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Neurogenic vestibular evoked potentials using a tone pip auditory stimulus

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Abstract

Objectives: *To obtain neurogenic vestibular evoked potentials (NVESTEPs) with surface scalp recording using a tone pip auditory stimulus.*

Methods: *Fourteen neurologically normal volunteers (Age range 26-45 years, 10 females and 4 males), and two patients with sensorineural hearing loss and possible multiple sclerosis respectively, were examined. Two channel recordings were obtained, the first channel being P3 referred to Fpz, and the second channel being P4 referred to Fpz. A 1 kHz tone pip stimulus with two cycles was delivered via headphones monoaurally with contralateral masking noise.*

Results: *A consistent negative wave with a mean absolute latency of 4.72 msec was obtained, which we have named N5. 25% of the ears tested had better responses at the ipsilateral parietal electrode. In the patient with bilateral sensorineural hearing loss, NVESTEPs was present, suggesting that the NVESTEP is not a cochlear response. In the patient with possible multiple sclerosis, an abnormal NVESTEP response and a normal BAEP response were found.*

Conclusion: *Use of a tone-pip rather than a click auditory stimulus allows a lower click intensity to be used in the production of NVESTEP responses, leads to a shorter testing time, and is therefore more comfortable for the patient. This study adds to our impression that the NVESTEP may be a physiological response that can be used to assess the vestibular system and is different from the BAEP response. Further testing in patients with symptoms of dizziness and with disorders specific for the vestibular nerve is required.*

Key-words: Vestibular, evoked potential, tone, neurogenic, brainstem

Introduction

Neurogenic electrophysiological evoked responses from vestibular nerve stimulation in humans have been attempted in the past, using rotation (7, 8, 13, 14, 25, 28, 29) and head drop (16). Myogenic vestibular evoked responses using high intensity clicks, recording mainly from the tonically activated sternocleidomastoid muscles, have recently been developed using a technique that can be easily performed in any neurophysiological laboratory that performs routine brainstem auditory evoked potentials (BAEPs) (3, 4, 5, 6, 9, 10, 11, 12, 19, 20, 22, 23, 26, 32). It is possible to use an auditory stimulus to test a vestibular pathway, that is, a pathway subserving posture and acceleration in movement, as it has been shown that saccular afferents are very sensitive to

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sound (3, 18, 21). This may be a consequence of the proximity of the saccule to the stapes footplate and eddy currents set up in the endolymph by sudden movement of the stapes (3, 31). Using high intensity clicks, we have previously shown that it is possible to record neurogenic vestibular evoked potentials (NVESTEPs) from the parietal areas, with a negative peak at around 3 msec after stimulus onset, and which may originate from the pons (24). In relation to myogenic vestibular potentials, Welgampola and Colebatch (33) have found that the use of a tone burst stimulus allows one to use a lower intensity auditory stimulus than with a click stimulus. The present study looked at the use of a tone pip auditory stimulus in the production of NVESTEPs. We have found that lower stimulus intensities may be used, although the absolute latencies are prolonged by about 1 msec compared to responses evoked by a click stimulus. In addition, use of the tone pip stimulus reduced the testing time from 30 minutes to 10-15 minutes and responses were found to be best obtained from the ipsilateral parietal area of the scalp. We show also that this response is within normal limits in a patient with bilateral sensorineural hearing loss, and abnormal in a patient with possible multiple sclerosis (M.S.) with small demyelinating plaques in the pons.

Methods and materials

The study was approved by the local ethics committee. Fourteen neurologically normal volunteers were examined (Age range 26-45 years of age, 10 females and 4 males). Surface silver/silver chloride EEG electrodes were placed at P3, P4, Fpz and Cz according to the internationally used 10/20 system (15). The scalp areas were cleaned with a skin preparation gel (Skinpure, Nihon Kohden Corporation, Japan) and applied using EEG paste (Elefix, Nihon Kohden Corporation, Japan). The subjects were then placed supine on a bed with the eyes closed, relaxed but awake. Two channel recordings were performed, with P3 referred to Fpz in the first channel and P4 referred to Fpz in the second channel. Cz was used as the ground. The instrumentation used was the Nicolet Viking IV. Filter settings were 100Hz-3kHz, with a horizontal sweep of 2 msec/division and a vertical resolution of 0.2 uV/division. Oscilloscope readings were displayed with the negative polarity in the upward direction. The rate of stimulation was 10.1 Hz delivered via headphones. A tone pip auditory stimulus with a frequency of 1 kHz was used with two total cycles per stimulus. 500-1000 stimulations were obtained. Monoaural stimulation was performed for the left and right ears separately. A contralateral masking noise was used that was 30 dB nHL in tone pip intensity lower than the intensity of the test stimulus.

Results

Figure 1 shows the result of a recording from ambient space and the amplifier inputs connected to themselves, to illustrate the stimulus artifact created by the tone pip stimulus. The stimulus was set to a minimum of two cycles so as to restrict this artifact to within 2 msec and not to affect the recording of evoked potentials. The recording system used did not provide the option of alternating polarity with tone-pip stimulation, which would have otherwise removed this stimulus artifact. An example of a result from a neurologically normal volunteer is shown in figure 2. Only one wave is consistently obtained among the neurologically normal volunteers, at an absolute latency of around 4-5 msec.

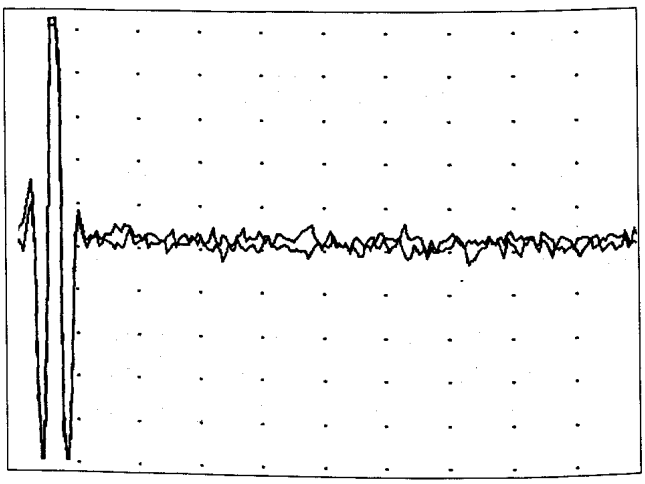

Fig.1. – A recording in ambient space, with the electrodes of the amplifier connected to themselves and placed in the vicinity of the headphones. The 1 kHz tone pip stimulus produces a prominent stimulus artifact. Setting the stimulus to two cycles restricts this artifact to within 2 msec. The sweep is 2 msec/division and the vertical resolution is 0.2 uV/division.

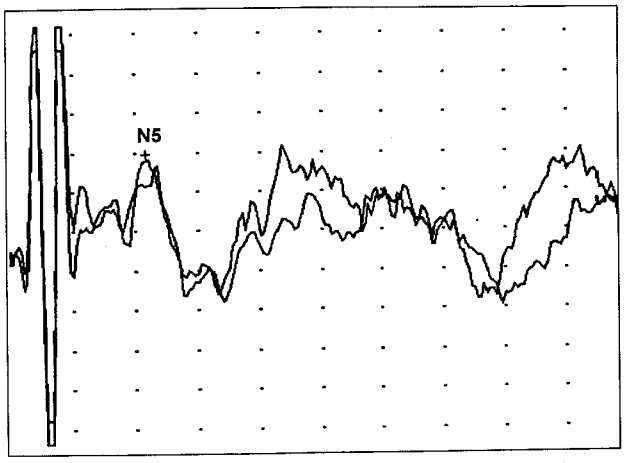

Fig. 2. – Result of an NVESTEP study in a neurologically normal volunteer recorded from the ipsilateral parietal electrode and referred to a frontopolar electrode. The sweep is 2 msec/division and the vertical resolution is 0.1 uV/division.

For seven of the 28 ears (25%) tested in total, the response was better obtained or only obtained at the parietal area ipsilateral to the test ear. The response was present only at the ipsilateral parietal area for both ears for two subjects (14.3%). In none of the volunteers was the response better at the contralateral parietal area. Normative values for this group are therefore reported only for the ipsilateral parietal area, which are summarized in Table 1. Because the mean absolute latency of the response is close to 5 msec and as it has a predominantly negative polarity, we have named this waveform N5. The response was unobtainable in all subjects at 60 dB nHL. In one subject the minimum tone pip intensity at which the response appeared was at 70 dB nHL, in six subjects the minimum was 80 dB nHL, in five subjects it was 90 dB nHL and in two subjects it was 100 dB nHL. In the latter group, the stimulus was not described by the subjects as being painful. The total testing time, including the procedure of measuring and placing the electrodes on the scalp and explaining the examination to the subject, was not longer than 15 minutes.

Case examples

In addition to healthy volunteers, two patients were examined. Both patients gave written informed consent for this study.

Table 1. – *Normal values for the absolute latency of the N5 response (n=14)*[3]

Parameter	Mean	S.D.	Range	Limit[2]
Absolute latency	4.72	0.52	3.92 – 5.76	< 6.02
IALD[1]	– 0.12	0.35	– 0.72 – 0.36	– 1.0 – 0.75

[1] IALD = interside absolute latency difference (left minus right).
[2] The limit for the absolute latency is defined as mean plus 2.5 standard deviations, and for the IALD mean plus and minus 2.5 standard deviations.
[3] The mean absolute latency was calculated by first averaging the responses from the left and right ears for each normal control.

Case 1

This 53-year-old man was referred to the CING with episodes of vertigo, unstable gait, and numbness in both upper and lower limbs, with a working diagnosis of multiple sclerosis. The MRI revealed plaques in the periventricular white matter and centrum semiovale bilaterally, and none in the brainstem. Brainstem auditory evoked potentials revealed unobtainable responses bilaterally at a click intensity of 70 dB nHL, and waveforms with normal absolute and interpeak latencies at a click intensity of 90 dB nHL, which was suggestive of the presence of sensorineural hearing loss bilaterally. Neurogenic tone pip evoked vestibular potentials, recorded from the ipsilateral parietal areas, were however within normal limits at a tone pip intensity of 90 dB nHL on the right and at 80 dB nHL on the left. To rule out the possibility that the latter are simply a BAEP response produced by a tone pip stimulus which is acoustically more focused than a click stimulus, a BAEP recording was obtained at a tone pip intensity of 80 dB nHL for the left ear, which revealed the presence of only wave V at 7.30 msec (Fig.3). This is a completely different and separate response from the NVESTEP tone pip response at the same intensity for the same ear, which appeared at 4.08 msec, providing evidence that the NVESTEP response recorded here is not at least a partial manifestation of a BAEP response, and is therefore not of cochlear origin.

Case 2

This 17-year-old woman is being followed for possible M.S., with a six month history of dizziness.

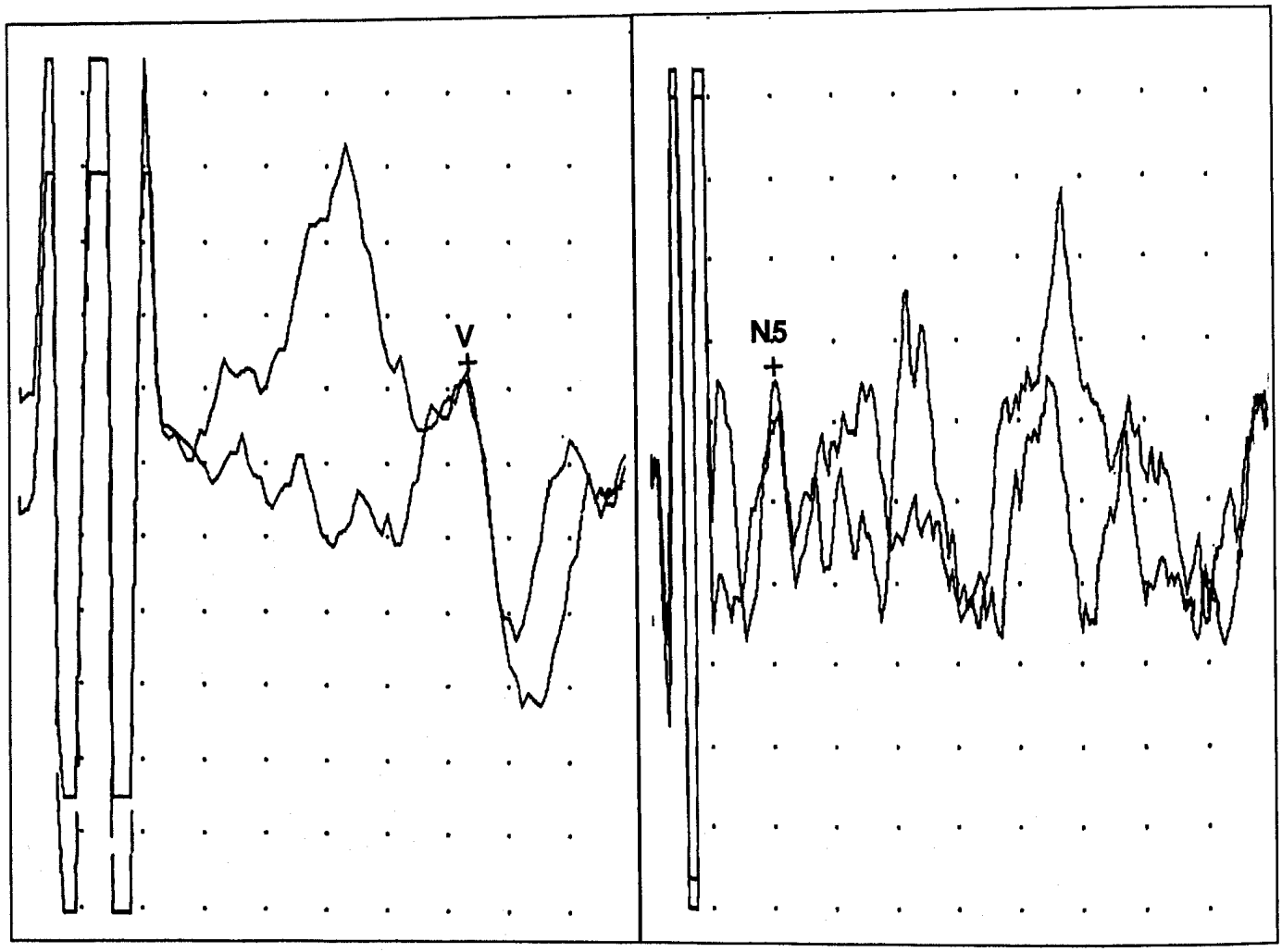

Fig. 3. – Results of a BAEP recording (left figure) and an NVESTEP recording (right figure) of a patient with bilateral sensorineural hearing loss, using a tone pip stimulus intensity of 80 dB nHL for the left ear. The BAEP revealed the presence only of wave V, at a latency much later than the NVESTEP response, suggesting that the latter is non-cochlear in origin and not the same response. The sweep and vertical resolution are 1 msec/division and 0.1 uV/division (left), and 2 msec/division and 0.1uV/division (right) respectively.

Several foci were reported in the brain MRI, with small lesions in the left dorsal pons and right ventral pontomedullary junction in the brainstem. Visual, brainstem auditory and short latency somatosensory evoked potentials were all within normal limits. Tone pip evoked NVESTEPs (Fig. 4) revealed a normal N5 response with left ear stimulation (4.48 msec), but a prolonged N5 response with right ear stimulation (6.18 msec). The interside absolute latency difference was significantly prolonged (1.70 msec). The presence of a possible cortical potential was noted with right ear testing at around 12 msec after stimulus onset.

Discussion

In this study we were able to record electrophysiologically a neurogenic signal from the scalp surface, using a tone pip auditory stimulus, that is possibly of vestibular origin. We have named the response N5 due to its predominantly negative polarity and appearance at approximately 5 msec after stimulus onset.

The N5 response is very similar to the N3 response obtained with a click auditory stimulus obtained in the same scalp area that we have reported previously (24). The N5 response we report here is

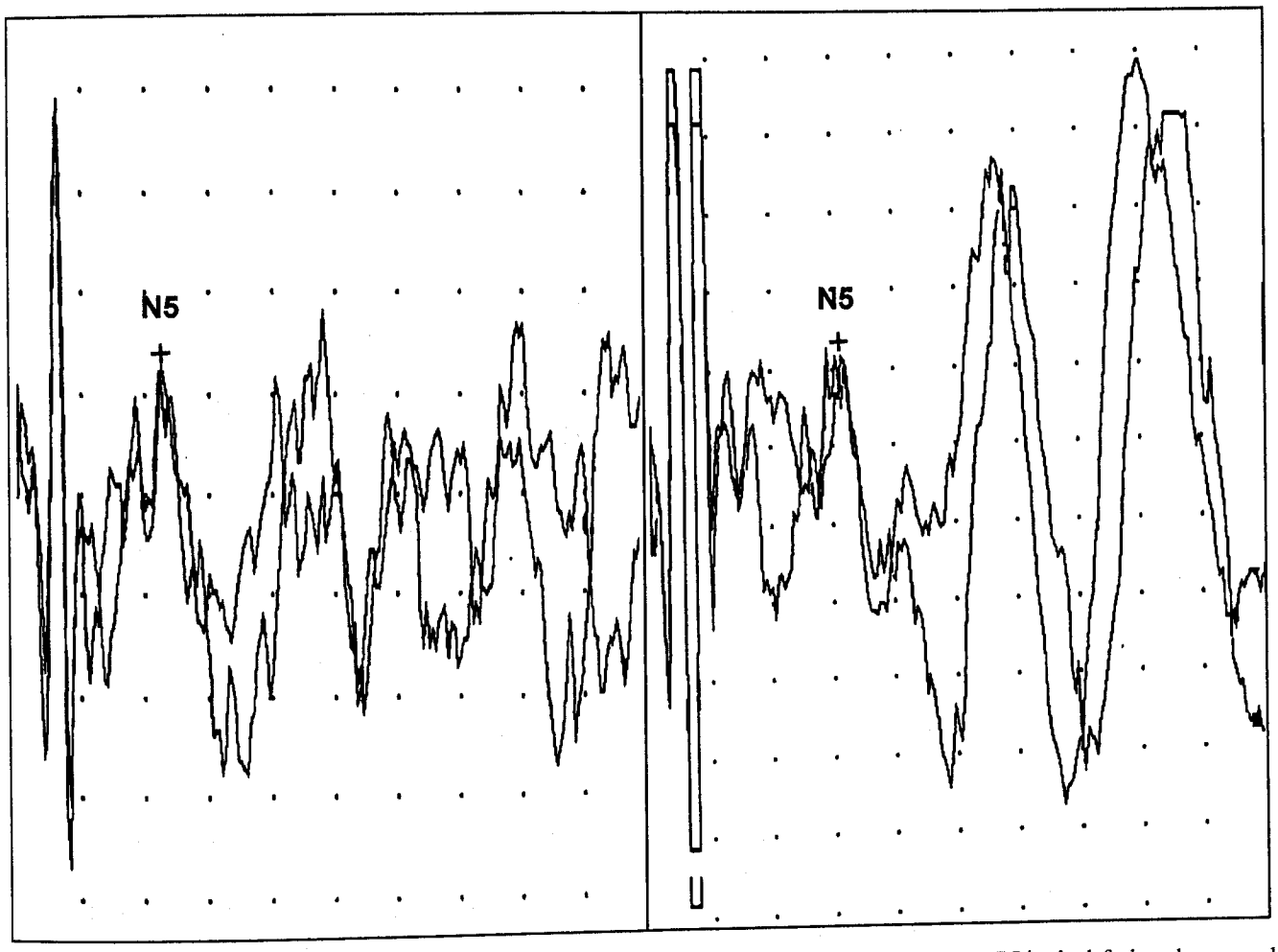

Fig. 4. – NVESTEP results in a patient with possible multiple sclerosis, with demyelinating lesions on MRI in the left dorsal pons and right ventral pons-medullar junction. A significant interside difference is seen, with right ear testing producing the longer latency (right figure). Both figures have a sweep of 2 msec/division and a vertical resolution of 0.1 uV/division. The presence of a possible cortical potential is noted with right ear stimulation at around 12 msec.

however longer in latency than the latter response. This is due to the use of a tone rather than a click stimulus and has also been reported for the BAEP response, where tone pip stimuli produce responses of longer absolute latency than click stimuli (30).

We noted in this study that in many neurologically normal individuals, the response was best obtained ipsilaterally to the test stimulus, and that in none of the subjects was the response better on the contralateral side. Therefore, one can perform this examination with a one-channel recording from the ipsilateral parietal area referenced to Fpz. In addition, this rules out the possibility that Fpz is contributing to the NVESTEP response. If it had, responses of equal amplitude and persistence would have appeared bilaterally in our recordings from both P3 and P4, as recordings from both parietal areas were referenced to the same Fpz electrode.

Lower sound intensities were used to obtain NVESTEP than in our previous study, in which a click auditory stimulus was used. Unlike our previous study where a click intensity of 105 dB nHL had to be used, here an average tone pip intensity of 80 dB nHL was sufficient. The lower intensity may be due to the more focused sound pressure wave frequency content of the tone pip, than the less focused click which consists of a wide range of frequencies (30). The lower tone pip intensity allowed continuous recording and shorter testing time. In our previous study, intervals of rest were introduced during

the test, as it is known that a high click intensity (greater than 100 dB) delivered over a long period of time may cause damage to the peripheral hearing apparatus (1), and this made testing time longer.

The stimulus had to be restricted to the minimum two cycles allowed by our recording system. The stimulus artifact in this way was restricted to within two seconds of the recording after stimulus onset. Therefore, if there was an evoked potential in the first two seconds, we would not have been able to see it. This artifact is present also with tone burst evoked myogenic vestibular potentials (Colebatch, personal communication), but because of the long absolute latency of the myogenic response (> 10 msec), the stimulus artifact did not affect their recordings (33). A tone pip was used in our study rather than a tone burst stimulus, as was used in the study by Welgampola and Colebatch (33), as the tone burst stimulus is of long duration (5msec) and the resulting stimulus artifact would have hidden the underlying early evoked potentials.

In this study, we used a longer time base than in our previous study, in the hopes of obtaining a more rostral response from the vestibular pathway. Apart from the N5 response, no other consistent reproducible response amongst the neurologically normal volunteers was seen. A possible reason for this may be the fact that a primary vestibular cortex does not exist (2,17). Another reason may be the fact that the conditions of our recording favor far-field recordings, rather that near-field recordings (30). The fast stimulus rate used may not allow us to record cortical potentials, which are on average of longer duration and longer latency than sub-cortical potentials and may interact with each other at high rates. Further studies are needed to clarify this. We did note however in our second case a possible cortical potential following the N5 response at around 12 msec after stimulus onset. We have seen this also in a few BAEP recordings using long sweep times. However, because it is not present in all neurologically normal individuals, it is not at the moment of good clinical utility.

The first patient case with sensorineural hearing loss and normal NVESTEP responses provides evidence, together with evidence provided in our previous publication (24) for the non-auditory origin of the NVESTEP response. To further prove this point, we will need to perform this examination in patients with unilateral peripheral vestibular dysfunction, and demonstrate a unilateral absence of the NVESTEP on the side of the lesion. Our second case though shows a unilateral prolongation of NVESTEP absolute latency with demyelinating plaques present in the left dorsal pons and right ventral pontomedullary junction on MRI. In this case the BAEP response was completely normal, further illustrating the dissociation between the BAEP and NVESTEP response. The second case also adds to our suspicion from our previous study that the origin of the NVESTEP response (in this case N5) originates at or close to the pons.

Conclusions

Use of a tone-pip rather than a click auditory stimulus allows a lower click intensity to be used in the production of NVESTEP responses, leads to a shorter testing time, and is therefore more comfortable for the patient. We have therefore further refined a neurogenic neurophysiological examination that possibly tests separately from the auditory system the vestibular pathway of the nervous system, using a tone pip auditory stimulus and recording from the parietal scalp areas. This test would eventually prove useful in patients with symptoms of dizziness, as well as in detecting subclinical abnormalities in multiple sclerosis, and in diseases specific to the vestibular nerve. Further validation in a larger number of patients and in normal controls is needed.

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