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# Normal pressure hydrocephalus: Increase of utricular input in responders to spinal tap test

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HIGHLIGHTS

- One third of patients with normal pressure hydrocephalus had impaired otolith function.
- Patients with an increase of walking velocity after spinal tap test only had a significant increase of oVEMP amplitude.
- Otolith dysfunction may contribute to imbalance in normal pressure hydrocephalus (NPH) and increased utricular function after spinal tap test may be relevant for gait improvement.

ABSTRACT

*Objective:* To investigate whether there is a change in ocular (oVEMP) and cervical (cVEMP) vestibular evoked myogenic potentials in patients with normal pressure hydrocephalus (NPH) before and after spinal tap test (STT).
*Methods:* In 25 patients (6 females, age 62–83 years) c/oVEMP were measured before and after STT. Patients with an increase of >20% of walking velocity were classified as responders ($n = 10$). VEMP were also measured in a control group of 13 non-NPH patients.
*Results:* All patients had reproducible oVEMP; 68% had cVEMP. There was a significant increase of the peak-to-peak (pp) oVEMP amplitude after STT in responders ($8.5 \pm 2.7$ to $18.9 \pm 7.5$ μV ($p = 0.010$)). No significant changes were found in non-responders ($13.4 \pm 7.6$ to $15.3 \pm 8.6$ μV) or controls ($12.4 \pm 7.6$ to $12.5 \pm 6.8$ μV). There were no significant differences in cVEMP before and after spinal tap test (STT).
*Conclusion:* One third of patients with suspected NPH had impaired otolith function. Responders to STT only had a significant increase of oVEMP and thereby utricular input, probably due to a decrease of pressure.
*Significance:* Both findings indicate that otolith dysfunction may contribute to imbalance in NPH and that increased utricular function after STT may be relevant for gait improvement.


## 1. Introduction

Idiopathic normal pressure hydrocephalus (NPH) is characterized by the clinical triad of cognitive impairment, urinary incontinence and gait disturbance (Hebb and Cusimano, 2001; Relkin et al., 2005). Although this disease was first described nearly 50 years ago, (Adams et al., 1965) the pathophysiology is still under discussion. There is some evidence that increased cerebrospinal fluid (CSF) pulse pressure (Lenfeldt et al., 2004) could lead to increased liquor diapedesis in the periventricular white matter following ventricular dilatation (Kristensen et al., 1996). Other theories discuss increased vascular compliance leading to, first, propagation of pulse waves into the brain parenchyma with

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subsequently subependymal white matter damage and, second, altered CSF reabsorption through the deep brain veins (Bateman, 2000, 2008). An essential aspect of diagnosis and treatment is a large-volume lumbar puncture or external lumbar drainage, which can lead to a partial recovery of the patient, especially to an improvement in walking speed and postural stability. Impaired postural stability is one of the main problems for the patients, leading to recurrent falls and loss of independence. Posturographic analysis revealed a higher sway path area in the sagittal plane and higher backward directed velocity of the center of pressure with reduced capacity for visual compensation in patients with NPH (Blomsterwall et al., 2000, 2011; Lundin et al., 2013). It was shown that the gait improvement after STT is connected to improved postural stability and better balance function (Blomsterwall et al., 1995; Czerwosz et al., 2009; Lundin et al., 2013). Linear accelerations of the body are detected by the otolith organs, providing signals for motionsense and subsequently appropriate motor response (Gresty et al., 1992). Over the last few years vestibular evoked myogenic potentials (VEMP) have been established as the standard test for the otolith system (Rosengren et al., 2010). Gait instability with pulling sensations similar to that in NPH patients can be partially mediated by impaired otolith function (Saka et al., 2014; Layman et al., 2015). Therefore we investigated otolith function using ocular VEMP (oVEMP) for utricular and cervical VEMP (cVEMP) for saccular function) as well as video-head-impulse-test (HIT) for the horizontal semicircular canal function in patients with probable idiopathic NPH before and after spinal tap test (STT).

## 2. Patients and methods

### 2.1. Participants

25 probable NPH patients according to the criteria of Relkin et al. (2005) were recruited from the Clinics of Neurology and Neurosurgery of the LMU in Munich. Patients had to be older than 60 years with enlarged ventricular size and an insidious onset gait disturbance plus cognitive impairment and/or urinary incontinence. Patients with increased opening pressure on lumbar puncture or evidence for intracerebral haemorrhage, meningitis or other known causes of secondary hydrocephalus were excluded. All 25 participants received o- and cVEMP testing together with gait analysis before and after spinal tap test (STT). 13 of these patients had a large-volume lumbar puncture of 30–50 ml, 12 an external lumbar drainage with a maximum of 120 ml per day. Patients with an increase of >20% of preferred walking velocity were classified as responders ($n = 10$).

VEMP were also measured before and after STT in a control group of 13 non-NPH patients with alternative neurological diseases (4 patients with Alzheimer's disease, one each with Binswanger's disease, amyotrophic lateral sclerosis, polyneuropathy, peripheral glossopharyngeal paresis, functional paresis, multiple sclerosis, primary progressive aphasia, chronic inflammatory demyelinating polyradiculoneuropathy, limbic encephalitis). 5 controls had a large-volume lumbar puncture, 8 a lumbar puncture with a small volume of CSF.

This study was approved by the Institutional Review Board of the ethics committee of the Ludwig-Maximilian University Munich and was conducted according to the principles expressed in the Declaration of Helsinki. All participants gave their informed written consent prior to their inclusion in the study.

### 2.2. Vestibular evoked myogenic potentials (VEMP)

In this study we used the Interacoustics Eclipse System and the standard protocol in our clinic described elsewhere (Bremova et al., 2013) for examination of vestibular evoked potentials. Subjects were examined lying supine on a chair with their back elevated 30° above the horizontal.

### 2.3. Ocular vestibular evoked myogenic potentials (oVEMP)

We used bone-conducted oVEMP, induced by a mini-shaker (Bruel and Kjaer Mini-Shaker Type 4810, 2 ms clicks of positive polarity, with a repetition rate of two per second). The patients were asked to gaze at a small target approximately 30° above their normal gaze position. The mini-shaker was placed at the Fz position. Ocular VEMP were recorded with an electrode alignment consisting of a recording electrode placed over the contralateral inferior oblique muscle, approximately 3 mm below the eye and centered beneath the pupil, a reference electrode on the chin, and a ground electrode placed under the chin. Because of the wider-spaced reference the amplitudes are higher than in other published VEMP data with reduced selectivity. Patients received two measurements for each eye to show reproducibility. Responses to 100 stimuli were averaged. The first reliable negative and positive peak were designated n1 (10) and p1 (15). For original waveforms before and after STT see Fig. 1.

### 2.4. Cervical vestibular evoked myogenic potentials (cVEMP)

For this examination patients were asked to lift their heads, which led to a maximal tonic muscle tension of the SCM during cVEMP stimulation. Air-conducted 500 Hz, 125 dB SPL tone bursts were delivered monaurally via intra-auricular speakers with foam ear-tips. cVEMP were recorded from an electrode alignment consisting of a recording electrode placed at the midpoint of the belly of the ipsilateral sternocleidomastoid muscle, a reference electrode placed on the manubrium, and a ground electrode placed on the forehead. The first reliable positive and negative peak were designated p1 (13) and n1 (23). The corrected amplitude is calculated by dividing the peak-to-peak amplitude by the mean rectified EMG level calculated over the pre-stimulus interval. For original waveforms before and after STT see Fig. 2.

### 2.5. Gait analysis

Gait analysis was performed using a 6.7-m-long pressure-sensitive carpet (GAITRite, CIR System, Havertown, USA). This system enables special gait parameters to be qualified. Patients were asked to walk at a self-selected comfortable velocity over the carpet. In reference to a previous study, which showed a specific significant improvement of self-chosen gait velocity and stride length after STT, we used this parameter for evaluation of clinical improvement (Stolze et al., 2001). Patients whose self-chosen velocity improved by more than 20% were called responders.

### 2.6. Video-head-impulse-test

Video-head-impulse-test (HIT) was measured using the EyeSeeCam System®. Ten head rotations to each side with a velocity between 100 and 200 °/s were recorded. We analyzed gain of HIT test, defined as a ratio of eye velocity to head velocity 60 ms after the beginning of the head movement. For original waveforms before and after STT see Fig. 3.

### 2.7. Dizziness Handicap Inventory (DHI)

To quantitatively assess the subjective impairment in daily life, subjects were administered the Dizziness Handicap Inventory (DHI). The DHI is a 25-item questionnaire developed to quantify the impact of dizziness on everyday life. It is divided into three