

ORIGINAL ARTICLE

Vertical acquired pendular nystagmus: oculomotor findings, localizing value and pathophysiology

Rosen IKONOMOV¹, Dolja PHILIPOVA¹, Katerina STAMBOLIEVA²

¹ Department of Neurology, UMHAT Sofamed, Sofia, Bulgaria; ² Institute of Neurobiology, Bulgarian Academy of Science, Sofia, Bulgaria.

Correspondence to: Rosen Ikonov, MD., PhD., Department of Neurology, UMHAT Sofamed, 16 G.M. Dimitrov Blvd, Sofia 1797, Bulgaria. TEL: +359888766461; FAX: +35924444460; E-MAIL: drros@abv.bg

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Abstract

OBJECTIVES: Evaluation of the localizing value and pathogenesis of vertical APN through examination of patients with this nystagmus form and different diagnosis.

DESIGN: Three patients with vertical APN with different diseases (brainstem infarct, brainstem encephalitis and brainstem haemorrhage), but with similar topic of lesions, are presented. For registration of the nystagmus AC-electrooculography (EOG) was used.

RESULTS: All patients were registered with spontaneous nystagmus with the following characteristics: vertical, conjugate APN with average frequency of 3.1 Hz and average amplitude of 7°.

THE MAIN FINDINGS: Several main theories about the etiology and pathogenesis of the APN exist. According to the first one, this nystagmus form is due to the primary demyelination of the optical nerves, leading to a delay in visual feedback. However, the more popular theory is the one, according to which APN is due to certain abnormalities of the internal brainstem circuits, such as the connections between the brainstem nuclei and the cerebellum.

CONCLUSIONS: Following the examinations, we were able to conclude that the lesions of the optical nerves are not the main reason, causing the APN, as all three patients did not have clinical and instrumental data for involvement of the visual pathways. From another point of view, all three patients had established brainstem lesions. The identical topic of the lesions suggested a connection between the vertical APN and this localization. The patients' lesions were observed in the midbrain, mainly tegmental, paramedian, ventrolateral from the oculomotor nucleus, in the area of the red nucleus.

Abbreviations:

APN – Acquired Pendular Nystagmus; CT – Computed Tomography; MRI – Magnetic Resonance Imaging; EOG – Electrooculography; AC – Alternating Current; CNS – Central Nervous System;

INTRODUCTION

The pendular nystagmus is an involuntary sinusoidal oscillation of the eyes. Compared to the jerk nystagmus, it does not have a quick phase (Gresty *et al* 1982; Leigh & Zee 2006). It can be congenital or acquired.

The acquired pendular nystagmus (APN) is caused by different diseases of the central nervous system and above all by disruptions of the central myelin, such as multiple sclerosis (Kori *et al* 1993; Leigh & Zee 2006). Its characteristics usually allow it to be clinically differentiated from the congenital one, which is most

frequently horizontal, binocular and conjugate, and changes into jerk nystagmus on lateral gaze. In comparison, APN may be monocular or binocular, conjugate or disconjugate, horizontal, vertical or torsional and largely independent of the eye position (Gresty *et al* 1982). In spite of its big frequency, the lesion topics and the pathogenesis in the APN are not completely cleared up (Barton & Cox 1993). This concerns especially the vertical forms, which occur more rarely. We have observed 3 patients with vertical APN with different diseases, but with similar topic of lesions in the brainstem, which allows us to draw conclusions about the localizing value of this nystagmus form.

MATERIALS AND METHODS

We have studied 3 patients in the age range of 42–72 years, which had vertical APN and different diseases (brainstem infarct, brainstem encephalitis and brainstem haemorrhage). Two of them had vertical gaze paresis and the third one – horizontal left and right gaze paresis. For visualization of the lesions the necessary additional tests were made (CT and/or MRI). We have used the visual acuity and visual evoked potentials to examine the visual pathways.

For registration of the nystagmus we have used electrooculography (EOG). The records were made on an electronystagmography system Tonies with AC amplifier and time-constant 2 s, followed by a computer analysis of the data. The eye-movements were registered during a gaze straight ahead and during gaze 40° right, left, up and down, and during a fixed gaze and eliminated fixation. The patients' saccadic movements (light stimuli with 1 s intervals at a distance 40° horizontally and vertically) and the smooth pursuit (sinusoidal laser stimulus with frequency 0.3 Hz) were also examined.

RESULTS

The MRI/CT visualization of the lesions of the three patients is presented in Figure 1. All had brainstem lesions, engaging the paramedian parts of the tegmentum in the midbrain. No clinical and instrumental data (including visual evoked potentials) for involving of the visual pathways were observed.

A spontaneous nystagmus was registered with the following characteristics: vertical, conjugate APN in all, third degree in two of them (with the biggest amplitude recorded during an up-gaze); first degree in the third one (Figure 2), with average frequency of 3.1 Hz and an average amplitude of 7°. The elimination of the fixation leads to disappearance of the nystagmus in two of the patients and to decrease in the third one.

The saccadic movements were disrupted in all patients, as decreased saccadic velocity without dysmetria was also observed. A decrease in the velocity was found mostly during an up-movement, with increased vertical asymmetry. The smooth-pursuing movements were also disrupted in all patients, as the most disrupted was the vertical, up-movement pursuit. In two of the patients the pursuit had decreased amplitude and saccadic character, and in the third one – it was severely disorganized (Table 1).

DISCUSSION

Undoubtedly, all patients had spontaneous nystagmus with characteristics of APN – acquired nystagmus with sinusoidal character, without a quick phase. This nystagmus form has always evoked great interest among the scientists, as the etiology, the pathogenetic mechanisms and its localizing value were broadly discussed. Generally accepted is the conception that APN is con-

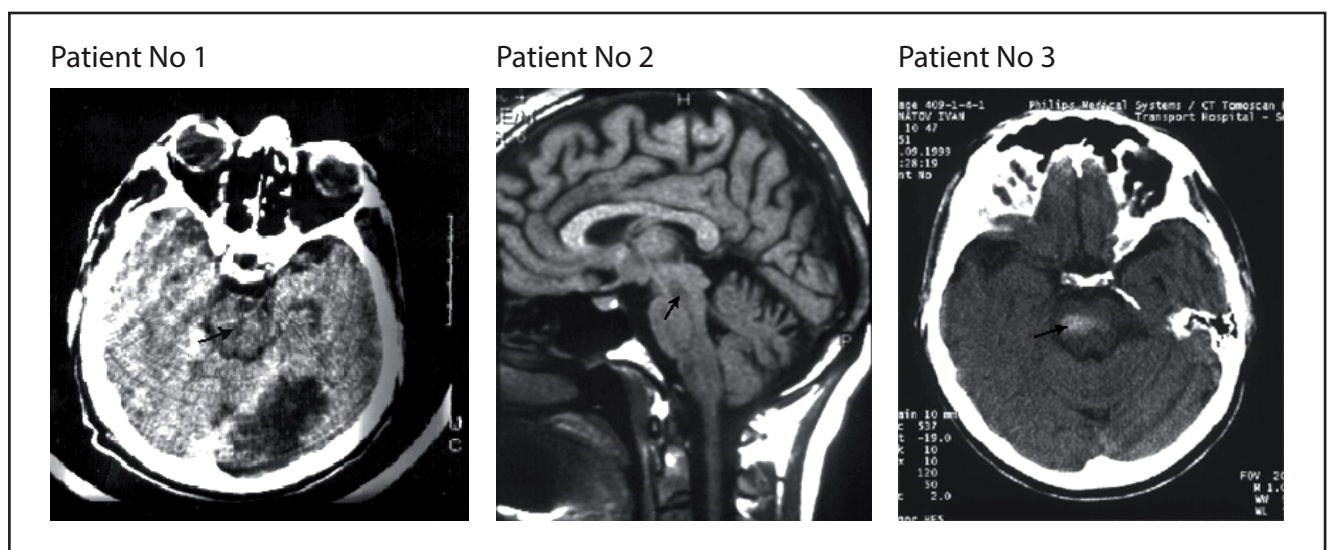


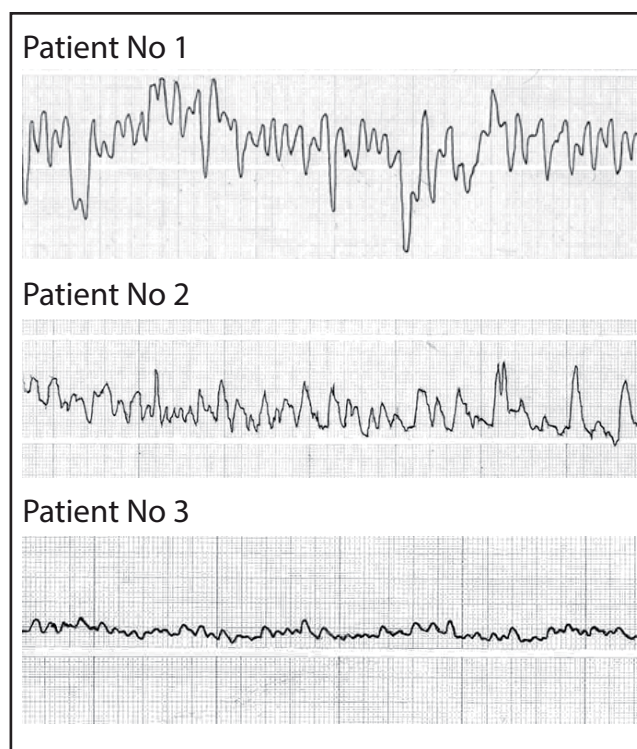
Fig. 1. CT/MRI findings in the patient (arrows indicate the lesions in the midbrain).

Tab. 1. EOG findings in the patients studied.

No	Spontaneous nystagmus				Saccadic movements					
	Direction	Degree	Frequency	Amplitude	right	left	asymmetry	up	down	asymmetry
1	Vertical	3 rd degree	2.5 Hz	12°	290°/s	264°/s	4.7%	144°/s	228°/s	22.7%
2	Vertical	3 rd degree	2.6 Hz	7°	213°/s	227°/s	3.2%	56°/s	219°/s	59.3%
3	Vertical	1 st degree	4.3 Hz	2°	142°/s	186°/s	13.3%	226°/s	337°/s	19.7%

nected with different pathological processes, concerning mainly the myelin in the central nervous system (Kori *et al* 1993; Leigh & Zee 2006). This is the reason why its highest frequency occurs in the demyelinating disorders – multiple sclerosis and the leucoencephalites (Tsutsumi *et al* 2014). However, it can also be observed in other diseases, engaging the brainstem – vascular, tumors, degenerative, dystrophic, toxic (Gresty *et al* 1982; Kori *et al* 1993; Lawrence & Lightfoote 1975; Leigh *et al* 1994; Leigh & Zee 2006; Yamamoto *et al* 1992; Yokota *et al* 1999). Another main reason for APN is the disruption or the loss of vision due to diseases of the visual pathways, especially at a younger age (Barton & Cox 1993; Leigh & Zee 2006). The characteristics of APN are various – horizontal, vertical, torsional or combined, conjugate or disconjugate, with different frequency and amplitude (Gresty *et al* 1982; Leigh & Zee 2006). Lopez *et al* (1995, 1996) describe 27 patients with APN with different direction (4 with horizontal, 5 with torsional, 3 with vertical and 8 with combined) and conjugation (15 with conjugate and 12 with disconjugate nystagmus). Most of the authors share the opinion that the frequency of APN is between 2 and 7 Hz, the average is around 3.5 Hz, and the amplitude is between 2° and 5° (Gresty *et al* 1982; Kori *et al* 1993; Leigh *et al* 1994; Lopez *et al* 1995; Lopez *et al* 1996). Our results confirm these limits for the frequency (average frequency 3.1 Hz), but the amplitude is larger (average 7°). The observed vertical direction of the APN is comparatively more rarely than the other forms (Averbuch-Heller *et al* 1995; Lopez *et al* 1995, 1996). However, it can also be observed, that while in multiple sclerosis the horizontal forms are predominant, in other etiological factors (vascular and infections) the vertical forms occur more often (Gresty *et al* 1982; Lawrence & Lightfoote 1975), as confirmed by our patients' diseases (2 with cerebrovascular disease and 1 with viral infection of CNS). APN can be associated with pendular movements of other structures, such as palate, facial muscles, tongue, pharynx, diaphragm and extremities, usually with the same frequency, as this state is called ocular myoclonus (Bassani *et al* 2011; Buckley 1997; Leigh & Zee 2006; Tilikete *et al* 2011).

The subjects for pathogenesis and localizing value of APN, including its vertical forms, are not completely cleared up. Several main theories about its etiology and pathogenesis exist (Averbuch-Heller *et al* 1995; Leigh *et al* 1994; Leigh & Zee 2006). According to the first one

**Fig. 2.** EOG findings in the patients (spontaneous nystagmus, up-gaze).

this nystagmus form is due to the primary demyelination of the optical nerves, leading to a delay in visual feedback (Averbuch-Heller *et al* 1995; Barton & Cox 1993; Kori *et al* 1993). In support of this theory Barton *et al* (1993) reports for 37 patients with APN all with multiple sclerosis and with involvement of the optical nerves. Only 7 of them had brainstem lesions in MRI. All the more, the patients with symmetric involvement of the optical nerves were with conjugate nystagmus and those with asymmetric – with disconjugate, as more outstanding nystagmus is registered always from the side with the more severe involvement. However, this does not fully explain why APN occurs, since it remains unchanged in darkness and experimental delay of visual feedback does not change its characteristics (Matthew *et al* 2012).

A more likely explanation is that APN arises due to an unstable “neural integrator”. The neural integrator has an important role in ensuring steady gaze. Components of the neural integrator are located in various

parts of the brainstem. Whereas impaired neural integrator function produces gaze-evoked nystagmus, APN might result from loss of normal feedback to the neural integrator, thereby producing instability, perhaps due to lesions affecting the paramedian tracts in the pons (Matthew *et al* 2012).

Some authors support the other theory according to which APN is due to abnormalities of internal brainstem circuits, such as the connections between brainstem nuclei and cerebellum (Averbuch-Heller *et al* 1995; Leigh *et al* 1994; Leigh & Zee 2006). Averbuch-Heller *et al* (1995) establish that the artificial electronically-evoked delay of the visual feedback leads to slow sinusoidal oscillations with frequency of 1Hz in normal subjects and in patients with APN without influencing the available nystagmus. Regarding the topic of lesions predominates the conception that large areas of the brainstem are involved: in the midbrain the red nucleus and around the oculomotor nucleus, in the pons the medial vestibular nucleus and paramedian tracts, in the medulla the inferior olivary nucleus and especially olivocerebellar fibres (Averbuch-Heller *et al* 1995; Gresty *et al* 1982; Grigorova & Stambolieva 2003; Leigh *et al* 1994; Lopez *et al* 1995, 1996). Lopez *et al* (1995, 1996) make an attempt to connect the directions of APN with a defined localization of the lesions. They accede that the lesions of the pons cause horizontal APN, midbrain lesions-vertical APN, and the bulbar lesions-torsion APN. According to the authors, the inferior olivary defines the rhythm and the frequency of ocular oscillation (Carota *et al* 2012).

The observed patients allow us to accede that the lesions of the optical nerves are less important for the occurrence of APN, as the three patients did not have clinical and instrumental (including visual evoked potentials) data for involvement of the visual pathways. From another point of view, all of them had CT and/or MRI brainstem lesions. The identical topics of the lesions suggested a connection between the vertical APN and this localization. The lesions observed in the patients were in midbrain, mainly tegmental, paramedian, ventro-lateral from the oculomotor nucleus, in the area of the red nucleus. This topic coincides with the described midbrain lesions in literature and proves the thesis for a connection of the vertical APN with the midbrain (Lopez *et al* 1995, 1996). The disruptions of the vertical saccadic and smooth pursuit eye-movements in the patients are explained with the connections of the vertical oculomotor mechanisms with the midbrain structures.

CONCLUSIONS

The presented clinical cases of patients with vertical APN show the importance of the untypical nystagmus forms, connected with lesions of different parts of the

brainstem. The similarity of the topic of the lesions in the patients supports the conception that the main reason for the appearance of APN is the disruption of the internal brainstem circuits, and its vertical forms are connected with tegmental paramedian midbrain lesions involving the areas around the red nucleus.

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