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TITLE:

Assessment of Static Graviceptive Perception in the Roll-Plane Using the Subjective Visual Vertical Paradigm

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KEYWORDS:
Otolith, vestibular, graviceptive, perception, subjective visual vertical, verticality, SVV, static, head-tilt, roll-plane, method

SUMMARY:
The perception of gravity is commonly determined by the subjective visual vertical in the head upright position. The additional assessment at head tilts of ± 15° and ± 30° in the roll plane ensures increased information content for the detection of impaired graviceptive perception.

ABSTRACT:
Vestibular disorders are among the most common syndromes in medicine. In recent years, new vestibular diagnostic systems have been introduced that allow the examination of all semicircular canals in the clinical setting. Assessment methods of the otolithic system, which is responsible for the perception of linear acceleration and perception of gravity, are far less in clinical use. There are several experimental approaches for measuring the perception of gravity. The most frequently used method is the determination of the subjective visual vertical. This is usually measured with the head in an upright position. We present here an assessment method for testing otolith function in the roll plane. The subjective visual vertical is measured in the head upright position as well as with head inclination of ± 15° and ± 30° in the roll plane. This extended functional paradigm is an easy-to-perform clinical test of otolith function and ensures increased information content for the detection of impaired graviceptive perception.

INTRODUCTION:
Impairment of otolith function can be caused by peripheral as well as by central vestibular conditions[1]. Peripheral vestibular causes include Meniere's disease, labyrinth infarction, as well as superior or inferior vestibular neuritis. Central otolith dysfunction can occur in lesions of central otolithic pathways from brain stem via thalamus[2] to the vestibular cortex[3]. In addition, diminished otolith reflexes are also found in cerebellar disorders[4]. While a number of standardized methods, such as caloric testing or video-head impulse test, are available for the

assessment of semicircular canal function, no standardized clinical measurement method exists for gravity estimation and verticality perception[5].

Since the otoliths are responsible for the perception of linear acceleration, otolith function can in principle be measured by linear acceleration by recording the so-called translational vestibulo-ocular reflex (t-VOR). However, this requires the use of special and complex equipment such as a parallel swing or linear sleds[4,6]. For the assessment of unilateral saccular and utricular function a specific off-center centrifugation test has been developed, which could be used clinically in balance laboratories with a specific rotational chair system[7]. When displacing the head by 3.5–4 cm from the rotation axis, the eccentrically positioned utricle is stimulated unilaterally by a resultant centrifugal force. In this paradigm otolith function can be determined either by measuring the resulting eye torsion or the subjective visual vertical (SVV). This procedure, however, also requires sophisticated equipment and the method still shows limited sensitivities for both SVV and eye torsion assessment[7]. Otolith function can further be quantified through eye movement recordings. Assessment can be done in horizontal or linear acceleration, but also during head- or body tilt in the roll plane with application of 3-D videooculography. The latter allows determination of ocular torsion. The clinical application of this method is also limited due to its low sensitivity[8]. The perception of body verticality (i.e., the sensation that I feel my body aligned with the true vertical) can be assessed by means of the so-called subjective postural vertical. In this experimental task, patients are seated in a chair in a motorized gimbal and asked to indicate when they entered and exited the upright position, while being tilted 15 ° in the pitch or roll plane. The disadvantage of this technique is not only its elaborate experimental approach, but also that it measures both otolith and body proprioceptive signals[9]. Whether vestibular evoked myogenic potentials (VEMPs) are useful clinical screening tools for otolith function in various clinical disorders is still controversial[10,11].

Visual tasks are currently the most frequently used clinical methods for measuring graviceptive function, which can be assessed through measurement of the subjective visual vertical (SVV)[12]. Seen from a precise physiological perspective, SVV is not a direct test of the otolith function alone, as the SVV is the result of a weighting between several sources of information (gravity, proprioceptive and also visual when they are available). However, for rapid clinical use, an easy application of this SVV task, the so-called bucket test, has been developed[13] especially for the emergency setting, enabling immediate detection of acute disturbances of graviceptive perception. The more precise and standardized procedure consists of letting an observer align a light bar or rod with the estimated vertical. Tested in darkness in healthy individuals in an upright position, deviations are limited to ± 2° from the earth vertical[14]. Using the SVV task, graviceptive function has so far been assessed in a variety of neurological conditions such as stroke[15,16] or Parkinson's disease[17]. Furthermore, impaired SVV-perception has also been reported in unilateral[18,19] or bilateral vestibular lesions[20], as well as in patients with benign paroxysmal positional nystagmus[21].

We here present a modified SVV assessment method, which measures SVV estimates not only in head-upright position but also at ± 15° and ± 30° head tilts in the roll plane. This paradigm increases the information content for the detection of graviceptive deficits and for systematic tilts of the SVV.

PROTOCOL:

The study was approved by the ethical committee of the Medical University of Vienna and has been performed in accordance with the ethical standards found in the Declaration of Helsinki. An informed consent was signed by all patients and controls before the study.

1. Installation of the patient in the chair

1.1. Perform the measurement binocularly. Install the patient in a stable chair with a backrest and a head fixation unit. The latter maintains the patient's head in a stable and defined position and consists of an elastic headband and a u-shaped headrest, which can be fixed to each other using an adhesive strap. Place the chair in a closable cabin allowing assessment of the SVV in the dark.

1.2. Position the headrest in the desired inclination angle (0°, ± 15° or ± 30°) by aligning it along the scale of a goniometer, which is attached to the chair´s backrest. At the beginning of the experiment adjust the headrest at 0° inclination at suboccipital height.

1.3. Place the elastic headband on the patient's head and fix it with the screw on the back. Ensure that the headband in not positioned too low on the patient´s forehead, so that it does not impair eye motility.

1.4. Connect the adhesive straps – on the headband and on the headrest – with each other. This ensures an optimal fixation of the head to the headrest on the chair.

2. Installation of the SVV unit

2.1. Mount the SVV unit by means of the fixation device on the chair in front of the patient (**Figure 1a**). The SVV unit consists of a LED light bar attached to a stick, allowing positioning in front of the patient. The position of the light bar can be adjusted in the roll plane through a connected potentiometer.

2.2. Make sure that the SVV unit is firmly fixed and that the light bar is positioned exactly opposite to the patient´s head and at the same level as the patient's eyes.

2.3. Connect the SVV unit to the electrical connection underneath the chair.

2.4. Place the potentiometer in the patient's left hand and instruct them on how to perform the SVV setting. While standing in front of the patient, adjust the position of the light bar again, if necessary, to ensure its position along the coronary plane.

2.5. Read the SVV deviation from the true vertical on the goniometer on the back of the SVV unit. The goniometer contains an angle display of ±20° at 2° intervals and is equipped with an infrared camera placed 3 cm in front of the display, allowing continuous data acquisition in complete darkness (**Figure 1b, 1c**).

2.6. Before continuing with the next step, check the visibility on the screen. The infrared-image of the angle display is transmitted to a screen outside of the cabin, ensuring that the patient´s SVV estimates can be collected continuously without having to open the cabin door between tests, therefore preventing visual re-orientation.

3. Calibration under visual control

3.1. Tilt the light bar 30° to the right or left relative to the absolute vertical (which serves as start position before each SVV task) and ask the patient to adjust it to the vertical position under visual control. This serves to self-calibrate the patient and to check the visuomotor ability of the patient.

3.2. If the patient confirms the displayed SVV position, compare it with the actual vertical.

3.3. If the patient's setting deviates significantly from the actual vertical, check the orthograde position of the SVV unit again. A deviation of ±1° is tolerable to confirm intact visuomotor function.

4. SVV setting in neutral head position

4.1. Open the examination protocol for simultaneous entry of the SVV estimates. The protocol allows the documentation of the measurements during the experiment and randomly determines whether the SVV task is performed from the +30° or -30° starting position.

4.2. Close the cabin door so that the patient is in complete darkness throughout the experiment. Check by intercom if the patient can understand the instructions well. Ask the patient now to tilt the light bar in the starting position: 30° to the right or to the left (randomization according to the protocol, **Figure 1d**).

4.3. After a waiting period of 15 s, instruct the patient to adjust the lightbar from the starting position until it reaches the subjective vertical. The patient is not under time pressure and can still correct the set position at any time. The patient confirms the setting verbally via the intercom system.

4.4. Enter the tilt angle shown on the display in degrees in the protocol. Per definition, mark clockwise angle deviations with a plus, while mark counterclockwise deviations with a minus**.** In total, let the patient adjust the SVV in 6 passes, whereby the starting position of ±30° is randomized.

4.5. After completion of the trial in neutral head position, perform the test with head tilting in the roll plane. The tilt direction sequence (-30°, -15°, +15° and +30°) is also randomized for each patient.

5. SVV setting with head tilt

5.1. Undo the initial head fixation by disconnecting the adhesive straps.

5.2. Loosen the headrest and adapt the tilt position according to the protocol: 15° or 30° to the right or to the left. Make sure that the headrest is exactly aligned along the respective angle at the goniometer, which is attached to the chair´s backrest. Fix the headrest in this position firmly.

5.3. Fix the patient's head with the elastic headband to the headrest. Ensure that this head tilt is tolerable for the patient and adapt the height of the headrest if needed. Instruct the patient to maintain this head position during the trial.

5.4. Close the cabin door and perform the trial as in the neutral head position.

5.5. Upon completion of the trial, undo the head restraint and adjust the headrest according to the randomized head-tilt position given by the protocol.

5.6. Close the cabin door again and perform the same procedures until all SVV settings in all head tilts have been recorded.

REPRESENTATIVE RESULTS:

SVV assessment was performed using a rotational chair system (**Figure 1a**) comprising a tiltable headrest and an adjustable LED light bar. The SVV adjustments were recorded via an infrared camera from a goniometer display on the back of the lightbar (**Figure 1b**). The devices used and the test protocol correspond exactly to the test methods presented here.

SVV measurement was performed in 13 healthy individuals at a mean age of 52.8 years. Gender distribution was 69.2% females and 30.8% males. They had no history of vestibular disorders and exhibited normal results in vestibular- and ocular motor function tests, which included assessment of spontaneous eye movements or spontaneous nystagmus, assessment of gaze-evoked nystagmus (at ±25°), horizontal and vertical saccades (±5-20°), smooth pursuit eye movements (at 0.1, 0.2 and 0.4 Hz), VOR-gain examination with sinusoidal rotational chair test (at 0.04, 0.08 and 0.32 Hz) and test of VOR-suppression (at 0.04 Hz). The absolute tilt of the SVV from the actual vertical at 0° head position was assessed (**Figure 2**) and showed an SVV median of 1.33 (95% CI 0 to 3.00), which correlates with values reported in the literature.

At a head tilt of 15° an SVV median of 1.66 was achieved (95% CI, 0.34 to 5.34; **Figure 2**) and measurements of the SVV at a head tilt of 30° yielded an SVV median of 5.33 (95% CI, 0.17 to 9.84; **Figure 2**). In conclusion, increased deviation and variability of the SVV was observed with higher head tilt angles, correlating with a higher information content for detecting graviceptive impairment in a dynamic setting.

The method was also used to analyze SVV tilts in patients suffering from cervical dystonia (CD). In total, 32 patients were tested. The patient group had a median age of 59.0 years and consisted of 36.7% males and 63.3% females. They exhibited a median habitual head deviation of either 10.0° clockwise or 8.5° counterclockwise. Assessment of the SVV at the patient's habitual head posture revealed major deviations from the actual vertical with a median of 2.65° (95% CI, 0.17 to 7.83; **Figure 3**, second bar). In comparison to healthy individuals at their habitual head posture (approximately 0° head tilt), the patient's response was significantly impaired with a median difference of – 1.34° (95% CI, -2.5 to -0.33, p=0.017; **Figure 3**, first bar).

The method was subsequently also used in a follow-up examination in order to assess possible treatment effects. Patients suffering from cervical dystonia were treated with botulinum toxin (BoNT) in order to improve the head posture into an upright position. Three weeks after injection of BoNT, the patients' SVV estimates in habitual head position (**Figure 3**) and at 30° head tilt (**Figure 4**) did not differ anymore from those of controls. A detailed discussion and interpretation of these results can be found in a preceding paper[22].

FIGURE AND TABLE LEGENDS:

Figure 1: Experimental setup. (**a**) A rotational chair system is used for SVV assessment, equipped with a tiltable headrest and an adjustable LED light bar. (**b**) The goniometer on the back of the lightbar covers a total measuring width of ±20° at 2° intervals. The SVV adjustments are recorded via an infrared camera (black box in front of the goniometer display), allowing data acquisition from outside the cabin. SVV was assessed in an upright sitting position in a completely dark cylindrical cabin with a diameter of 2 meters. In front of the participants, at a distance of 50 cm, there was a dim light bar, 2 mm wide and 10 cm long, which could be rotated about its midpoint by means of an electronic motor and a remote control device, so that a coaxial rotation around the middle eye of the test subject was guaranteed. All participants adjusted the bar six times from randomized starting positions at ±30° (relative to the absolute vertical) for parallel alignment with the perceived gravitational vertical. The six estimates were averaged for further analysis. (**c**) The headrest can be tilted 15° or 30° to the right or to the left. Through an adhesive strap on the headband and the headrest, the patient's head can be firmly fixed in the desired position. (**d**) Schematic map of the arrangement of the experimental setup.

Figure 2: SVV tilts in healthy individuals. Absolute SVV tilt in degree assessed at head tilts of 0°, 15° and 30° in healthy individuals. Increase of the SVV tilt was observed with higher head tilt angles. With permission from Elsevier (This figure has been modified from Platho-Elwischger et al. 2017[22]).

Figure 3: SVV tilts in patients suffering from cervical dystonia upon injection of botulinum toxin. Absolute SVV tilt in degree assessed in healthy controls, patients suffering from cervical dystonia at baseline (CD baseline) and three weeks after injection of botulinum toxin (CD week 3) at habitual head posture. SVV deviations of CD patients at baseline were significantly increased

compared to controls (p=0.017), but not after botulinum toxin injection (CD week 3). With permission from Elsevier (This figure has been modified from Platho-Elwischger et al. 2017[22]).

Figure 4: SVV tilt in CD patients and controls during head tilt. Absolute SVV tilt during 0° (**A**), 15°(**B**) and 30° (**C**) head tilt in controls, CD patients at baseline (CD baseline) and three weeks after injection of botulinum toxin (CD week 3). SVV estimations of CD patients at baseline with 30° head tilt showed significantly increased deviations compared to controls, which was not the case after botox therapy (CD week 3). With permission from Elsevier (This figure has been modified from Platho-Elwischger et al. 2017[22]).

Table 1: Descriptive data of absolute SVV tilt and differences within head-positions in healthy individuals. SVV was measured in degree (°). Statistically significant values ($p<0.05$) are marked with *. CI: confidence interval; N: number of patients; SVV: subjective visual vertical. With permission from Elsevier (This table has been modified from Platho-Elwischger et al. 2017[22]).

DISCUSSION:

SVV is a method to ensure the sense of verticality. It results from the integration of several information. The vestibular system being of paramount importance in this perception, it has been shown that a lesion at any level of vestibular information pathway leads to SVV errors.

The measurement of SVV in the head upright position is now regarded as the clinical standard method for recording otolith function. However, this method is hampered by low sensitivity as SVV-deviations in darkness in healthy individuals are limited to ±2° from the earth vertical[14]. Previous experimental studies have suggested that tilting the head in the frontal plane increases the sensitivity of the SVV test[23]. Several reports have been published on the effects of head tilts on SVV estimates in normal subjects, confirming a higher variability of the responses and thus possibly higher sensitivity in terms of graviceptive assessment in this paradigm. Whether this dynamic method definitely also increases the sensitivity in the detection of otolith function has still to be confirmed by direct method comparison. However, none of these previous experimental studies used a standardized protocol for applied head tilts, which ranged from 7° up to 20°, 30°, 35° or even 45° in the roll plane[24,25,26,27], thus making a comparison of results difficult.

The SVV paradigm at different head tilts has so far scarcely been applied in patients with central or peripheral vestibular disorders. Previous studies also used either different techniques in patients with peripheral lesions[28,21] or applied different head tilts (i.e., 20° or 25°) in patients with central disorders like neglect or vestibular migraine[29,30]. These different procedures for the determination of the SVV make it reasonable to introduce a standardized test procedure in order to make test results more comparable.

The test protocol has several advantages compared to other test methods. First of all, it is characterized by a simpler applicability than the application of linear accelerations, centrifuges or whole body tilts for measuring otolith function in patients. While there are efforts to improve the quality of VEMPs in research and practice[31,32], this clinically easy method still has a low sensitivity for the assessment of otolith impairment[11]. Thus, the easiest method to use in the clinical setting today is SVV measurement. The modified technique presented by us yields an increased variability of the responses and thus an increased information content by measuring under different head positions (**Table 1**), as previous data on normal subjects have also demonstrated[23,27]. Both our approaches of SVV assessment with head tilt and the bucket method represent feasible techniques of measurement of the otolith function. While the bucket test[13] is a validated, easily performed bedside test accessible to everyone, our approach offers high sensitivity but still needs certain technical equipment. Zwergal et al. found an SVV deviation of 0.9° ± 0.7° for binocular measurements[13]. The validated technique of SVV assessment without head tilt resulted in an SVV median of 1.33 with 0 to 3.0 (95% CI) in the healthy cohort. With the approach of assessment with 15% head tilt, an SVV median of 1.66 with 0.34 to 5.34 (95% CI) was obtained.

The measurement in four different head tilt angles (i.e., ±15° and ±30° in the roll plane) is tolerable for patients and increases the robustness of the SVV responses in the test arrangement (**Figure 2**); the method is therefore also an ideal instrument for demonstrating the effect of interventions in a more sensitive way, as we were able to show in a Botox treatment study with cervical dystonia patients (**Figure 3,4**). Furthermore, the presented method can also be extended for experimental questions by the additional projection of a pattern rotating around the visual axis, so that the so-called dynamic SVV can be determined[5].

In order to carry out the test method correctly, some points should be observed during the test procedure. For instruction and practice, as well as to check the patient's visuomotor abilities, we recommend that the patient makes the first SVV adjustments under visual control. It is also important that the cabin is always completely closed during the SVV settings so that the patient is actually in complete darkness, as any visual reference point can influence the settings. The order of the head positions should always be randomized, as should the start position of the lightbar before the respective SVV adjustment. Experiences from previous pilot tests showed that a continuous change of the head position, for example from -30° to -15°, to 0°, +15° and finally +30°, leads to a directional bias in the SVV adjustments, apparently due to a learning effect. Previous studies have also shown that a prolonged retention of head tilt leads to an after-effect in SVV settings that falsifies the results[27]. Therefore, it is recommended not to allow too long a latency between head position changes.

Furthermore, the goniometer allows measurement of ±20° at 2° intervals. However, although the goniometer used shows 2° intervals, the pointer used has a very high sensitivity and thus also enables the recording of numerical values between the intervals. This allows a visual resolution of 1° without any problems when viewed on an external screen. The resolution of 1° is also reflected in the representative test results shown.

Despite the simple handling of the method, it cannot or should not be used for some patient groups. These naturally include patients with severe visual impairments, with operative fixations in the area of the cervical spine, or patients who are cognitively or for other neurological reasons unable to adequately adjust the SVV. It is also not recommended for patients with cervical disc prolapse or severe cervical pain syndrome. Patients suffering from cervical dystonia can also only be examined to a limited extent with this method. However, previous studies from our laboratory show that these patients can still be examined as long as the head tilt does not exceed an angle of 30° in the roll plane[22].

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DISCLOSURES:
The authors have nothing to disclose.

REFERENCES:
1. Dieterich, M., Brandt, T. Perception of Verticality and Vestibular Disorders of Balance and Falls. *Frontiers in Neurology*. **10**, 172 (2019).
2. Elwischger, K., Rommer, P., Prayer, D., Mueller, C., Auff, E., Wiest, G. Thalamic astasia from isolated centromedian thalamic infarction. *Neurology*. **78** (2), 146 – 147 (2012).
3. Wiest, G., Zimprich, F., Prayer, D., Czech, T., Serles, W., Baumgartner, C. Vestibular processing in human paramedian precuneus as shown by electrical cortical stimulation. *Neurology*. **62** (3), 473 – 475 (2004).
4. Wiest, G., Tian, J.R., Baloh, R.W., Crane, B.T., Demer, J.L. Otolith function in cerebellar ataxia due to mutations in the calcium channel gene CACNA1A. *Brain*. **124** (Pt 12), 2407 – 2416 (2001).
5. Dakin, C.J., Rosenberg, A. Gravity estimation and verticality perception. *Handbook of Clinical Neurology.* **159**, 43 – 59 (2018).
6. Demer, J.L., Crane, B.T., Tian, J.R., Wiest, G. New tests of vestibular function. *Annals of the New Yorc Academy of Sci*ence. **942**, 428-45 (2001).
7. Clarke, A.H., Schonfeld, U., Helling, K. Unilateral examination of utricle and saccule function. *Journal of Vestibular Research.* **13** (4–6), 215 – 225 (2003).
8. Kingma, H. Clinical testing of the statolith-ocular reflex. *ORL Journal for Otorhinolaryngology and its Related Specialties.* **59** (4), 198–208 (1997)
9. Bisdorff, A.R., Wolsley, C.J., Anastasopoulus, D., Bronstein, A.M., Gresty, M.A. The perception of body verticality (subjective postural vertical) in peripheral and central vestibulardisorders. *Brain,* **199** (5), 1523 – 1534 (1996).
10. Welgampola, M.S. And Colebatch, JG. Characteristics and clinical applications of vestibular-evoked myogenic potentials. *Neurology*, **64** (10), 1682 – 1688 (2005).
11. Kingma, H. Function tests of the otolith or statolith system. *Current Opinion in Neurol*ogy, **19** (1), 21 -25 (2006).
12. Kheradmand, A., Winnick, A. Perception of Upright: Multisensory Convergence and the Role of Temporo-Parietal Cortex. *Frontiers in Neurology*, **8**, 552 (2017).
13. Zwergal, A., Rettinger, N., Frenzel, C., Dieterich, M., Brandt, T., Strupp, M. A bucket of static vestibular function. *Neurology*. **72** (19), 1689 – 1692 (2009).
14. Bronstein, A.M. The Interaction of Otolith and Proprioceptive Information in the Perception of Verticality: The Effects of Labyrinthine and CNS Disease. *Annals of the New York Academy of Science,* **871**, 324–333 (1999).

15. Saeys, W., Herssens, N., Verwulgen, S., Truijen, S. Sensory information and the perception of verticality in post-stroke patients. Another point of view in sensory reweighting strategies. *PLOS ONE*. **13** (6), e0199098 (2018).

16. Baier, B., Thömke, F., Wilting, J., Heinze, C., Geber, C., Dieterich, M. A pathway in the brainstem for roll-tilt of the subjective visual vertical: evidence from a lesion-behavior mapping study. *Journal of Neuroscience,* **32** (43), 14854 – 14858 (2012).

17. Huh, Y.E., Kim, K., Chung, W., Youn, J., Kim, S., Cho, J.W. Pisa Syndrome in Parkinson's Disease: Pathogenic Roles of Verticality Perception Deficits. *Science Reports*, **8** (1) 1804 (2018).

18. Ogawa, Y., Otsuka, K., Shimizu, S., Inagaki, T., Kondo, T., Suzuki, M. Subjective visual vertical perception in patients with vestibular neuritis and sudden sensorineural hearing loss. *Journal of Vestibular Research.* **22** (4), 205 – 211 (2012).

19. Toupet, M., Van Nechel, C., Bozorg, Grayeli A. Influence of body laterality on recovery from subjective visual vertical tilt after vestibular neuritis. *Audiology and Neurootology,* **19** (4), 248-55 (2014).

20. Lopez, C., Lacour, M., Ahmadi, A.E., Magnan, J., Borel, L. Changes of visual vertical perception: a long-term sign of unilateral and bilateral vestibular loss. *Neuropsychologia*. **45** (9), 2025 – 2037 (2007).

21. Kitahara, T. et al. Idiopathic benign paroxysmal positional vertigo with persistent vertigo/dizziness sensation is associated with latent canal paresis, endolymphatic hydrops, and osteoporosis. *Auris Nasus Larynx*, **46** (1), 27–33 (2019).

22. Platho-Elwischger, K. et al. Plasticity of static graviceptive function in patients with cervical dystonia, *Journal of the Neurological Sciences*, **373**, 230–235 (2017).

23. Aranda-Moreno, C., Jáuregui-Renaud, K. The subjective visual vertical in vestibular disease. *Revista de Investigación Clínica*. **57** (1), 22 - 27 (2005).

24. Guerraz, M., Luyat, M., Poquin, D., Ohlmann, T. The role of neck afferents in subjective orientation in the visual and tactile sensory modalities. *Acta Otolaryngologica*, **120** (6), 735-738 (2000).

25. Luyat, M., Noël, M., Thery, V., Gentaz, E. Gender and line size factors modulate the deviations of the subjective visual vertical induced by head tilt. *BMC Neurosci*ence, **13,** 28 (2012).

26. Fraser, LE., Makooie, B., Harris, L..R. The Subjective Visual Vertical and the Subjective Haptic Vertical Access Different Gravity Estimates. *PLOS ONE*. **10** (12), e0145528 (2015).

27. Otero-Millan, J., Kheradmand, A. Upright Perception and Ocular Torsion Change Independently during Head Tilt. *Frontiers in Human Neuroscience,* **10**, 573 (2016).

28. Kim, S.H., Kim, J.S. Effects of Head Position on Perception of Gravity in Vestibular Neuritis and Lateral Medullary Infarction. *Frontiers in Neurology*, **9**, 60 (2018).

29. Funk, J., Finke, K., Müller, H.J., Utz, K.S., Kerkhoff, G. Effects of lateral head inclination on multimodal spatial orientation judgments in neglect: Evidence for impaired spatial orientation constancy. *Neuropsychologia*, **48** (6), 1616–1627 (2010).

30. Winnick, A., Sadeghpour, S., Otero-Millan, J., Chang, TP., Kheradmand, A. Errors of Upright Perception in Patients With Vestibular Migraine. *Frontiers in Neurololgy,* **9**, 892 (2018).

31. Deriu, F., Ginatempo, F., Manca, A. Enhancing research quality of studies on VEMP in central neurological disorders: a scoping review. *Journal of Neurophysiology*, **122** (3), 1186-1206 (2019).

32. Rosengren, S.M., Colebatch, J.G., Young, A.S., Govender, S., Welgampola, M.S. Vestibular

evoked myogenic potentials in practice: Methods, pitfalls and clinical applications. *Clinical Neurophysiology Practice*, **4**, 47-68 (2019).

Figure1

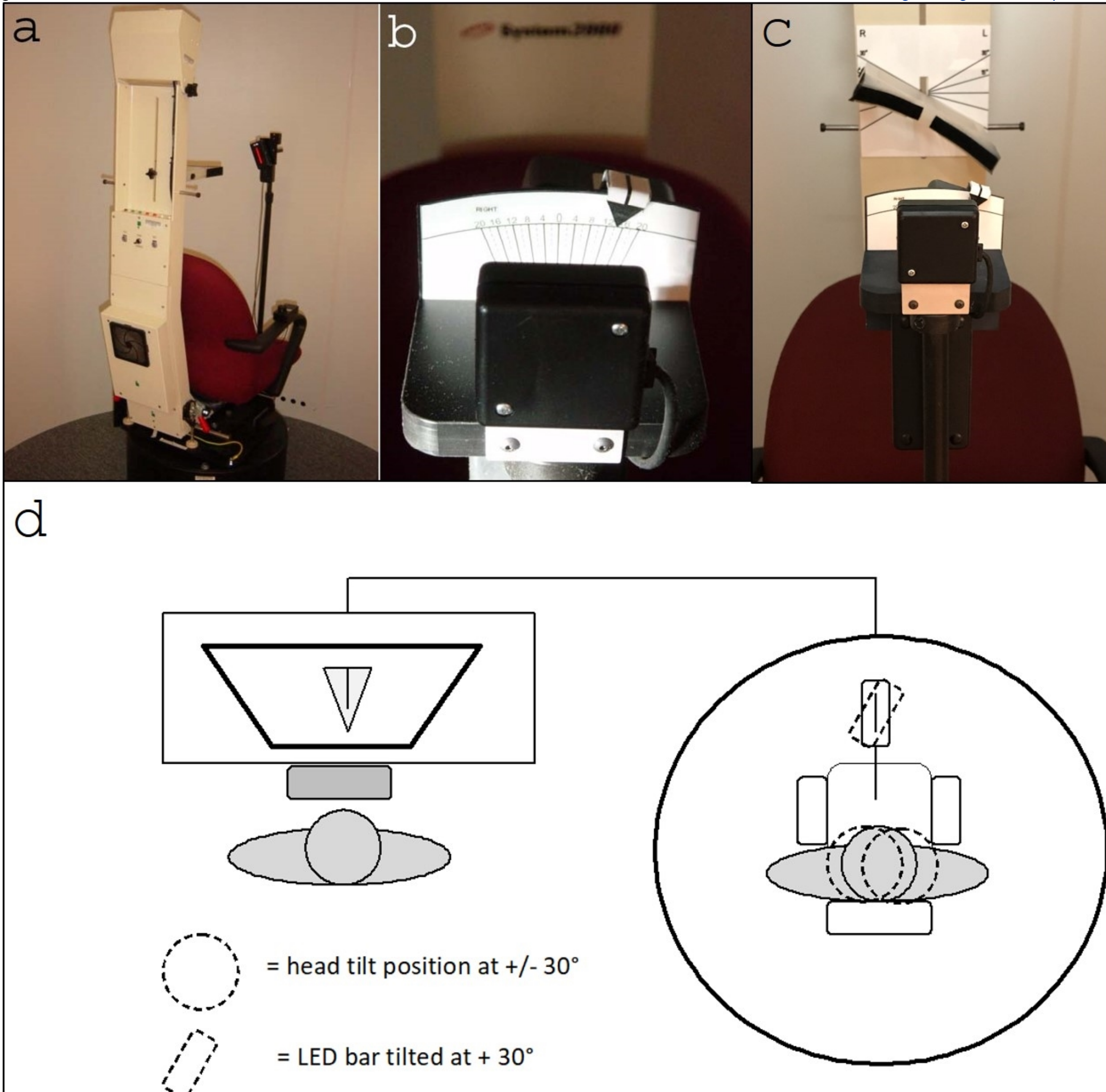


Figure 2

Click here to access/down

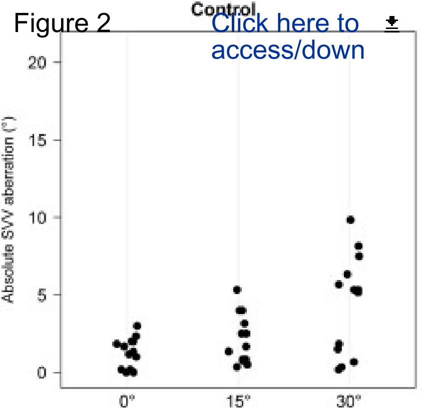


Figure3

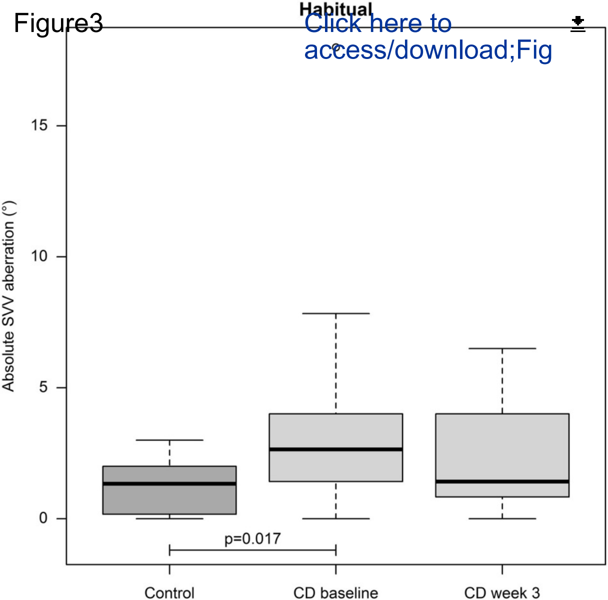
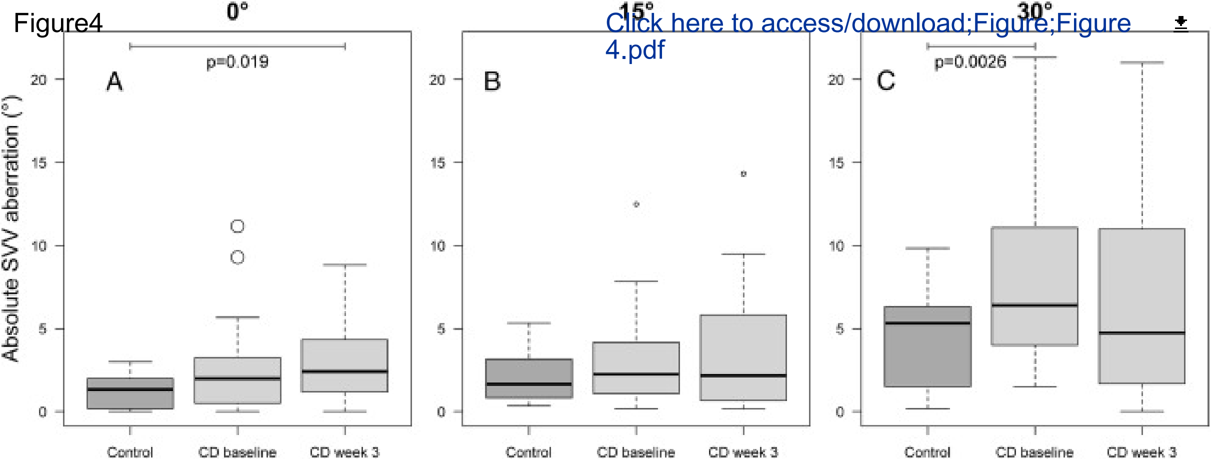

Habitual
Absolute SVV aberration (°)
15
10
5
0
p=0.017
Control
CD baseline
CD week 3

Figure4


0°
15°
30°
A
B
C
p=0.019
p=0.0026
Absolute SVV aberration (°)
0
5
10
15
20
Control
CD baseline
CD week 3

Patients	N	Head tilt	SVV median (95% CI)	Within group differences
				Mean difference (95% CI)
Controls	13	0°	1.33 (0 to 3.00)	0° vs. 15°: – 0.85° (– 2.1 to 0.36)
		15°	1.66 (0.34 to 5.34)	15 vs. 30°: – 2.31° (– 3.72 to – 0.90)
		30°	5.33 (0.17 to 9.84)	0° vs. 30°: – 3.17° (– 5.39 to – 0.94)

p-Values
0.1525
0.0039*
0.009

Name of Material/ Equipment	Company
Adjustable plastic goniometer board 7,87" x 7,87", (marked tilt angles of 0°, 15° and 30°)	self-produced
Elastic head band with adjustable screw on the back	Micromedical Technologies Inc
HD LCD display, 1366 x 768p resolution, 19"	Philips
Subjective Visual Vertical Set including infrared video camera (black/white, resolution 0,25°)	Micromedical Technologies Inc
Sytem 2000 (Rotational Vestibular Chair System with Centrifuge)	Micromedical Technologies Inc 10 Kemp Dr Chatham, IL 62629-9769 United States
Tiltable headrest	Micromedical Technologies Inc

Catalog Number	Comments/Description
6	for fixation at the backrest and for adjustment of neckrest along the given tilt angles (0°,15°,30°)
4	modified with attached adhesive strap
5	for monitoring SVV-adjustments outside the cabin (infrared camera recording)
2	
1	
3	modified with attached adhesive strap

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Signature: [signature] Date: 6/13/2019

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Title of Article: ASSESSMENT OF STATIC GRAVICEPTIVE PERCEPTION IN THE ROLL-PLANE USING THE SUBJECTIVE VISUAL VERTICAL PARADIGM

Author(s): FIONA I. JÄGER, KIRSTEN PLATHO-ELWISCHGER, GERALD WIEST

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Medical University of Vienna
Department of Neurology

Vienna, 10.12.2019

Dear Editors,

Thank you for sending us the reviewers' helpful comments on our manuscript. We carefully reviewed each one and have revised the manuscript accordingly.

EDITORIAL COMMENTS

1. The manuscript was again thoroughly proofred.
2. Step.1.2 was written in imperative tense.
3. Commercial instrument names were removed from the manuscript.

REVIEWER'S COMMENTS

Reviewer #1
This is a well structured manuscript on an interesting issue.
It is clear that the authors have put significant time and effort into this manuscript.
Efficacy of the protocol was edited to the better and point out a clear step by step methodology.
Therefore, I recommend publication.

Reviewer #4:
In the introduction and in the summary, you present SVV as a means of detecting otolithic disturbances. However, SVV is not a direct test of the otolith function. The SVV (see for instance the work of Harris and collaborators, 2017) is the result of a weighting between several sources of information (gravity, proprioceptive and also visual when they are available). Besides patients with no otolithic defect such as more central lesion or other pathology (see Guardia et al. 2013) can produce abnormal deviations of the SVV. In your experiment, the patients have a cervical dystonia and not a vestibular defect but they showed abnormal deviations.
If I may, I would introduce the paradigm rather as you do in the first paragraph of your discussion. "SVV is a method to ensure the sense of verticality. It results from the integration of several information. The vestibular system being of paramount importance in this perception, it has been shown that a lesion at any level of vestibular information pathway leads to SVV errors." Something like that…

In the introduction the following sentence has been added to explain that physiologically SVV is not a direct test if the otolith function:

Seen from a precise physiological perspective, SVV is not a direct test of the otolith function alone, as the SVV is the result of a weighting between several sources of information (gravity, proprioceptive and also visual when they are available). However, for rapid clinical use an easy application of this SVV task, the so-called bucket test, has been developed[13] especially for the emergency setting, enabling immediate detection of acute disturbances of graviceptive perception.

Furthermore, the following sentence has been added to the discussion, as suggested by the reviewer:

SVV is a method to ensure the sense of verticality. It results from the integration of several information. The vestibular system being of paramount importance in this perception, it has been shown that a lesion at any level of vestibular information pathway leads to SVV errors.

More detailed results are missing. For example, it would be absolutely necessary to have the algebraic deviations, the min and the max in each group, if possible the individual results. An equivalence on ages and sex between groups would be appreciated.

As explained in the manuscript and demanded by the journal the presented data is exemplary from a study published several years ago. Therefore the raw data set wasn‘t available anymore. However, the equivalence on ages (CD: 59.0 years, healthy controls: 52.8 years) and sex (CD: 36.7% males and 63.3% females, healthy controls: 69.2% females and 30.8% males) between groups is documented in the paper. The attached table additionally shows the means and confidence intervals for healthy controls.

Finally, since the SVV is sensitive to several methodological factors, in particular the size of the line to be oriented, it would be necessary to be very precise on this point: actual and angular size of the led-bar, observer distance. Also specify if the light-bar always stays centered on the subject's middle eye (coaxial rotating?). You should add a figure of your chair in a tilted position to help the reader to understand it.

The diameter of the cabin, the sizes of the LED-bar as well as the observer distance were measured and added to the manuscript (see legend Figure 1: Experimental setup):

SVV was assessed in an upright sitting position in a completely dark cylindrical cabin with a diameter of 2 meters. In front of the participants, at a distance of 50 cm, there was a dim light bar, 2 mm wide and 10 cm long, which could be rotated about its midpoint by means of an electronic motor and a remote control device, so that a coaxial rotation around the middle eye of the test subject was guaranteed. All participants adjusted the bar six times from randomized starting positions at +/- 30° for parallel alignment with the perceived gravitational vertical. The six estimates were averaged for further analysis.

We also included a figure of the chair showing the headrest tilted at 30° (Figure 1c).

The starting angle of the rod is 30 °. Well specify if it is 30° relative to the head or relative to the absolute vertical. Moreover if it is 30 ° relative to the absolute vertical, when tilting the head does that mean that there are conditions where the head and the rod are aligned?

The starting angle of the rod at +/- 30° is relative to the absolute vertical, resulting in a condition where head and rod are aligned at 30° relative to the absolute vertical. This has been specified in the text (see in the Protocol: Calibration under visual control, as well as legend Figure 1: Experimental setup).

In the method, first describe the arrangement of the experimental piece: the cabin, the position of the experimenter etc (a map perhaps would help)

Additional details about the experimental setup was added to the first step of the protocol and more precisely to the figure and table legends (Figure 1: Experimental setup). Exact positioning of each unit can be seen in Figure 1a. An additional schematic map of the experimental setup has been produced to present the position of the experimenter and the subjects in a more understandable way (Figure 1d).

For calibration under visual control, if I well understood, the visual context (the vision of the room) is available. It seems to me that a sensitivity of 2° is not much, check this because we could expect a sensitivity a little stronger in this condition.

We agree with the reviewer that a sensitivity of 2° for the visual control condition is very low. After we did not find any normative data for this visual control condition in the literature, we adopted the sensitivity of the dark condition from previous publications, which is 2.

After re-checking the literature we still did not find any normative data regarding the sensitivity under visual control condition.

However, we can report from another currently ongoing own study that the average deviation of SVV in the visual control condition in 26 patients with idiopathic downbeat nystagmus (i.e. vertically beating nystagmus) ranged from - 1° to + 0.66° (unpublished data). This would confirm the reviewer's assumption that the sensitivity is also higher in healthy individuals under the visual control condition, i.e. about +/- 1°.

If the reviewer agrees, we would write the following sentence (3. Calibration under visual control, 3.3): A deviation of ± 1° is tolerable to confirm intact visuomotor function.

We have made every effort to ensure that the comments are implemented as effectively as possible and hope to have significantly improved the paper in the sense of the reviewers.

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