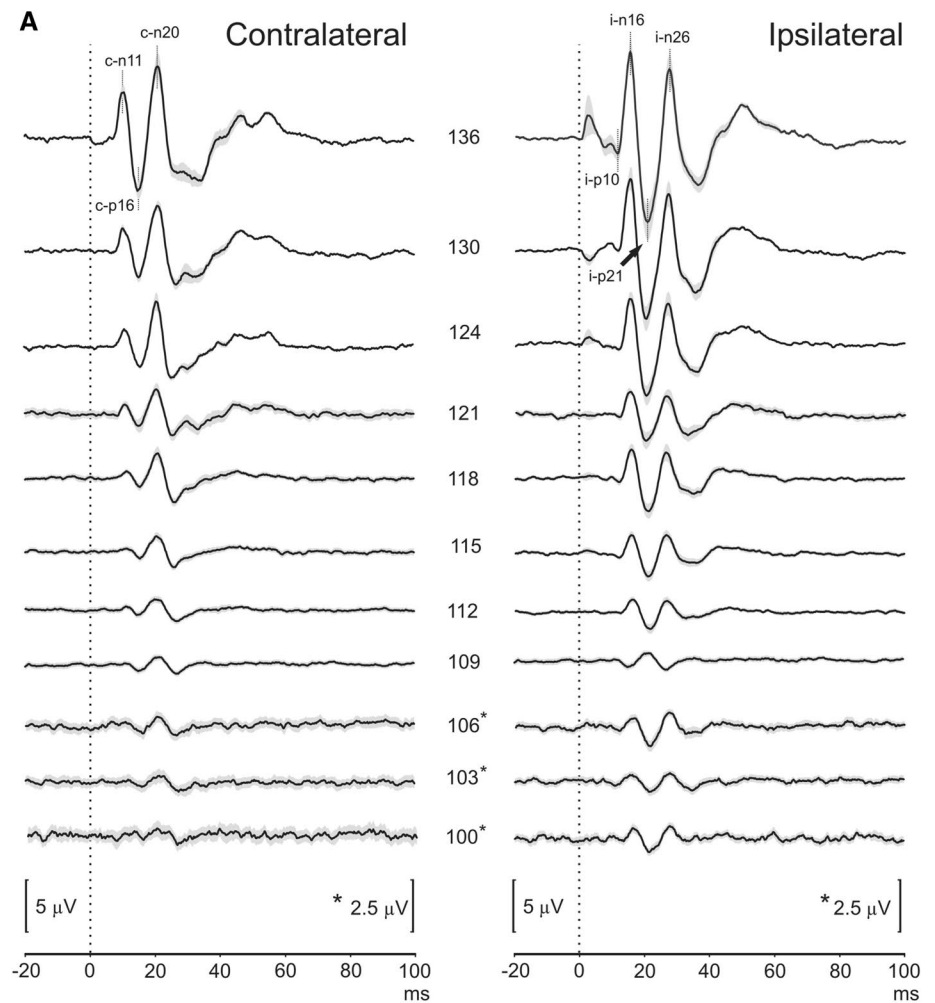


Where the quadratic term was significant, separate regressions were performed for the lower and upper intensities. Regression gradients were compared using the method of Gardner and Altman (1989).

Results

ANOVA showed a significant side to side difference for several of the extraocular peaks: the ipsilateral p10

Fig. 3 Grand mean recordings ($n = 14$) for the impulse evoked extraocular reflexes at each stimulus intensity (136–100 dB FL). **a** The responses from the eyes contralateral and ipsilateral to the side of stimulation have different waveforms, corresponding to the two different directions of acceleration with respect to the midline (Todd et al. 2008b). The earliest peaks tended to show higher thresholds than later peaks for both eyes. Contralaterally, the n20 response can be seen to the lowest intensity, while ipsilaterally, the n16, p21 and n26 responses persist to the lowest intensity. The grey areas show the SE of the mean (SEM). Note higher gains for three lowest intensities, indicated by the asterisks. **b** Shows the (raw) amplitudes of the different peaks plotted against stimulus intensity



($p = 0.039$), n16 ($p = 0.022$), p21 ($p = 0.002$) and n26 ($p = 0.012$) responses, but not for any of the cervical responses. In all cases, the ocular reflex response evoked from left-sided stimulation was larger than for the right (on average less than half the amplitude from the left).

Overall, the responses contralateral to the side stimulated were also smaller for right-sided stimulation, but these did not reach statistical significance. The side to side differences were much less for the cervical reflexes. There was no significant difference in background SCM EMG

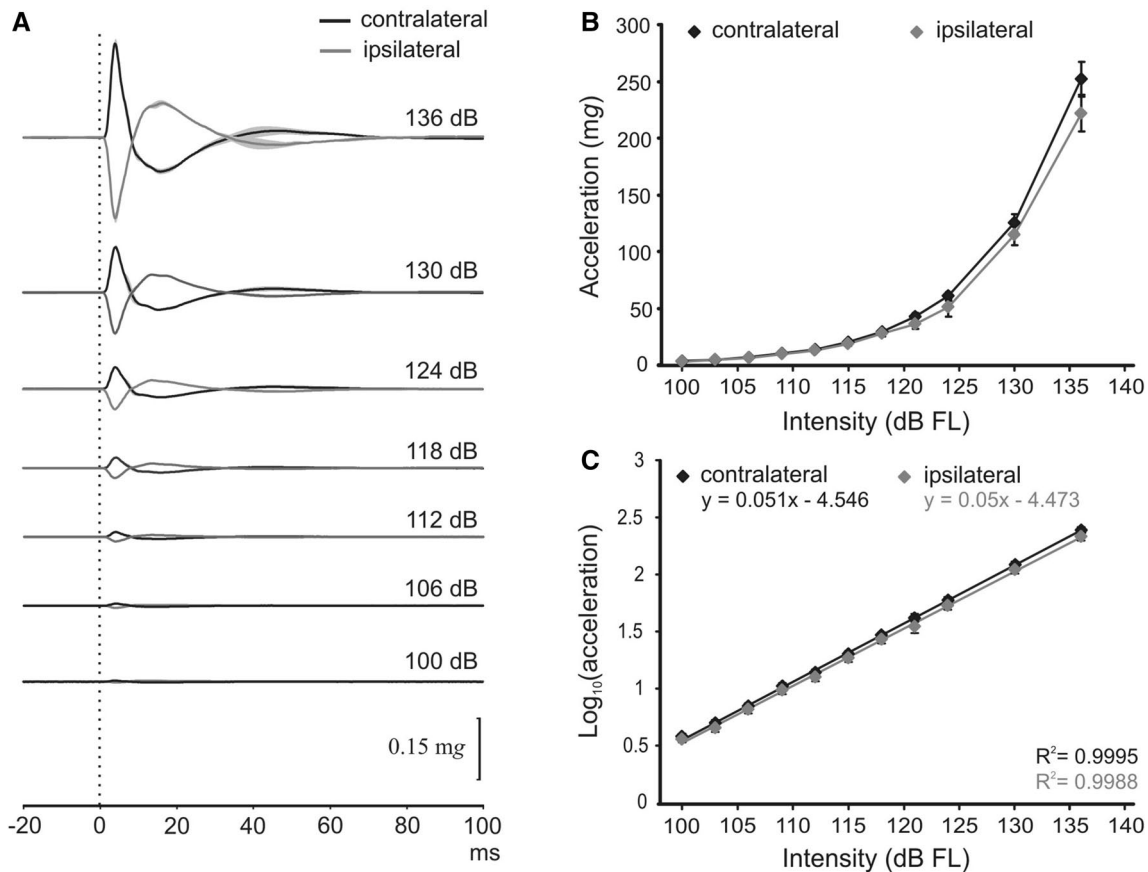


Fig. 4 Grand mean recordings of ($n = 14$) of accelerometry traces (**a**) for a range of stimulus intensities (136–100 dB) measured on the side (ipsilateral) or opposite side (contralateral) to the stimulus. Acceleration values decreased exponentially with decreasing intensity

activity ($105.5 \pm 30.0 \mu\text{V}$) across intensities ($F_{10,266} = 0.8$, $p = 0.583$). The prestimulus standard deviation was $1.9 \mu\text{V}$ for the grand-averaged cervical reflexes and $0.1 \mu\text{V}$ for the grand-averaged ocular recordings. For the individual subjects, these values were higher, being on average $5.4 \mu\text{V}$ for the cervical and $0.3 \mu\text{V}$ for the ocular recordings.

Accelerometry

The largest mean acceleration amplitudes were recorded at 136 dB FL (contra: $251.8 \pm 57.1 \text{ mg}$; ipsi: $221.6 \pm 60.8 \text{ mg}$) and decreased exponentially with decreasing intensity (Fig. 4; $F_{10,268} = 289.4$, $p < 0.001$, Supplementary Table 1). Acceleration amplitudes for the contralateral side were slightly larger than for the ipsilateral side ($F_{1,268} = 4.0$, $p = 0.046$). At the lowest stimulus intensity (100 dB FL = -36 dB from initial), mean acceleration amplitudes for the contralateral and ipsilateral sides were $3.8 \pm 0.8 \text{ mg}$ (-35.5 dB) and $3.7 \pm 0.8 \text{ mg}$ (-36.4 dB), respectively. There was no overall effect of intensity on acceleration peak latency (mean range: 4.0–4.3 ms:

(b) and a log plot of the values demonstrates the highly linear relationship between head acceleration and intensity (c). Ordinate values can be converted to dB with respect to 1 mg by multiplying by 20

Supplementary Table 1). In the text, where approximate acceleration is given, it is the mean of the values derived for the ipsilateral and contralateral sides.

Response amplitudes and thresholds: grand average results

Grand average traces are shown in Fig. 2 (cervical) and 3 (extraocular) and represent the mean of over 2,000 individual trials. The baseline recordings indicated that multiple peaks were significant by our criteria. The signal-to-noise ratio (SNR) for the baseline response varied from 103 (c-n30) to 11 (c-n14; Table 1). For the cervical montage, the significant peaks were the ipsilateral i-p15, n22, n36 and contralateral c-n14, p20, n30. For the extraocular montage, the contralateral c-n11, p16, n20 and the ipsilateral i-p10, n16, p21, n26 peaks were above our criterion. These peaks were therefore measured for this and the remaining intensities in all subjects. The extraocular reflex peaks c-n20, i-n16, i-p21 and i-n26 changes with intensity were all highly correlated ($r^2 = 0.99$) and had similar amplitudes and thresholds (Table 1), and the same was true for the cervical c-p20 and

Table 1 Grand-averaged peaks at baseline

| | Cervical montage (SCM) | | | | | Ocular montage (IO) | | | | | | | |
|--------------------------------------|------------------------|-------------|-------------|-------------|-------------|---------------------|-------------|-----------|-------------|--------------|-------------|-------------|--------------|
| | i-p15 | i-n22 | i-n36 | c-n14 | c-p20 | c-n30 | c-n11 | c-p16 | c-n20 | i-p10 | i-n16 | i-p21 | i-n26 |
| Amplitude (μV) | 87.0 | 66.8 | 92.2 | 18.1 | 118 | 178 | 4.5 | 5.2 | 7.0 | 1.5 | 8.4 | 8.1 | 6.8 |
| SD (μV) | 2.0 | 2.0 | 2.0 | 1.7 | 1.7 | 1.7 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| Grand average threshold (dB FL) | 109 | 100 | 103 | 106 | 100 | 100 | 106 | 103 | 100 | 124 | 100 | 100 | 100 |
| Population average threshold (dB FL) | 114.9 ± 7.2 | 109.9 ± 6.2 | 105.6 ± 6.2 | 123.5 ± 5.4 | 105.4 ± 4.1 | 104.1 ± 3.8 | 120.1 ± 8.9 | 112 ± 7.9 | 105.6 ± 3.1 | 122.7 ± 12.4 | 106.2 ± 6.2 | 106.2 ± 6.9 | 106.2 ± 10.3 |

Measurements made using the grand-averaged recordings

SD standard deviation of prestimulus recording (noise), FL force level, SCM sternocleidomastoid, IO inferior oblique

Population average refers to the average of measurements made in individual subjects

c-n30 peaks ($r^2 > 0.99$); thus, the extraocular i-p21 and i-n26 and cervical c-p20 peaks will not be discussed in detail. For the grand-averaged cervical reflexes, the i-p15-n22 response was above the criterion to 109 dB FL and the i-n22 peak to 100 dB FL, while for the extraocular reflexes, the c-n11 response exceeded criterion to 106 dB FL.

Response amplitudes and thresholds: individual results

The mean amplitudes obtained with the 136 dB stimulus for the cervical peaks were 93.1 μV (i-p15), 92.7 μV (i-n22), 139.4 μV (i-n36), 25.2 μV (c-n14), and 188.8 μV (c-n30). For the extraocular reflexes, the amplitudes were 5.6 μV (c-n11), 6.4 μV (c-p16), 9.4 μV (c-n20), 2.4 (i-p10), and 9.5 μV (i-n16). At this intensity, nearly all subjects showed all potentials, the exceptions being, for the neck, the c-n14 (9/14) and for the ocular recording site, the c-n11 (12), the c-p16 (13) and the i-p10 (7 subjects: Supplementary Tables 2 and 3).

The mean thresholds measured from the individual data (the “population average”) were mostly similar to those using the grand average, and only two peaks (cervical c-n14 and ocular c-n11) showed a discrepancy of more than 10 dB (Table 1). For the cervical montage, the c-n30 had the lowest threshold overall (104.1 dB FL, equivalent to 5.6 mg acceleration or -45 dB vs 1 g) and the c-n14 the highest (123.5 dB FL, equivalent to 52.9 mg acceleration or -26 dB vs 1 g). For the extraocular responses, the i-n16, i-p21 and c-n20 peaks had the lowest thresholds of about 106 dB FL (6.9 mg or -43 dB vs 1 g), while the c-n11 threshold was 120.1 dB FL (35.6 mg or -29 dB vs 1 g). ANOVA analysis of individual thresholds (excluding peaks c-p20, c-p21 and c-n26), with Bonferroni correction, confirmed that the short latency potentials had higher thresholds; thus, the cervical i-p15, c-n14 and the extraocular c-n11 and i-p10 peaks all had significantly higher thresholds than the cervical c-n30 and the extraocular c-n20 and i-n16 ($p < 0.001$ for all) potentials.

Relationship between amplitude and intensity

The relationship was curvilinear for the raw amplitudes versus stimulus intensity (dB FL) plots for all the potentials measured (Fig. 5). The raw amplitudes were transformed to dB and plotted against stimulus intensity. We combined the data for right and left stimulation for the extraocular recordings, having shown there was no significant difference for the gradient using all or just the left-sided stimulation results. The gradients then ranged from 0.353 to 0.768 for the peaks in the cervical montage and from 0.365 to 0.728 for those with the extraocular montage (Table 2). The cervical c-n14 and extraocular i-p10 gradients were both lower than the other gradients. Testing for linearity showed a significant

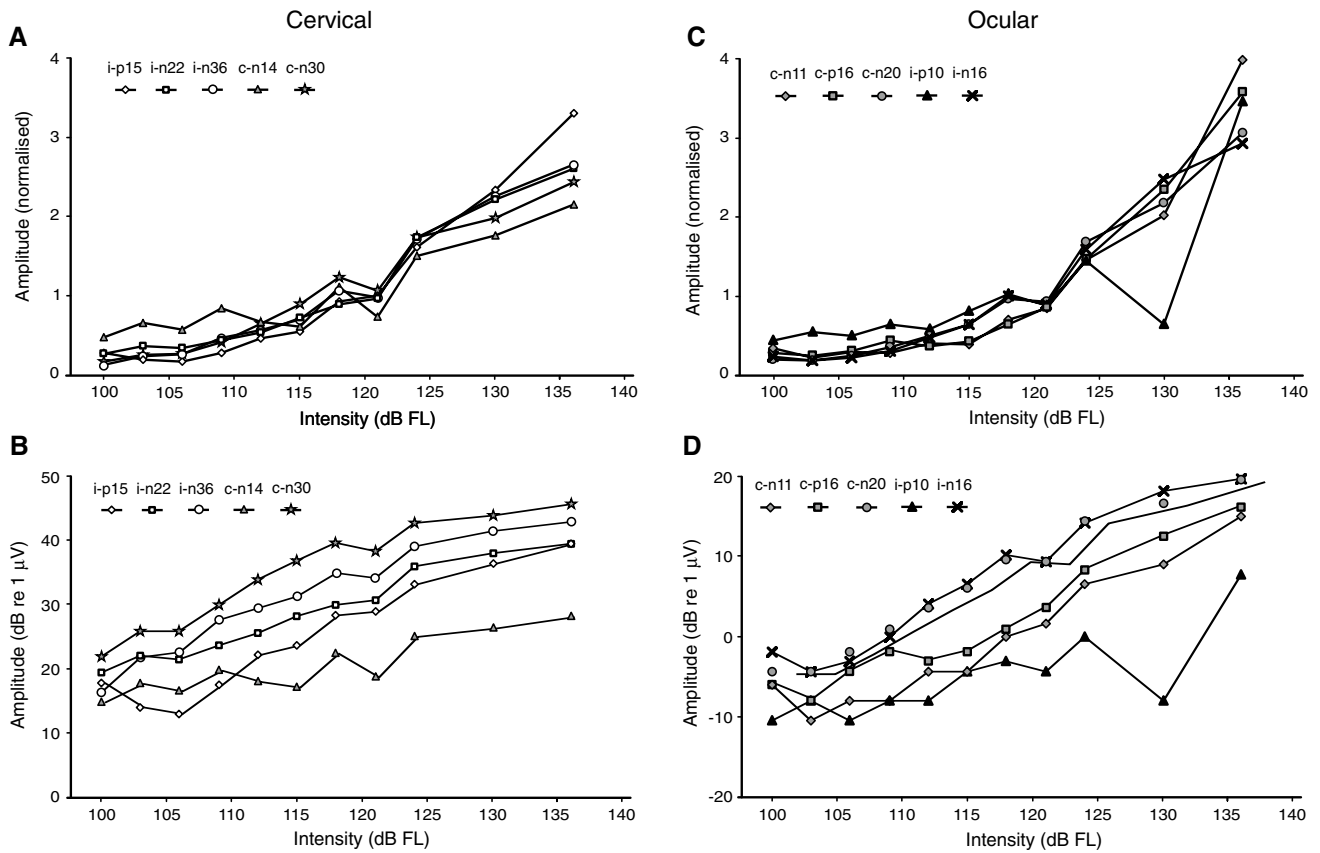


Fig. 5 Averaged, transformed responses. The *upper half* of the figure shows the superimposed averaged responses for the subjects’ cervical potentials (**a**) and extraocular potentials (**c**), plotted against stimulus intensity. The upper relationships have been normalised so the average amplitude is 1. Both sets of relationships are nonlinear, with

increasing rates of increase for stronger stimuli. The *lower half* of the figure shows the effect of the logarithmic transform of reflex amplitude. It can be seen that the relationships are more linear, although significant curvature was still present for the later cervical potentials (**b**) and the early crossed extraocular reflex responses (**d**)

Table 2 Regressions for cervical and ocular responses

| Peak | Cervical montage (SCM) | | | | | | Ocular montage (IO) | | | | | | |
|----------|------------------------|--------|--------|-------|--------|--------|---------------------|-------|-------|-------|-------|-------|-------|
| | i-p15 | i-n22 | i-n36 | c-n14 | c-p20 | c-n30 | c-n11 | c-p16 | c-n20 | i-p10 | i-n16 | i-p21 | i-n26 |
| Gradient | 0.768 | 0.602 | 0.736 | 0.353 | 0.670 | 0.687 | 0.677 | 0.665 | 0.728 | 0.365 | 0.728 | 0.644 | 0.621 |
| r^2 | 0.928 | 0.972 | 0.953 | 0.820 | 0.943 | 0.932 | 0.911 | 0.935 | 0.978 | 0.652 | 0.960 | 0.965 | 0.953 |
| $F(1,8)$ | 0.124 | <0.001 | 16.9** | 0.989 | 17.3** | 18.0** | 10.0* | 7.87* | 1.22 | 0.62 | 0.11 | 1.52 | 0.56 |

Gradients for $20 \times \log$ (raw amplitude) versus intensity

SCM sternocleidomastoid, IO inferior oblique. F values apply to the test of significance of the quadratic fit (see text)

* $p < 0.05$, ** $p < 0.01$

nonlinear component for the cervical i-n36, c-p20 and c-n30 peaks and for the extraocular c-n11 and c-p16 peaks. This was confirmed with testing the gradients for the low and high intensities. The gradients for the i-n36, c-p20 and c-n30 cervical peaks were significantly *reduced* for stimuli over 118 dB FL, and the gradients for the c-n11 and c-p16 ocular peaks were significantly *increased* for stimuli over 118 dB FL (Table 3). Figure 6 shows the contrasting fits obtained using the low and high intensity regressions for the initial

responses for the cervical i-p13/n23 response compared with the early extraocular responses (c-n10/p16), showing the increased gradient that occurred for the ocular response.

Discussion

We have previously shown that the stimulus used here evokes a near-pure lateral head acceleration, the adequate

Table 3 Cervical and ocular regressions for log raw data for low and high intensities

| Peak | Cervical montage (SCM) | | | | | | Ocular montage (IO) | | | |
|-------------------|------------------------|--------|---------|--------|--------|--------|---------------------|--------|--------|--------|
| | c-p20 | | c-n30 | | i-n36 | | c-n11 | | c-p16 | |
| | Low | High | Low | High | Low | High | Low | High | Low | High |
| Gradient | 0.897 | 0.378 | 0.976 | 0.375 | 0.979 | 0.506 | 0.203 | 0.829 | 0.291 | 0.833 |
| r^2 | 0.968 | 0.902 | 0.969 | 0.839 | 0.960 | 0.875 | 0.361 | 0.978 | 0.664 | 0.973 |
| p (vs 0) | 0.000** | 0.013* | 0.000** | 0.029* | 0.001* | 0.020* | 0.207 | 0.001* | 0.048* | 0.002* |
| p (low vs high) | 0.002* | | 0.002* | | 0.016* | | 0.005* | | 0.004* | |

Gradients for $20 \times \log$ (raw amplitude) versus intensity for peaks with significant quadratic curvature

Gradients for normal subjects using stimuli 100–115 dB FL (“Low”) and 118–136 dB (“High”)

SCM sternocleidomastoid, IO inferior oblique

* $p < 0.05$, ** $p \leq 0.0001$

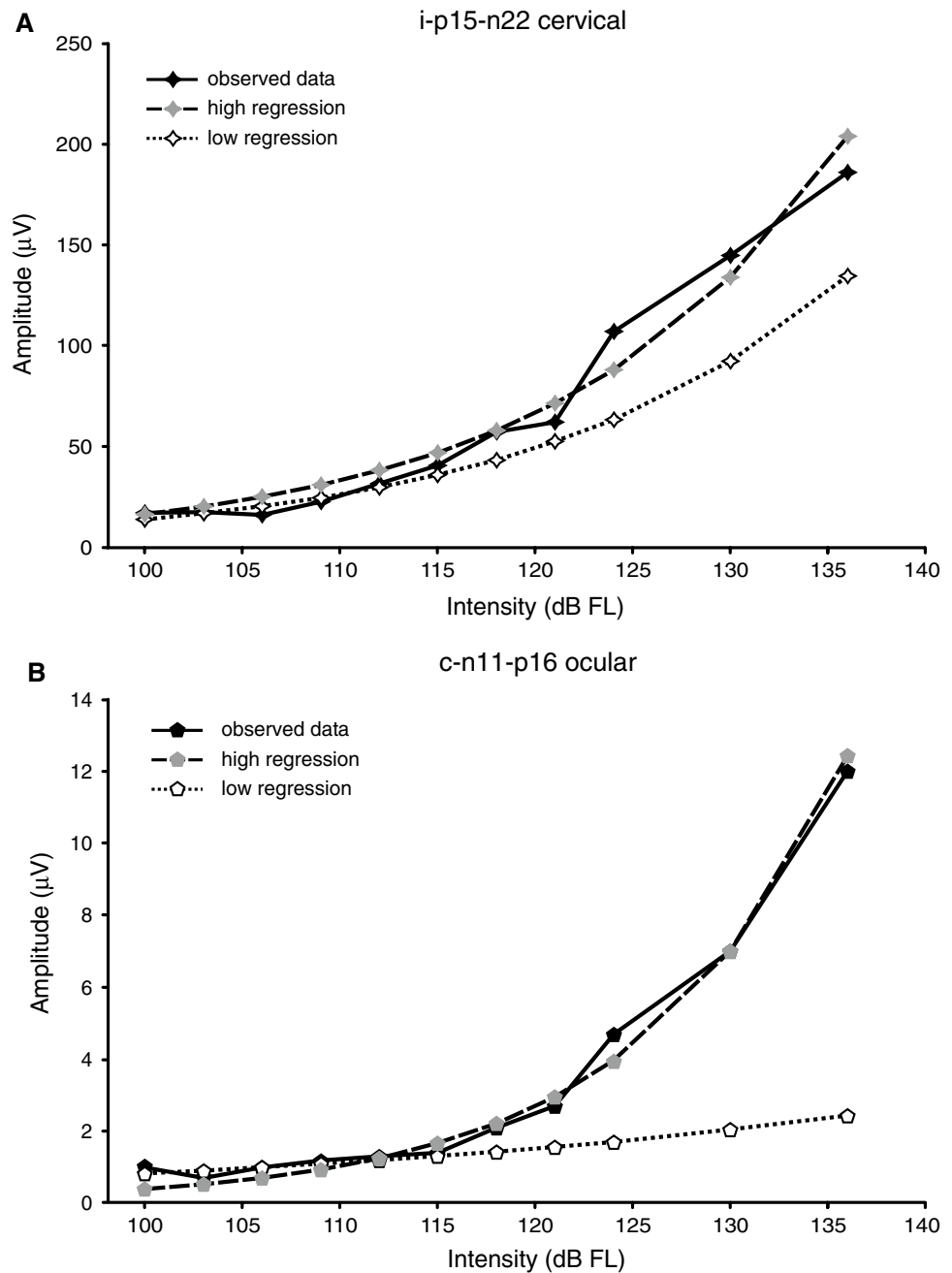
stimulus for utricular afferents (Fernández and Goldberg 1976). Consistent with this, short latency, acceleration direction-dependent reflexes can be evoked from ocular muscles (oVEMPs: Todd et al. 2008b), the neck (cVEMPs: Rosengren et al. 2009) and the legs (postural reflexes: Laube et al. 2012). Positive (medial) head accelerations were associated with an initial crossed negativity (Westin and Brantberg 2014), and it is likely that all the extraocular responses recorded here are vestibular dependent (Todd et al. 2009). It has been proposed that the oVEMP response is an expression of either the sound-evoked VOR (Welgampola et al. 2009) or the linear (translational) VOR (Todd et al. 2012). Agrawal et al. (2013) have provided evidence that the amplitudes of oVEMP reflexes evoked by an impulsive head acceleration correlate with perceptual thresholds for linear motion, consistent with an effect on the utricle. Todd et al. (2008a) originally reported that oVEMPs evoked by short duration low-frequency whole-head vibrations were well fitted by a power law over more than a 30 dB range of stimuli, and we have confirmed that this applies to most of the peaks investigated. In addition, the average gradient of the four later ocular peaks that we found here (0.68, Table 2) was close to that reported by Todd et al. (0.66). We have also confirmed a higher threshold for the initial crossed ocular response than for the later responses (Paillard et al. 2014).

Laterality effects were not the main focus of this investigation, and the numbers of subjects stimulated on each side were not balanced. However, left-sided stimulation gave larger crossed and ipsilateral ocular responses than right-sided stimulation. Interestingly, the effect was much less marked for the neck. In our previous study (Dennis et al. 2014), there was a significantly larger left-sided response for the ocular c-p16 response only. Vestibular projections to the thalamus are predominantly crossed (Lopez and Blanke 2011), but utricular projections may be the opposite (Meng et al. 2001). Hemisphere asymmetries to vestibular

stimulation have been shown using functional imaging, in which the activation within the non-dominant hemisphere is stronger (Dieterich et al. 2003; Todd et al. 2014). Our findings are novel in suggesting that vestibular asymmetries may be expressed at a brainstem level, and a feature of vestibular otolith fibres projecting rostrally rather than caudally. These findings will need to be confirmed with further experiments specifically designed to investigate laterality effects.

Using the conventional oVEMP recording site, as here, Govender et al. (2011) reported that only the c-n11 behaved as if it was solely of (crossed) unilateral origin, confirming earlier observations (Iwasaki et al. 2007). Likewise, the i-p10 probably arises as a crossed response from the contralateral utricle. There may be a parallel for this unilaterality in the present findings for recruitment. Using unilateral (sound) stimulation, Dennis et al. (2014) found that all the crossed responses had evidence of an increased response gradient after a threshold was passed. In the present case, this applied only to the earliest (unilateral) crossed responses with the later (bilateral) responses showing consistent power law relationships with higher gradients. While the c-n11-p16 response has obvious diagnostic applications, it may be that unilateral utricular excitation is associated with a change of gradient and higher threshold than for bilateral, coherent responses, perhaps explaining the difficulty in demonstrating this projection using utricular nerve stimulation and intracellular recordings (Uchino et al. 1996). Our findings make it unlikely that the change in gradient reported by Dennis et al. (2014) for the AC-evoked c-n10 was due to a change in the receptor being stimulated (e.g., from saccule to utricle with increasing intensity), because the present stimulus showed the same features, but appears to target utricular receptors (see above). The gradient change is also unlikely to be due to excitation of utricular receptors per se, because, if so, it should also have been a feature of the ipsilateral oVEMP

Fig. 6 Observed versus predicted data. **a** Shows the observed (*solid line*) and predicted amplitudes of the group-averaged i-p15-n22 (cVEMP) responses against intensity, using regressions based upon the lower (*dotted line*) and higher (*dashed line*) intensities. **b** Shows similar data using the oVEMP c-n11-p16 responses, fitted using the low (*dotted line*) and high (*dashed line*) intensity responses



response to AC stimulation. Thus, we tentatively conclude that the gradient change is a property of the crossed oVEMP pathway, when excited unilaterally.

A major role of vestibular reflexes is to stabilise eye position despite head motion. The translational VOR compensates for retinal displacement in response to lateral and fore-aft accelerations and is a relatively recent evolutionary development (Baloh et al. 1988; Bronstein and Gresty 1988; Angelaki 2004). Retinal signals also contribute, but at longer latencies (Gellman et al. 1990). Irregular otolith afferents are most sensitive to bone-conducted stimuli (Curthoys et al. 2006) and also contribute to the tVOR

(Angelaki et al. 2000). Ocular responses to rapid translations begin with similar latencies to the earliest peaks shown here (Bush and Miles 1996; Angelaki and McHenry 1999; Crane et al. 2003). The ocular reflex responses recorded here have been shown to originate from the inferior oblique muscle (Weber et al. 2012), which is a target of short latency utricular reflexes (Suzuki et al. 1969). The inferior oblique muscles are not the primary targets of the tVOR, and indeed, Aw et al. (2003) found only small torsional responses to their impulsive roll stimuli. However, this could be a consequence of the (neutral) eye position normally used in such studies. If the eye is elevated,

Listing's Law implies a substantial amount of ocular torsion occurs with abduction and adduction (Ferman et al. 1987). In the case of a lateral acceleration, this would require intorsion of the eye contralateral to the stimulated side and extorsion of the ipsilateral eye. However, the earliest oVEMP excitability change contralaterally is a negativity (indicating excitation: Colebatch and Rothwell 2004), and the first ipsilateral potential is a positivity (indicating inhibition: Colebatch and Rothwell 2004). Given that the inferior oblique extorts the eye (Leigh and Zee 2006), these excitability changes are not consistent with a role in compensating for torsional changes associated with eye elevation. A lateral acceleration, however, cannot be distinguished initially from a lateral tilt to the opposite side (Telford et al. 1997) and a tilt would be expected to evoke the torsional VOR, a reflex with a relatively fixed gain (Migliaccio et al. 2006). Our observations are consistent with those reported by Telford et al. (1997), who found in monkeys that torsional movements were induced by lateral accelerations designed to excite the utricle, effects that appeared to be tilt responses. The size of the torsional responses was found to decrease rapidly with increasing stimulus frequency, in contrast to the compensatory linear eye movements. The increase of the oVEMP previously observed with eye elevation (Govender et al. 2009) raises the question of whether the gain of the torsional responses might also be modulated by eye elevation.

The translational vestibulocollic reflex (tVCR) has been little investigated (Goldberg and Cullen 2011). The acceleration amplitudes we have used in this study are similar to those encountered physiologically during walking (Pozzo et al. 1991). We have previously reported upon the nature of the short latency reflex in the sternocleidomastoid muscles evoked by short duration lateral accelerations (Rosengren et al. 2009). These consist of a series of responses, the polarities of which are determined by the direction of acceleration. The responses on both sides are dominated by initial positive waves (i-p15 and c-p20), earlier on the side of the positive acceleration, and which are generated by the vestibular apparatus on each side. Because the initial response is inhibitory and the sternocleidomastoid muscles flex and rotate the head to the opposite side, these responses, due to their asynchrony, would tend to extend as well as rotate the head towards the side of the applied acceleration. The latter response is consistent with a role in gaze stabilisation during translation (Angelaki 2004). In contrast to the extra-ocular responses, the later ipsilateral negativity, i-n36, is unaffected by vestibular lesions and is likely to represent a stretch reflex in the ipsilateral SCM (Rosengren et al. 2009). Our findings support the exquisite sensitivity of the muscle spindles to small disturbances, including sensitivity to acceleration (Matthews and Stein 1969; Hasan and Houk 1975; Honeycutt et al. 2012).

Matthews and Stein (1969) showed that the muscle spindle sensitivity to acceleration occurred with high frequencies of vibration and, at 100 Hz, a displacement of 0.1 μm (equivalent to a peak acceleration of 4 mg) was sufficient to modulate the discharge of a primary spindle ending. We found the population thresholds were as low or lower for the stretch reflex i-n35 peak as for the vestibular-dependent responses. The i-n35 and other potentials with presumed segmental input (c-p20 and c-n30) deviated from a power law relationship, but this was due to a reduction in gradient with the larger stimuli. The responses differed from the otolith-dependent responses as they showed very little directional specificity and thus are consistent with excitation by transmitted vibration (Lance and De Gail 1965). The neck appears to be unusual in having both vestibular and segmental stretch reflex responses to transient accelerations. Our findings indicate that while both were activated by all the accelerations we applied, and had similar average thresholds, their effects differed. The otolith-dependent reflexes tended to rotate and extend the neck while the segmental stretch reflexes evoked a co-contraction, stiffening the neck and thereby damping any potential oscillation (Goldberg and Cullen 2011). Most of the ocular and cervical reflexes showed a power law relationship to the provocative stimulus over the range of accelerations that we investigated, and the same might therefore be expected for the mechanical responses evoked.

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