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Spatial orientation in patients with chronic unilateral vestibular hypofunction is ipsilesionally distorted

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HIGHLIGHTS

- Visual vertical (VV) was measured in 13 patients with chronic unilateral vestibular hypofunction.
- VV shifts in the patients were significant only when rolled ipsilesionally.
- Thus VV testing in roll-tilted positions is recommended to identify more subtle vestibular deficits.

ABSTRACT

Objective: Acute unilateral peripheral–vestibular hypofunction (UVH) shifts the subjective visual vertical (SVV) ipsilesionally, triggering central compensation that usually eliminates shifts when upright. We hypothesized that compensation is worse when roll-tilted.
Methods: We quantified SVV errors and variability in different roll-tilted positions (0°, ±45°, ±90°) in patients with chronic UVH affecting the superior branch (SVN; $n = 4$) or the entire (CVN; $n = 9$) vestibular nerve.
Results: Errors in SVN and CVN were not different. When roll-tilted ipsilesionally 45° (9.6 ± 5.4° vs. −0.2 ± 6.4°, patients vs. controls, $p < 0.001$) and 90° (23.5 ± 5.7° vs. 16.8 ± 8.8°, $p = 0.003$), the patient's SVV was shifted significantly towards the lesioned ear. When upright, only a trend was noted (3.6 ± 2.2° vs. 0.0 ± 1.2°, $p = 0.099$); for contralesional roll-tilts shifts were not different from controls. Variability was larger for CVN than SVN ($p = 0.046$). With increasing disease-duration, adjustment errors decayed for ipsilesional roll-tilt and upright ($p \leqslant 0.025$).
Conclusions: The reason verticality perception was distorted for ipsilesional roll-tilts, may be the insufficient integration of contralesional otolith-input. Similar errors in SVN and CVN suggest a dominant utricular role in verticality perception, albeit the sacculus may improve precision of SVV estimates.
Significance: With deficiencies in central compensation being roll-angle dependent, extending SVV-testing to roll-tilted positions may improve identifying patients with chronic UVH.

1. Introduction

Innervation of the vestibular organs is provided by two branches of the vestibular nerve: the superior branch receives input from the horizontal and anterior semicircular canal (SCC) and the utriculus, the inferior branch contains axons from the posterior SCC and the sacculus (Gianoli et al., 2005; Curthoys, 2010). Sudden unilateral peripheral–vestibular hypofunction (UVH) typically presents as acute vestibular syndrome (AVS) (Tarnutzer et al., 2011a), i.e., prolonged vertigo/dizziness accompanied by nausea/vomiting nystagmus, gait ataxia and motion intolerance, and may result from isolated superior vestibular neuropathy (SVN), inferior vestibular neuropathy (IVN) or a combination of both (CVN). The most frequent cause of UVH is inflammation of the vestibular nerve (Strupp and Magnusson, 2015). After acute UVH, symptoms such as vertigo/dizziness, imbalance of stance and spontaneous nystagmus resolve within days to weeks (Okinaka et al., 1993; Halmagyi et al., 2010). This is usually achieved by central compensatory mechanisms including re-weighting of multisensory (vestibular, somatosensory, visual) input (Angelaki and Cullen, 2008; Sadeghi et al., 2010) and by minimizing the vestibular tone

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imbalance between the affected and the healthy side (Halmagyi et al., 2010), as the vestibular nerve remains hypofunctional in the majority of cases. Whereas compensation allows about 80% of patients to resume normal activities of daily life (Reid et al., 1996; Halmagyi et al., 2010), these mechanisms are insufficient to compensate for fast movements, causing brief spells of vertigo and oscillopsia during rapid head movements (Okinaka et al., 1993; Halmagyi et al., 2010).

Patients with UVH misperceive the direction of gravity, as assessed behaviorally for example by the subjective visual vertical (SVV) (Van Beuzekom and Van Gisbergen, 2000; Tarnutzer et al., 2009a, 2012a). The SVV thereby shifts towards the lesioned side when upright (Friedmann, 1971; Curthoys et al., 1991; Bergenius et al., 1996; Anastasopoulos et al., 1997; Lopez et al., 2008). Healthy humans show a distinct pattern of roll-angle dependent SVV errors: while roll over-compensation occurs at small (<60°) and very large (>120–135°) (Tarnutzer et al., 2009a) angles (E-effect) (Mueller, 1916), roll under-compensation is found for medium-sized (60–135°) angles (A-effect) (Aubert, 1861). Most likely the A- and E-effect are of central origin and a consequence of the processing of visual input as previous studies reported an accurate percept of vertical for the subjective postural horizontal (Mittelstaedt, 1983) and the subjective haptic vertical (Schuler et al., 2010) and horizontal (Wade and Curthoys, 1997). The trial-to-trial variability of SVV adjustments is roll-angle dependent, showing an m-shaped pattern with minimal variability when upright, maximal values around 120–135° roll and intermediate values in upside-down position (Tarnutzer et al., 2009a).

To which extent the estimates of the direction of gravity recover over time after acute UVH and whether this holds true both for upright and roll-tilted positions is unclear. Albeit decreasing in size, adjustment errors may remain abnormal years after UVH (Tabak et al., 1997). It seems reasonable to assume that also for roll-tilted positions errors decrease over time, though since upright is a more common posture when walking, the rate of improvement may be different at roll-tilted angles. Both more extensive exposure to upright position or the brain prioritizing accurate verticality perception when upright may explain such differences. Therefore, the offset of the estimated direction of gravity may rather be roll-angle dependent than constant. With otolith sensors being polarized, i.e., preferentially sensing ipsilateral roll (Dai et al., 1989), unilateral loss may result in more pronounced errors when roll-tilted towards the lesioned side. Alternatively, as a strategy to compensate for acute UVH, the brain could rely more on body-fixed orientation cues, resulting in an increased A-effect and a decreased E-effect on both sides (Tarnutzer et al., 2011b). The few studies that have addressed adjustment errors in chronic UVH while roll-tilted suggest a tendency towards roll under-compensation at small angles (Dai et al., 1989; Böhmer and Rickenmann, 1995; Bergenius et al., 1996; Betts et al., 2000), while no data is available for larger angles. The aim of this study was to characterize both the accuracy and precision of SVV adjustments in chronic UVH over a larger range of roll-tilted positions. Assessing the SVV in roll-tilted positions may be a more sensitive test to detect residual deficits after UVH and will shed more light on potential compensatory mechanisms and the role of the different macular organs. The relative contribution of utricular and saccular afferents to internal estimates of vertical remains debated. While preserved verticality perception in patients with isolated acute inferior vestibular neuropathy suggests no significant saccular contribution to the SVV, combining utricular and saccular input and taking a higher number of utricular compared to saccular afferents (1:0.6 (Rosenhall, 1972)) into account, resulted in accurately simulated SVV responses (Tarnutzer et al., 2009a). Likewise, for the otolith-ocular reflex a ratio of utricular-to-saccular input of 3:1 was proposed (De Graaf et al., 1996). Numerical simulations demonstrated a smaller but still significant contribution of saccular afferents to the detection of head roll (Jaeger and Haslwanter, 2004). Based on these observations we would predict larger SVV errors and trial-to-trial variability in case of CVN compared to SVN. The completeness of utricular/saccular damage may also influence verticality perception. Partial utricular function may be sufficient for verticality perception, while only in case of complete utricular/saccular loss would adjustment errors emerge.

2. Material and methods

2.1. Subjects

We compared 13 right-handed patients with chronic UVH (CVN = 9, SVN = 4) with 17 healthy controls (Table 1). All patients had a history of vestibular neuropathy (VN; symptom onset 11.3 ± 5.9 months ago, mean ± 1 standard deviation, range = 3–21 months) except two patients with vestibular schwannoma. Written informed consent was obtained after a full explanation of the experimental procedure in all participants. The protocol was approved by the Cantonal ethics commission Zurich (KEK-ZH-2013-0054) and was in accordance with ethical standards laid down in the 2013 Declaration of Helsinki for research involving human subjects.

2.2. Experimental setting

All potential study participants received vestibular testing before inclusion and the pattern of the peripheral–vestibular deficit was determined. The video-head-impulse test (vHIT; GN Otometrics, Taastrup, Denmark) was used to evaluate horizontal and vertical canals. SCC-hypofunction was defined as a reduction in angular vestibulo–ocular reflex (aVOR) gain and/or the occurrence of compensatory saccades. For gains, cut-off values of 0.8 (horizontal canals) and 0.7 (vertical canals) were proposed by the manufacturer, which have recently been confirmed over a broad range of ages (McGarvie et al., 2015).

Sacculus function was assessed by cervical vestibular-evoked myogenic potentials (cVEMPs) and utriculus function by ocular vestibular-evoked myogenic potentials (oVEMPs). In all participants air-conducted cVEMPs (brief clicks at 500 Hz, 2 ms duration, 2 series with 200 stimuli each) were obtained at two different intensities (90 and 95 dB normal hearing level) and responses from the sternocleidomastoid muscle were recorded. Additional air-conducted cVEMPs at 100 dB hearing level were applied if responses at 90 and 95 dB were insufficient (see Rosengren et al. (2010)) for further details on cVEMPs). If air-conducted cVEMPs at 100 dB were inconclusive (e.g. bilaterally absent responses), bone-conducted cVEMPs were obtained as well. Only the asymmetry ratio (AR) derived from the highest stimulus intensity was considered and if both air-conducted and bone-conducted cVEMPs were obtained, only results from bone-conducted cVEMPs were used. For recording of oVEMPs, brief vibrations (500 Hz, 4 ms duration, two times 200 stimuli, provided by a Minishaker, 4810 from Brüel and Kjaer, Denmark) were applied to the forehead and responses from the inferior oblique muscles were recorded (see Weber and Rosengren (2015)) for details). Differences in response amplitude (left vs. right) of >30% or absent responses were considered abnormal for both oVEMPs and cVEMPs.

Hypofunction of the horizontal and the anterior semicircular canal on the video-head-impulse test (reduction in gain and/or presence of compensatory saccades) and significant loss of utricular function (AR > 30% with stronger responses on the opposite side on oVEMP-testing) accompanied by normal saccular function (AR ⩽ 30% on cVEMPs) were required to meet the criteria for a