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Analysis of retinal nerve fibre layer, visual evoked potentials and relative afferent pupillary defect in multiple sclerosis patients

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HIGHLIGHTS

- We evaluated RNFL, pVEPs studies and RAPD changes in multiple sclerosis patients.
- pVEPs were more frequently abnormal than RNFL in eyes with and without optic neuritis (ON).
- RNFL damage in eyes without ON may indicate neurodegenerations in CNS of MS patients.

ABSTRACT

Objective: The aim of this study was to analyse retinal nerve fibre layer (RNFL), pattern-reversal visual evoked potentials (pVEPs) and relative afferent pupillary defect (RAPD) changes in multiple sclerosis (MS) patients with the consideration of past optic neuritis (ON).
Methods: Ophthalmological, neurological, OCT, RNFL and pVEP studies were conducted in 59 MS patients. RAPD tests were performed in 47 of them. Control group consisted of 28 healthy volunteers.
Results: Abnormal RNFL was found in 59% of cases of eyes with ON and 28% of eyes without ON. In eyes with ON, significantly lower RNFL values were indicated in the temporal and lower quadrants. Elongation of pVEP latency was found in 83% of eyes with ON and 60% of eyes without ON. The average value of pVEP latency was larger and the amplitude was lower in the subgroup of eyes with RNFL at the borderline or below the norm. RAPD was observed only in eyes with ON and with RNFL thinning. No association was found between the RAPD and pVEP parameters.
Conclusions: VEPs were more frequently abnormal than RNFL in MS patients. RNFL damage in eyes without ON may indicate neurodegenerations in CNS of MS patients; it can also be the consequence of subclinical ON.
Significance: An analysis of RNFL and VEP can be useful for evaluating the optic nerve in MS patients.

1. Introduction

Retrobulbar optic neuritis (ON) is the most frequent ocular manifestation of multiple sclerosis (MS) (Hoorbakht and Bagherkashi, 2012). It is characterised by three symptoms: (1) one-sided subacute impairment of vision, which develops within hours up to 2 weeks, (2) periorbital pain, mainly when moving the eyeballs and (3) dyschromatopsia (Hoorbakht and Bagherkashi, 2012; Voss et al., 2011). Other symptoms of typical ON include: a decrease of the sensitivity of vision to contrast and vision with bright light, photopsia and flashes when moving the eyeballs, defect of the field of vision, Uhthoff's phenomenon (worsening eye symptoms after physical effort and in high temperature), Pulfrich's phenomenon (difficulties in determining the direction of movement of the seen object), Moore's phenomenon (vertical flashes, usually appearing in poor lighting in the temporal part of the field of vision after moving the eyeballs) and relative afferent impairment of the pupil reflex to light (Burton et al., 2011). The optic disc is not usually swollen. Sometimes periphlebitis may occur, which is connected with a much greater risk of developing MS and the chronic inflammation of the front and intermediate uvea (Hoorbakht and Bagherkashi, 2012; Voss et al., 2011; Shams and Plant, 2009). The worsening of vision in the case of ON is

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usually slight, although there are rare cases (~3%) of a considerable loss of vision, until the loss of the sense of light (Burton et al., 2011). In more than 80% of patients, vision improves independently within 2–3 weeks, and in the majority of cases vision recovers with full sharpness. However, in approximately 30% of patients, blurred vision, decreased sense of contrast, disorders of colourful vision and defects in the field of vision may remain. In the acute ON phase, the elongation of latency and the decrease of visual evoked potentials (VEP) amplitude are found, and in MRI in approximately 90% of the cases, gadolinium strengthening in the area of the diseased nerve is observed, connected with a reversible disorder of the vascular brain–nerve barrier (Burton et al., 2011). Several weeks or months after the acute phase of neuritis, fading of the optic disc may appear, which is connected with axonal damage and astrocyte proliferation in the area of the optic nerve (Hoorbakht and Bagherkashi, 2012; Burton et al., 2011; Shams and Plant, 2009; Oreja-Guevara et al., 2010).

In approximately 40% of patients, ON is the first symptom of MS, and in approximately 30–70%, ON occurs in the course of previously diagnosed MS (Burton et al., 2011; Costello et al., 2011).

Diagnosing ON is mainly based on the presence of typical signs; however, in some cases, the course of the disease may have a subclinical nature or an atypical form. In such cases, additional tests can be useful for both determining the diagnosis and prescribing appropriate treatment, as well as monitoring the course of the disease. Hence, there is much interest in research, which makes it possible to verify vision dysfunctions.

The purpose of this article was to analyse retinal nerve fibre layer (RNFL), pattern-reversal visual evoked potentials (pVEPs) and relative afferent pupillary defect (RAPD) changes in MS patients with the consideration of past ON.

2. Methods

2.1. Clinical material

A total of 59 MS patients (34 women and 25 men) aged 21–72 years (average 45) were examined. The diagnosis was made in accordance with McDonald criteria. The Bioethics Committee of Wroclaw Medical University gave its consent, No. KB-131/2013, to conduct the research. The time of MS duration was on average 13 years (range 4–39). In total, 43 patients (73%) were diagnosed with relapsing-remitting MS and 16 (27%) with secondary progressive MS. The degree of disability of patients assessed according to EDSS ranged from 2 to 6.5 (average 4.5) and MSSS from 2 to 9.08 (average 5).

There were 31 patients (53%) who, before or during the test, underwent immunotherapy (interferon (IFN)-β, Copaxone, fingolimod, and imuran). The duration of immunotherapy did not exceed 2 years, while the longest interval between this test and the ceasing of immunotherapy amounted to 8 months. In the remaining 28 patients (47%), immunotherapy has never been applied.

All the patients were previously treated with corticosteroids, and there were 15 patients (25%), who, at the time of this study, were treated with Solu-Medrol because of the relapse of the disease without ON.

In the group of patients, the average best corrected sharpness of vision BCVA, measured with Snellen's tables, amounted to 0.8 (range 0.05–1.2). All patients had correct intraocular pressure measured with the noncontact air-puff method. Each eye was analysed separately in the examination. A total of 34 eyes (29%) with ON with a history of retrobulbar ON were distinguished, and 73 eyes (62%) without ON; and in 11 eyes, past ON was considered doubtful.

Both eyes of 28 age- and gender-matched healthy controls were tested. In all of them, glaucomatous neuropathy and other causes of optic nerve damage were excluded.

2.2. Methodology of research

In the examined groups, an interview and the following physical tests were conducted: ophthalmological, neurological, OCT-RNFL, pVEP and RAPD. These tests were performed in the duration not shorter than 6 months from the potential ON.

2.2.1. OCT-RNFL

The RNFL was measured by using the Spectralis HRA + OCT device from Heidelberg Engineering GmbH, Germany, according to a report of round RNFL scans, after prior mydriasis with 1% tropicamide. The device is equipped with software that calculates RNFL thickness automatically in four quadrants of the field of vision in relation to a control group comparable in age. The scans were analysed with signal quality of at least seven in the scale up to 10.

2.2.2. pVEPs

pVEPs were registered by using a Tomey EP-1000 device, with software VEP extension at a distance of 80 cm from the screen with a chequered pattern of angular quantity of individual squares of 1.0°. The contrast between the checkerboard squares amounted to 100%. In sum, 80 answers were averaged. The electrode was placed in the central line in the occipital area – Oz, the reference electrode in the central Fz area, and the grounding electrode on the right earlobe. The left and right eyes were subsequently stimulated with a frequency of 2 Hz. Sampling rate was 2000 Hz. Electrode impedance was kept below 5000 Ω. Values of pVEPs were obtained by using a filter bandpass of 1–100 Hz. Each evoked potential was the result of summation of 100 responses. The analysis time was 250 ms. At least two separate averages of pVEPs were superimposed to demonstrate replicability. The methodology of research was in accordance with the ISCEV standards updated in 2009. The P100 wave was identified as the first major positive peak response to pattern reversal expressed at the occiput with a latency of approximately 100 ms. P100 wave latency and amplitude were assessed. The obtained values were compared with the data obtained in the group of 28 healthy volunteers, selected suitably in terms of age and sex.

2.2.3. RAPD

Pupil functions were assessed in 47 patients. The pupils of the examined patients were even and showed the correct reaction to light: direct and consensual. The swinging-flashlight test was used to assess RAPD. During the test, a patient was made to look at a fixed point in the distance. Then, the pupils were lit always starting from the bottom of the right eye at an angle of 45°. After 3 s, the location of light was immediately changed to light the pupil in the left eye. The procedure was repeated 4 times. The point at which the instantaneous dilation of a pupil on which the source of light was directed or the lack of the evident narrowing as a reaction to light occurred was considered as RAPD presence. This assessment is in accordance with Kawasaki's standards (Kardon et al., 2006).

2.3. Statistical analysis

Statistica 10.0 software was used for the statistical analysis of the obtained data. The associations between the chosen parameters were determined by using: cross-tabulation, Pearson's chi-square test, chi-square HR (highest reliability) test, Yates'

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