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Vestibulo-cochlear function in inflammatory neuropathies

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HIGHLIGHTS

- Peripheral vestibular deficits were quantified in inflammatory neuropathy patients.
- Decreased vestibular function was frequent but large parts of the vestibular apparatus were intact.
- Our data does not support routine vestibular testing in inflammatory neuropathy patients.

ABSTRACT

Objective: We aimed to quantify peripheral-vestibular deficits that may contribute to imbalanced stance/gait in patients with inflammatory neuropathies.
Methods: Twenty-one patients (58 ± 15 y [mean age ± 1SD]; chronic-inflammatory-demyelinating-poly neuropathy = 10, Guillain-Barré Syndrome = 5, Anti-MAG peripheral neuropathy = 2, multifocal-motor-neuropathy = 4) were compared with 26 healthy controls. All subjects received video-head-impulse testing (vHIT), caloric irrigation and cervical/ocular vestibular-evoked myogenic-potentials (VEMPs). The Yardley vertigo-symptom-scale (VSS) was used to rate vertigo/dizziness. Postural stability was assessed using the functional gait-assessment (FGA). Pure-tone audiograms (n = 18), otoacoustic emissions (n = 12) and auditory brainstem responses were obtained (n = 12).
Results: Semicircular-canal hypofunction was noted in 9/21 (43%) patients (vHIT = 6; caloric irrigation = 5), whereas otolith function was impaired in 12/21 (57%) (oVEMPs = 8; cVEMPs = 5), resulting in vestibular impairment of at least one sensor in 13/21 (62%). On average, 2.4 ± 1.1 vestibular end organs (each side: anterior/posterior/horizontal canal, utriculus, sacculus; total = 10) were affected. The VSS-scores were higher in patients (16.8 ± 8.6 vs. 9.5 ± 6.2, p = 0.002) but did not correlate with the number of affected organs. Auditory neuropathy was found in 1/12 (8%) patients.
Conclusion: Impairment of one or more vestibular end organs was frequent, but usually mild, possibly contributing to imbalance of stance/gait in inflammatory neuropathies.
Significance: While our data does not support routine vestibular testing in inflammatory neuropathies, this may be considered in selected cases.

1. Introduction

Inflammatory neuropathies are a heterogeneous group of peripheral nerve disorders linked by their immune-related pathogenesis. They are caused by auto-immune inflammation within the peripheral nerves associated with destruction of myelin and/or axons (Lunn and Willison, 2009). Inflammatory neuropathies may be acute (e.g., Guillain-Barré Syndrome, GBS) or chronic (e.g., Chronic Inflammatory Demyelinating Neuropathy, CIDP; Multifocal Motor Neuropathy, MMN) and are closely related to neuropathies associated with paraproteinemia (Lunn and Willison, 2009).

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Our understanding of the underlying mechanisms that lead to impaired balance in patients with inflammatory neuropathies is limited. Postural control relies on information provided by the visual, vestibular, and somatosensory systems. It is assumed that, in polyneuropathies, proprioceptive sensory loss causes sensory ataxia leading to postural instability (Rinalduzzi et al., 2016). However, imbalance of gait and stance has also been linked to vestibular impairment in patients with polyneuropathy (PNP) of various causes (Fujikawa and Starr, 2000, Samaha and Katsarkas, 2000, Palla et al., 2009) (see also (Buetti and Luxon, 2014) for review). This includes metabolic-toxic (Biurrun et al., 1991), hereditary (Lemieux and Neemeh, 1967, Hanson et al., 1970; Butinar et al., 2000; Jen et al., 2005; Poretti et al., 2013; Perez-Garrigues et al., 2014) and inflammatory (Frohman et al., 1996, Jacot and Wiener-Vacher, 2008) neuropathies as well as the cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) (Szmulewicz et al., 2011). Identifying concomitant vestibular impairment may therefore be clinically important given the evidence that vestibular rehabilitation improves postural stability in patients with vestibulopathy (Whitney et al., 2016). We hypothesized that in analogy to other neuropathies, gait imbalance in patients with inflammatory or paraproteinemic neuropathies may be linked to vestibular impairment. In the current study, we set out to determine the frequency, pattern and clinical relevance of vestibular and cochlear impairment in such patients using state-of-the-art diagnostics. By studying different underlying disorders leading to inflammatory neuropathies, we hypothesized that the pattern of vestibulo-cochlear impairment could be disease-related.

2. Methods

Written informed consent was obtained from all participants after full explanation of the experimental procedure. The protocol was approved by the local ethics committee (KEK-ZH-Nr. 2014-0112) and was in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments for research involving human subjects.

2.1. Study cohort and eligibility criteria.

Between September 2014 and October 2015 patients referred to our tertiary neuromuscular center for further evaluation of neuropathic symptoms were screened for eligibility. Fifty patients were screened and 14 patients were excluded because they did not fulfill the inclusion criteria. Thirteen patients declined to participate in the study, one patient died prior to inclusion, one patient was excluded due to comorbidities. Twenty-one patients participated in our study. The diagnosis of GBS was made according to the criteria of Doorn and co-workers (van Doorn et al., 2008). Two GBS patients (ID 18 and 19) were examined in both the acute setting and again after about 5 months, whereas the three other GBS patients (ID 17, 20 and 21) were examined only once either at acute or chronic stage (see Table 1). We adhered to the EFNS/PNS guidelines for diagnosing CIDP and paraproteinemic demyelinating neuropathy associated with high serum-titers of anti-MAG (MAG = myelin-associated glycoprotein) IgM (>1/6400) (Joint Task Force of the EFNS and the PNS, 2010a,b; Van den Bergh et al., 2010).

2.2. Experimental setup

Detailed history taking and a comprehensive neurologic examination were performed in all patients by M.B. and one board-certified neurologist (A.P., J.A.P., H.H.J., A.A.T., or K.P.W.). Motor and sensory nerve conduction studies and vestibulo-cochlear tests (details see below) were obtained in all participants. Additional examinations such as MRI, lumbar puncture and serologic tests were ordered to increase diagnostic accuracy when required. Vestibular testing is illustrated in a representative case (ID 14) in Fig. 1.

2.2.1. Otolith testing – vestibular-evoked myogenic-potentials

Otolith function was quantified by means of vestibular-evoked myogenic-potentials (VEMPs) (Curthoys, 2010). Cervical VEMPs (cVEMPs) assess mainly saccular function, ocular VEMPs (oVEMPs) mainly utricular function.

Air-conducted sound stimuli for cVEMPs (500 Hz, 6 ms tone bursts at 90–100 dB normal hearing level, total of 200 bursts) were provided through calibrated headphones (Telephonics TDH-39P; Telephonics Corp., Farmingdale, NY, USA) monaurally to the right and left ears. During stimulation, subjects were asked to sit and turn their head as much as possible to the side to tense their sternocleidomastoid muscle (SCM). EMG activity was recorded (Viking V system; Nicolet Biomedical, Madison, WI, USA) from the upper half of the SCM contralateral to the side of acoustic stimulation. A reference electrode was placed on the upper part of the sternum. The background SCM contraction was monitored online and measured over the 20-ms prestimulus interval (using root-mean-square EMG amplitude). Signals of 200 air-conducted cVEMP stimuli were averaged, as previously reported by (Poretti et al., 2013). Note that in case of inconclusive or negative air-conducted cVEMPs, bone-conducted cVEMPs were obtained and judgment was based on the findings from the latter. Vibrations (unshaped 500 Hz bursts resulting in inter-aural accelerations of about 0.1 g, duration 4 ms, 200 stimuli in total) were applied using a Minishaker (Model 4810, Brüel & Kjaer, P/L, Naerum, Denmark) placed over the hairline near Fz, as previously described by (Weber et al., 2012). Again, responses from the contralateral SCM were recorded.

To improve reproducibility of measurements and to reduce noise from asymmetric muscle tension in individuals, response amplitudes were normalized. This procedure is based on the assumption, that there is a linear relationship between the level of muscle contraction and the response amplitude. This was demonstrated for moderate to strong muscle contractions (McCaslin et al., 2014) and confirmed by Rosengren more recently (Rosengren, 2015). Reported values for air- and bone-conducted cVEMPS will therefore be unitless.

Bone-conducted oVEMPs (unshaped 500 Hz bursts resulting in inter-aural accelerations of about 0.1 g, duration 4 ms, 200 stimuli in total) were applied by the same Minishaker, placed again over the hairline near Fz. Stimuli were recorded with surface electrodes placed beneath the eyes during up-gaze. For further details see also (Rosengren et al., 2010; Weber and Rosengren, 2015).

Differences in response amplitude (left side vs. right side; asymmetry ratio (AR)) of more than 30% or absent responses on cVEMPs or oVEMPs were considered abnormal, i.e., indicating unilateral or bilateral hypofunction. For comparison of VEMP latencies, we used data from a group of 26 healthy controls (aged 38.4 ± 15.8 years; 11 females), which were recorded with the same setup. Cut-off latency values (diverging >2SD from the mean of the controls) for cVEMPs were 17.78 ms (p13) and 31.13 ms (n23), while for oVEMPs cut-off latencies were 13.95 ms (n10) and 18.84 ms (p15).

2.2.2. Semicircular canal testing – video-head-impulse testing

We used quantitative video-head-impulse testing (vHIT) to assess the function of all six semicircular canals (McGarvie et al., 2015). The standard vHIT-procedure at our institution requires 20 valid head impulses for each canal (MacDougall et al., 2009, 2013a). For video-oculography an infrared camera recorded the right eye with a 250 Hz frame rate (ICS Impulse, Otometrics, Taastrup, Denmark). Head velocity was determined by three orthogonal

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