Case Report

Case Report: Acquired Periodic Alternating Nystagmus and Vestibular Weakness in West Nile Virus Encephalitis

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Short running title: Case Report: Acquired Periodic Alternating…

Highlights:
- West Nile encephalitis can cause dizziness through two mechanisms
- Cerebellar dysfunction, manifesting as periodic alternating nystagmus
- Vestibular weakness, identified on video head impulse testing and VEMP

ABSTRACT
Background: West Nile Virus (WNV) encephalitis is reported to cause "ataxia" in up to 31% of patients, and "vertigo" in up to 14% of patients. The mechanism of these symptoms is unclear.
The Case: We report the case of a lady who contracted WNV encephalitis at age 74 years. When evaluated 15 months later she complained both of baseline unsteadiness, and of a fluctuating component of disequilibrium. Instrumented vestibular testing identified bilateral vestibular weakness (in a different pattern on each side). It also identified Periodic Alternating Nystagmus (PAN), presumably acquired (rather than congenital). Acquired PAN has been observed in other encephalidites, but has not been previously reported in association with WNV encephalitis.
Conclusion: In this case, WNV encephalitis appears to have caused both vestibular weakness (likely accounting for the baseline unsteadiness) and periodic alternating nystagmus (likely accounting for the fluctuating disequilibrium).
Keywords: Nystagmus; West Nile virus; encephalitis; vestibular; case report

Introduction

When West Nile Virus (WNV) causes neuroinvasive disease, symptoms resemble those of other encephalidites,

including fever, headache, photophobia and meningeal signs. Symptoms in more severe cases may include encephalopathy, parkinsonism (and other extrapyramidal signs) and myoclonus. WNV encephalitis is also reported to cause "ataxia" in 31% of patients and "vertigo" in 14% of patients [1]. The "ataxia" is often ascribed to cerebellar dysfunction (in cases of encephalitis). The mechanism of "vertigo" is unclear; "WNV vestibular neuritis" is plausible —given that WNV is documented to cause other cranial neuropathies [2-11] —but unproven. Those mechanisms might account for some baseline degree of unsteadiness, but would not easily explain the fluctuating pattern of disequilibrium described by the patient in this case. Instrumented vestibular testing in this case did show bilateral vestibular weakness, which would account for the baseline degree of unsteadiness. However, examination also revealed Periodic Alternating Nystagmus (PAN), presumably acquired rather than congenital. Acquired PAN has been observed in other encephalitides [12], but has not been previously reported in association with West Nile virus encephalitis, and correlates with the fluctuating nature of symptoms in this case.

Case presentation

In this case, in the late autumn, a lady at age 74 years developed fever and mental status changes that prompted hospitalization, during which a diagnosis of West Nile virus encephalitis was made based on serological and cerebrospinal fluid studies. She was eventually discharged to a nursing facility for several weeks, during which time she received physical therapy (target diagnosis unclear) and then returned home. After that she was able to ambulate with a walker, but complained of chronic unsteadiness that fluctuated in intensity. She also attempted chiropractic manipulation, without benefit. The patient's son brought her to our institution's otoneurology clinic about 15 months after the original diagnosis of West Nile virus encephalitis. Her son specifically noted, "She can sometimes get up and be walking around pretty well, but then I can sort of see in her eyes that she feels unsteady. She sits down and it passes after a few minutes, but recurs throughout the day." The patient clarified that her baseline level of unsteadiness had been improving very slowly over the course of about a year, whereas the "spikes" in that symptom had remained about the same. Past medical history included restless leg syndrome (treated with ropinirole), gastroesophageal reflux disease (treated with famotidine), type 2 diabetes (treated with metformin) and hysterectomy. There was no relevant family or psychosocial history.

Serial brain MRIs performed at the beginning of the illness (in the first weeks after the diagnosis of encephalitis) reported stable hypodense subdural fluid collections overlying both frontotemporal convexities without mass effect that were interpreted as subdural effusions. IgM antibodies to the West Nile virus were 6.67 (normal range <1.30) in the serum, and 9.33 (normal range <1.30) in the cerebrospinal fluid. MRI of the internal auditory canals without and with contrast performed about 12 months after the diagnosis of encephalitis showed normal labyrinths and vestibular nerves.

When we examined this patient (at 15 months after the onset of illness), pertinent positive findings on physical examination included diffuse hyperreflexia, bilateral extensor plantar responses, a wide-based gait, and use of a rolling walker. Bedside infrared video oculography showed periodic alternating nystagmus (to be characterized further below). Pertinent negatives included the absence of bradykinesia, the absence of appendicular and cerebellar findings, the absence of dysarthria, and the absence of palatal tremor.

She underwent videonystagmography at an outside institution that reported spontaneous left beat nystagmus, yet also reported a 25% left unilateral caloric weakness, which was unexpected because a unilateral caloric weakness would usually provoke spontaneous nystagmus whose fast phase beats away from the deficient side (rather than toward it). This outside study did not report Periodic Alternating Nystagmus (PAN), or (more likely) did not observe the spontaneous nystagmus long enough to recognize that its horizontal direction changed in a cyclical fashion.

When the patient came to us for evaluation, during bedside examination with infrared video oculography (Micromedical VisualEyes 525b by Interacoustics) we observed spontaneous nystagmus for several minutes and appreciated PAN, which may have distorted the outside videonystagmogram's calculation of caloric weakness. We then undertook an audio-vestibular workup, starting with an audiogram, displayed in Figure 1, that showed moderate high frequency sensorineural hearing loss, 5–10 dB more pronounced on the left side.

We then performed videonystagmography (Micromedical VisualEyes 525b by Interacoustics) to document the periodic alternating nystagmus clearly, and a selection of those results is shown in Figure 2, but we did not rely on videonystagmography to assess peripheral vestibular function. We elected instead to assess peripheral vestibular function with tests whose results would not be altered by the presence of PAN; bilateral vestibular

weakness involving the high frequency range of horizontal semicircular canal afferents was identified on video Head Impulse Testing (vHIT) (VisualEyes EyeSeeCam by Interacoustics) as shown in Figure 3; right-sided vestibular weakness involving saccular afferents was identified on cervical vestibular evoked myogenic potentials (cVEMP) (Eclipse EP25 by Interacoustics) as shown in Figure 4; and left-sided vestibular weakness involving utricular afferents was identified on ocular Vestibular Evoked Myogenic Potentials (oVEMP) (Bio-Logic NavPro by Otometrics) as shown in Figure 5. In other words, there were different patterns of peripheral vestibular weakness on each side.

We also performed Rotatory Chair Testing (RCT) (Orion with VisualEyes 525b by Interacoustics), which showed several findings. First, step velocity testing showed normal gains and time constants (Figure 6); and slow harmonic acceleration showed modest phase lead, but normal gain (Figure 7); these suggest that the low- to middle-frequency range of the vestibulo-ocular reflex was spared (in contrast to the results of vHIT described earlier). Second, visual fixation suppression of the vestibulo-ocular reflex was impaired (Figure 8), suggesting cerebellar dysfunction.

It may be that the outside institution was uncertain whether to ascribe importance to the videonystagmography findings since they appeared internally inconsistent. Our conclusion was that the West Nile encephalitis had involved both vestibular nerves (though resulting in a different pattern of vestibular weakness on each side), causing a baseline level of unsteadiness that had been very slowly improving, whereas the fluctuating component of disequilibrium was instead due to the acquired PAN, likely due to encephalitic damage of the cerebellar nodulus.

The prognosis of acquired periodic alternating nystagmus is poor since it reflects irreversible damage to the cerebellar nodulus from which is not possible to compensate. Some improvement of vestibular weakness is possible (through central compensation), and can be accelerated with appropriately targeted vestibular rehabilitation therapy.

There is modest literature from case series suggesting that the nystagmus of PAN itself may diminish on treatment with baclofen [13] including in cases of acquired PAN [14, 15], but in this case there would have been some risk of interaction with ropinirole, and the patient also expressed reluctance to add any medications to her regimen.

We therefore encouraged this patient to re-attempt physical therapy, but this time specifically targeting vestibular weakness. The rationale was that although vestibular therapy would not improve PAN, it stood some chance of accelerating recovery from vestibular weakness, and would incur no medical risk. The patient was lost to follow-up, despite three attempts at contacting her and her family.

Discussion

Several hypotheses have been proposed regarding the underlying mechanism of periodic alternating nystagmus [12, 16], but these remain speculative. When a circumscribed lesion is discernible, it usually involves the cerebellar nodulus or uvula [17-19], less commonly the medulla [20, 21].

In this case a detailed history revealed that the disequilibrium had both a baseline (chronic) component, on which (episodic) exacerbations were superimposed. This history dovetailed with the findings of a static vestibular weakness (causing chronic unsteadiness) that may improve slowly (though incompletely) over time, and the fluctuating ocular motor finding of periodic alternating nystagmus (causing episodic exacerbations).

A clinical take-home point from this case is that if a patient's symptoms include fluctuating disequilibrium and their physical examination reveals spontaneous nystagmus, it may be helpful to observe that nystagmus for long enough to recognize whether it changes direction. In this case, the spontaneous nystagmus had a periodicity of about 4 minutes, which is fairly common in PAN [16], and would have been easily missed on a rushed examination.

Ethical Considerations

Compliance with ethical guidelines

The data for this case were collected as part of a research protocol approved by our institutional review board (University of Chicago IRB23-1045).

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Conflict of interest

The author declares no conflicts of interest.

References

1. Pepperell C, Rau N, Krajden S, Kern R, Humar A, Mederski B, et al. West Nile virus infection in 2002: morbidity and mortality among patients admitted to hospital in southcentral Ontario. CMAJ. 2003;168(11):1399-405.
2. Al-Hashimi I, Okon E. West Nile Virus: A Neglected Cause of Bell's Palsy? Cureus. 2024;16(6):e62486. [DOI:10.7759/cureus.62486]
3. Anninger WV, Lomeo MD, Dingle J, Epstein AD, Lubow M. West Nile virus-associated optic neuritis and chorioretinitis. Am J Ophthalmol. 2003;136(6):1183-5. [DOI:10.1016/s0002-9394(03)00738-4]
4. Ayça S, Akkoç G, Özdemir H, Selçuk-Duru HN. An unusual neurologic presentation of pediatric neuroinvasive West Nile virus infection: ophthalmoplegia. Turk J Pediatr. 2021;63(5):909-12. [DOI:10.24953/turkjped.2021.05.019]
5. Cunha BA, Eisenstein LE, Wirkowski E, Klein NH, Johnson DH. West Nile encephalitis relapse presenting with abducens and facial nerve palsies. Am J Med. 2006;119(6):e1-2. [DOI:10.1016/j.amjmed.2005.09.061]
6. Gilad R, Lampl Y, Sadeh M, Paul M, Dan M. Optic neuritis complicating west nile virus meningitis in a young adult. Infection. 2003;31(1):55-6. [DOI:10.1007/s15010-002-3039-4]
7. Hart J Jr, Tillman G, Kraut MA, Chiang HS, Strain JF, Li Y, et al. West Nile virus neuroinvasive disease: neurological manifestations and prospective longitudinal outcomes. BMC Infect Dis. 2014;14:248. [DOI:10.1186/1471-2334-14-248]
8. Koevary SB. Ocular involvement in patients infected by the West Nile virus. Optometry. 2005;76(10):609-12. [DOI:10.1016/j.optm.2005.08.015]
9. Rosenheck MS, Higham C, Sanzone K, Caprio C. New-onset Bell's palsy after neuroinvasive West Nile virus. BMJ Case Rep. 2022;15(7):e249770. [DOI:10.1136/bcr-2022-249770]
10. Ross JJ, Worthington MG. Bilateral sixth nerve palsy in West Nile meningoencephalitis. J Neuroophthalmol. 2004;24(1):97-8. [DOI:10.1097/00041327-200403000-00034]
11. Vaispapir V, Blum A, Soboh S, Ashkenazi H. West Nile virus meningoencephalitis with optic neuritis. Arch Intern Med. 2002;162(5):606-7. [DOI:10.1001/archinte.162.5.606-a]
12. Baloh RW, Honrubia V, Konrad HR. Periodic alternating nystagmus. Brain. 1976;99(1):11-26. [DOI:10.1093/brain/99.1.11]
13. DiBartolomeo JR, Yee RD. Periodic alternating nystagmus. Otolaryngol Head Neck Surg. 1988;99(6):552-7. [DOI:10.1177/019459988809900603]
14. Halmagyi GM, Rudge P, Gresty MA, Leigh RJ, Zee DS. Treatment of periodic alternating nystagmus. Ann Neurol. 1980;8(6):609-11. [DOI:10.1002/ana.410080611]
15. Isago H, Tsuboya R, Kataura A. A case of periodic alternating nystagmus: with a special reference to the efficacy of baclofen treatment. Auris Nasus Larynx. 1985;12(1):15-21. [DOI:10.1016/s0385-8146(85)80074-2]
16. Daroff RB. Periodic alternating nystagmus and the shifting null. Can J Otolaryngol. 1974;3(3):367-71.
17. Furman JM, Wall C 3rd, Pang DL. Vestibular function in periodic alternating nystagmus. Brain. 1990;113 (Pt 5):1425-39. [DOI:10.1093/brain/113.5.1425]
18. Jeong HS, Oh JY, Kim JS, Kim J, Lee AY, Oh SY. Periodic alternating nystagmus in isolated nodular infarction. Neurology. 2007;68(12):956-7. [DOI:10.1212/01.wnl.0000257111.24769.d2]
19. Oh YM, Choi KD, Oh SY, Kim JS. Periodic alternating nystagmus with circumscribed nodular lesion. Neurology. 2006;67(3):399. [DOI:10.1212/01.wnl.0000219818.35451.10]
20. DE Silva L, Cooper BP, McLeod JG. Periodic alternating nystagmus. Proc Aust Assoc Neurol. 1975;12:157-60.
21. Tsutsumi T, Ikeda T, Kikuchi S. Periodic alternating nystagmus caused by a medullary lesion in acute disseminated encephalomyelitis. Otol Neurotol. 2014;35(5):861-5. [DOI:10.1097/MAO.0000000000000344]

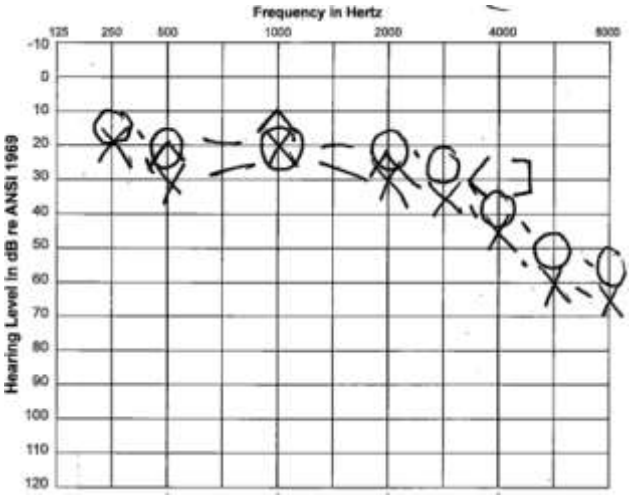

Figure 1. Audiometry showed moderate high frequency sensorineural hearing loss that was 5–10 dB more pronounced on the left side

Figure 2. Selected videonystagmography tracings (Micromedical VisualEyes 525b by Interacoustics) demonstrating periodic alternating nystagmus. In these tracings of horizontal eye movements, by convention an upward deflection represents a rightward eye movement, and a downward deflection represents a leftward eye movement; the red tracing represents the right eye, and the blue tracing represents the left eye; the numbers along the horizontal axis of the tracing are the number of seconds since the start of the recording; the numbers along the vertical axis of each tracing represent the deflection (in degrees) of the eye from the center (primary position of gaze). Panel A shows spontaneous nystagmus, initially right beat. Panel B shows that around 115 seconds the spontaneous right beat nystagmus ceased, and by about 140 seconds had shifted to spontaneous left beat nystagmus. Panel C shows crescendoing of the left beat nystagmus. Panel D shows that around 240 seconds the left beat nystagmus subsided, and by around 255 seconds began to shift back to right beat nystagmus

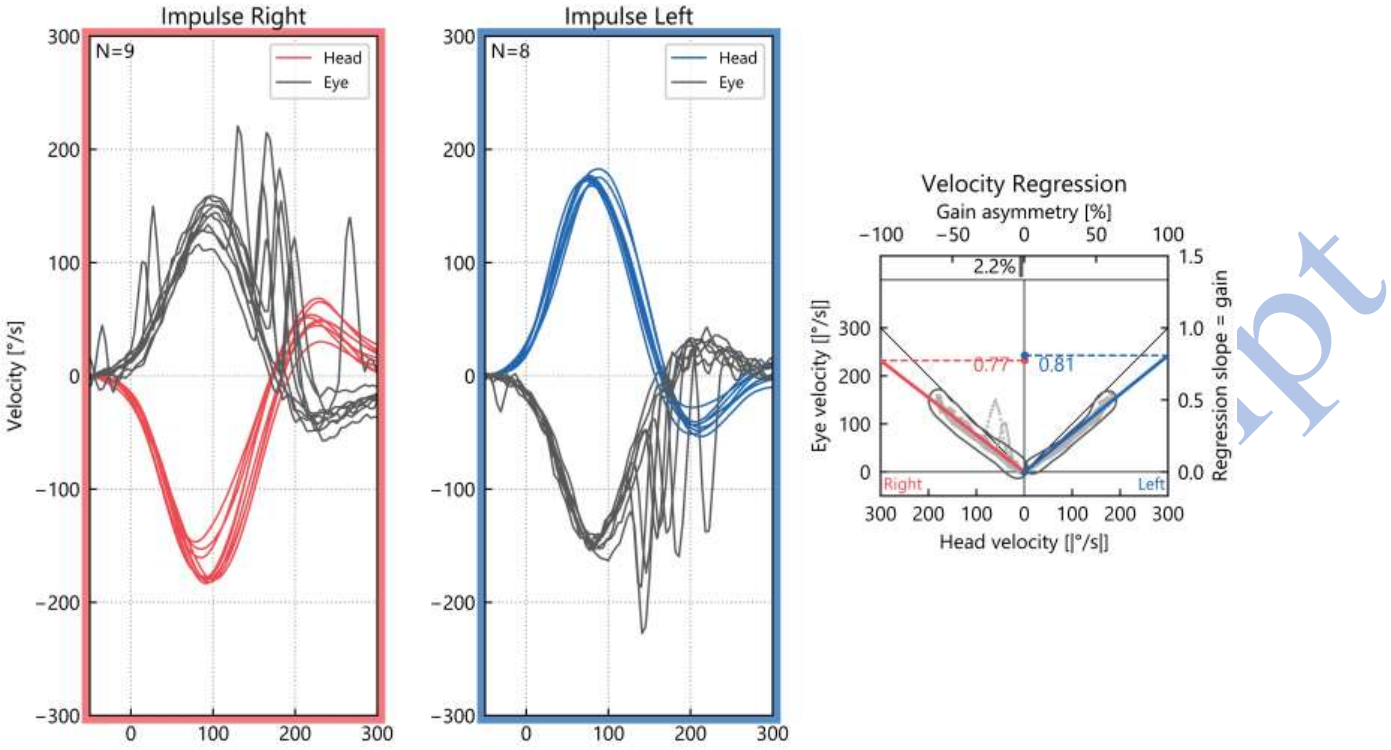

Figure 3. Video head impulse testing (VisualEyes EyeSeeCam by Interacoustics) showed low gain (0.77 on the right, 0.81 on the left, shown on the right of the figure) and covert compensatory saccades for both horizontal canals (shown in the left and middle of the figure)

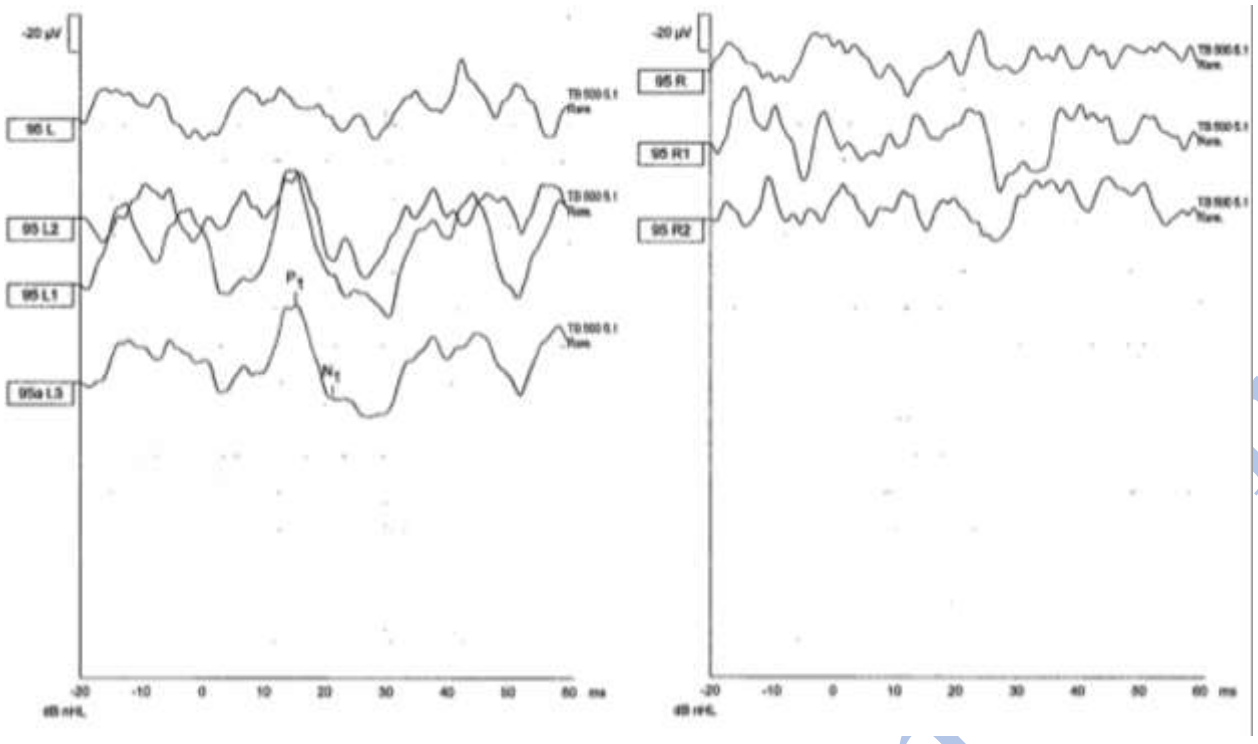

Figure 4. Cervical vestibular evoked myogenic potentials (Eclipse EP25 by Interacoustics) were present on the left with an inter-peak (p1-n1) amplitude of 51 microvolts (left side of figure) but absent on the right (right side of figure)

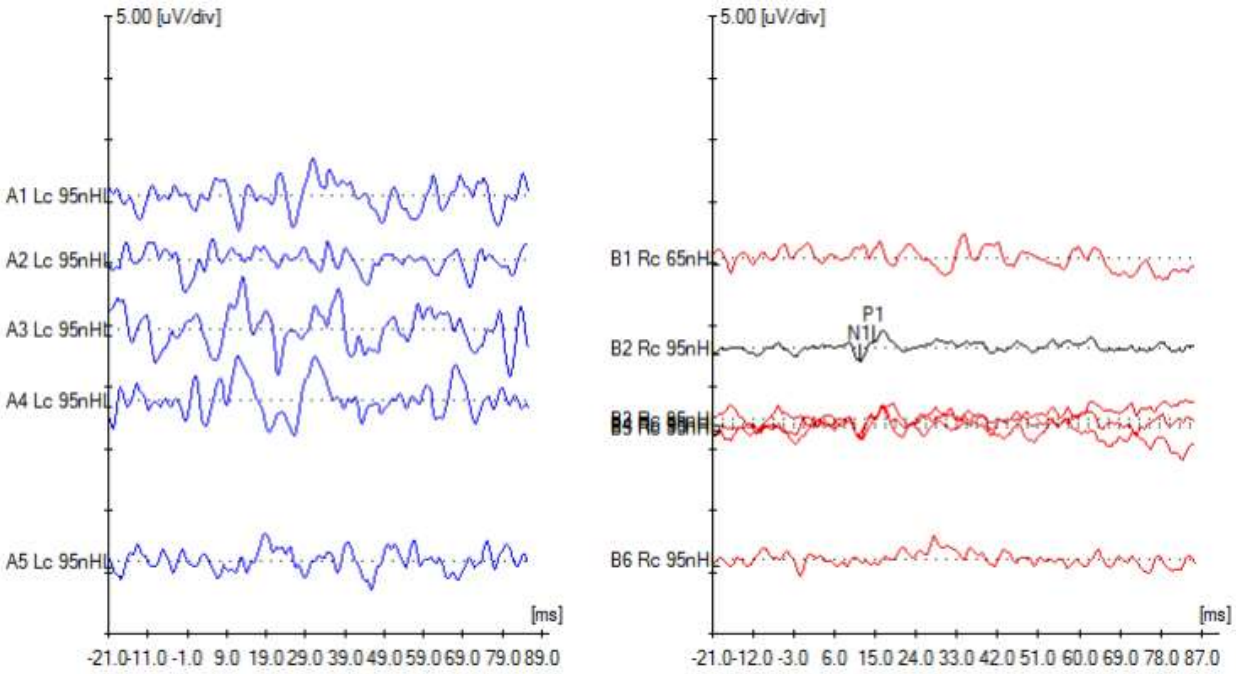

Figure 5. Ocular vestibular evoked myogenic potentials (Bio-Logic NavPro by Otometrics) were present on the right with an inter-peak (n1-p1) amplitude of 1.52 microvolts (right side of figure) but absent on the left (left side of figure)

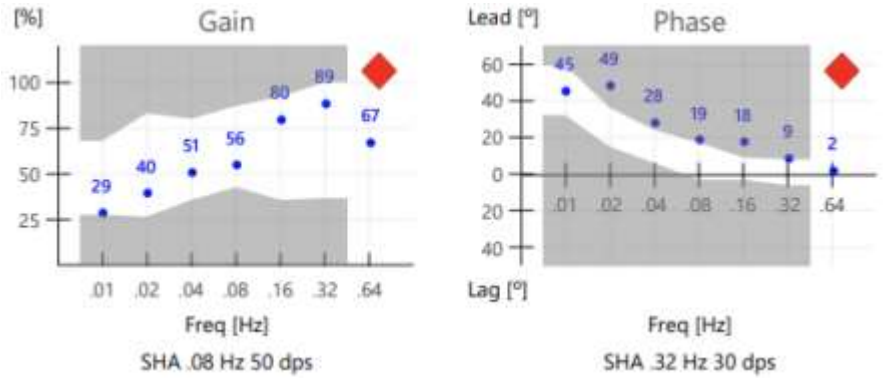

Figure 6. Rotatory chair testing (Orion with VisualEyes 525b by Interacoustics). Slow harmonic acceleration showed normal gains at 0.01–0.32 Hz (left panel), despite modest phase lead at several frequencies (right panel)

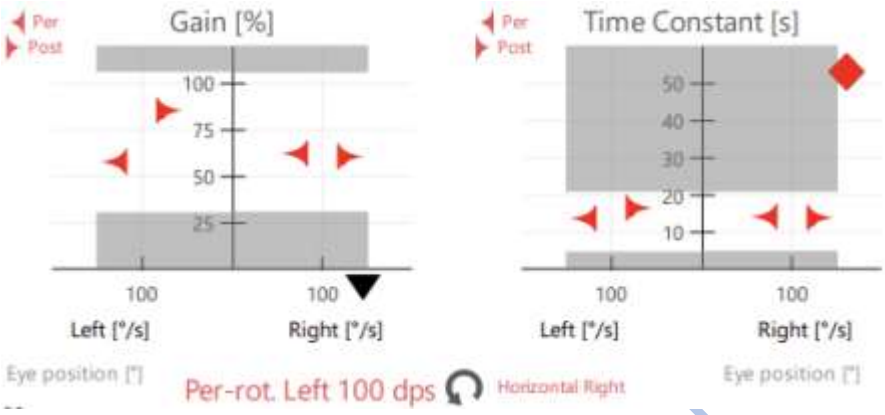

Figure 7. Rotatory chair testing (Orion with VisualEyes 525b by Interacoustics). Step velocity testing showed normal gains (left panel) and time constants (right panel)

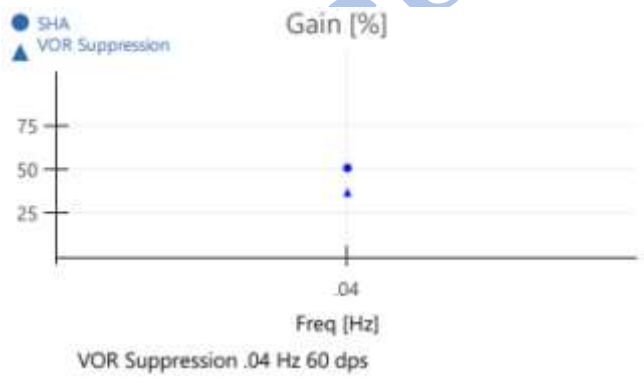

Figure 8. Rotatory chair testing (Orion with VisualEyes 525b by Interacoustics). Visual vestibulo-ocular reflex suppression was poor with a gain of about 0.35. VOR; vestibulo-ocular reflex