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7 **Pattern and motion related visual evoked potentials in Neuroborreliosis: follow-up study**  
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46 **Running title:** VEP follow-up study of Neuroborreliosis  
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## ABSTRACT

**Purpose:** Visual evoked potentials (VEPs) were used for objective testing of visual functions during treatment courses of Lyme neuroborreliosis (LNB) in adult patients in the Czech Republic.

**Methods:** In 30 LNB patients with originally delayed VEP latencies, pattern-reversal (R-VEP) and motion-onset (M-VEP) VEPs were repeatedly examined within one to eight years.

**Results:** Six patients had Lyme optic neuritis (ON), five from them displayed prolonged latencies in both R-VEPs and M-VEPs, and one had only abnormal R-VEPs. VEP recovery to normal latency values was in three of them. In the group of 24 LNB patients without ON, 14 patients displayed prolonged latencies only to motion stimuli and 10 patients had abnormal latencies both in R-VEPs and M-VEPs. During the follow-up period, 7 patients displayed shortening to normal latencies. In 5 patients VEPs latencies improved only partially and in the remaining 12 patients VEPs did not improve at all.

**Conclusions:** This study provides objective evidence that in LNB majority of patients without clinically manifesting ON display optic pathway involvement - predominantly magnocellular system/dorsal stream function changes. In cases with ON, however, mainly the parvocellular system is affected. About half of cases without ON improved with a relatively long time course of latency shortening.

**Key words:** Lyme neuroborreliosis (LNB), Visual evoked potentials (VEPs), Optic neuritis (ON), magnocellular system/dorsal stream

## INTRODUCTION

1  
2 Lyme disease or borreliosis is a widely distributed multisystem disease caused by a tick-borne  
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4 spirochete, *Borrelia burgdorferi* (Burgdorfer et al 1982). Lyme neuroborreliosis (LNB)  
5  
6 designates neurological involvement during systemic infection. Two forms of LNB have been  
7  
8 identified, the acute or early LNB and the chronic or late LNB with symptoms persisting for  
9  
10 more than 6 months. Substantial clinical difference in LNB depends on whether infection  
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12 occurred in the USA or Europe, because of genetic differences between the strain that causes  
13  
14 all cases of US LNB - *B. burgdorferi sensu stricto*, and the European strains - *B. garinii* and  
15  
16 *B. afzelii* (Hildenbrand et al 2009; Pachner & Steiner 2007).  
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22 In the United States, dissemination to central nervous system (CNS) is predominantly  
23  
24 hematogenous, leading to meningoencephalitis. This feature contrasts with the European  
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26 variant of predominant nerve root involvement, suggesting dissemination through the  
27  
28 peripheral nerves (Rupprecht et al 2008).  
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31  
32 Differences between European and American LNB are in a percentage of all Lyme disease  
33  
34 cases, more than 35% of European patients versus less than 10% of American patients.  
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37 Presence of erythema migrans lesions is uncommon in Europe, and common in US.

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39 Moreover, intrathecal antibody production is common in Europe, but in minority of cases in  
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41 America (Steere et al 1990). Involvement of the optic nerves in European LNB seems to be more  
42  
43 common than previously thought (Lesser 1995).  
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47 In this article extended data of our previous study (Kubova et al 2006) are presented. The goal  
48  
49 of this study was to evaluate objectively the long-term development of the visual pathway  
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51 involvement in LNB patients during treatment courses of LNB. Two types of visual stimuli were  
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53 used for VEP eliciting – pattern-reversal and motion stimuli with the aim to test the function  
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55 of the two fundamental subsystems of the visual pathway (the magno- and parvocellular ones)  
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57 and their cortical projections (the dorsal and ventral streams).  
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1 The first visual stimulation, activating predominantly the primary visual area V1, was the  
2 pattern reversal of black/white checkerboard. As the second type of stimulation we used two  
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4 variants of monochromatic moving stimuli (translating and expanding/contracting motion)  
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6 that are supposed to activate extrastriate visual areas (Hollants-Gilhuijs et al 2000; Kuba &  
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8 Kubova 1992; Kubova et al 1995).  
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## 11 12 13 14 **PATIENTS AND METHODS**

### 15 16 17 **Patients**

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19 From April 1999 till May 2010, we investigated a total number of 100 patients with an  
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21 evidence of LNB obtained at the Department of Infectious diseases, Faculty Hospital. 46  
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23 patients had pathologic VEP that could be attributed only to LNB (since they did not display  
24  
25 any other disorder possibly influencing VEPs). We monitored only 30 of them (24 women  
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27 and 6 men, mean age of  $46 \pm 12$  years, range 14 – 72 years) who were willing to undergo our  
28  
29 VEP examination repeatedly. VEPs were examined in the Electrophysiological lab at Faculty  
30  
31 of Medicine in Hradec Králové, Czech Republic. All 30 patients were followed up for a  
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33 period of 3 – 95 months. The first VEPs were usually obtained 1 – 12 months after the onset  
34  
35 of LNB symptoms. Second recording was made during the subsequent one year in 20 patients  
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37 and between 2 – 7 years in the remaining 10 patients. More than two VEP examinations were  
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39 done in 15 patients; two of them were examined six times. The course of the VEP  
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41 examinations shows Table 1.  
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48 The local medical ethics committee gave its approval for the study and a written informed  
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50 consent was obtained from all subjects (according to Helsinki declaration).  
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### 53 *Diagnosis*

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55 Diagnosis of LNB was based on medical history and on laboratory evidence of infection with  
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57 *B. burgdorferi* (Stanek et al 2010). The intrathecal production of anti-Bb antibodies with  
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1 increased CSF-to-serum-antibody index (AI) or a positive polymerase chain reaction (PCR)  
2 were the most reliable indicators of CNS infection (Table 2). CSF analysis and magnetic  
3  
4 resonance imaging (MRI) were performed in all patients.  
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6  
7 Only one patient had acute LNB, all remaining 29 patients suffered from chronic LNB.  
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14 Insert Tab 1 and Tab 2 about here  
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### 18 19 *Therapy*

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21 Ten patients were treated with intravenous ceftriaxone or penicillin G in one 3-week course.

22  
23 Repeated treatment courses with intravenous ceftriaxone or penicillin G for 2 – 3 weeks  
24  
25 underwent 20 patients - twice (14 persons), three times (4 persons), four and five times (1  
26  
27 person only in both cases) (Tab 1). Continuing disease activity was detected according to the  
28  
29 reappearance of clinical symptoms and rising AI.  
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### 32 33 34 *LNB symptoms and signs*

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36 Of the 30 patients, three had a history of a definite erythema migrans. Majority of patients  
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38 showed non-specific complaints as headache (n = 21), fatigue and sleep disorders (n = 11),  
39  
40 arthralgia and myalgia (n = 13), vertigo (n = 4), and tinnitus (n = 2). Painful radiculitis was  
41  
42 found in 7 cases, cranial neuritis in 6 cases, motor nerves paresis six times, aseptic meningitis  
43  
44 in 1 occurrence, and chronic encephalomyelitis in four cases.  
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### 47 48 49 *Visual manifestations*

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51 Ophthalmologic evaluation revealed chronic conjunctivitis (n = 1), iridocyclitis (n = 1),  
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53 neuroretinitis (n = 1), neuritis retrobulbaris (n = 6).  
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The most reported visual symptoms were vision impairment (n = 14), blurred vision (n = 8), pain or pressure behind eyes (n = 7), diplopia (n = 2), and other “non-specific” visual symptoms.

## Methods

*Visual evoked potentials (VEPs)* were recorded within one to eight years, two to six times.

The following variants of VEPs were used for objective testing of function of the visual pathway and its cortical projection during treatment courses:

*Pattern-reversal VEPs* evoked by 2 Hz reversal of high contrast (96% according to Michelson’s formula) checkerboard with two pattern element sizes of 40' and 20' (Odom et al 2010), were used to test the function of the parvocellular system/ventral stream.

*Motion-onset VEPs* were examined to test magnocellular system/dorsal stream function changes (Kuba et al 2007). Four variants of moving visual stimuli were used. The first consisting of translating motion (random order of fundamental directions, velocity 10 deg/s) of low contrast (10 %) isolated checks (40' check size and 120' check-to-check distances) (Kuba & Kubova 1992; Kubova et al 1995). Second motion stimulus consisted of low contrast (10 %) gray concentric circles with randomly changing expanding/contracting motion. Circles showed decreasing spatial frequency towards periphery of the visual field (1 – 0.2 c/deg) to account for cortical magnification, and increasing motion velocity (5 – 25 deg/s) to account for different motion sensitivities in the center versus the periphery of the visual field (Kremlacek et al 2004). The third and fourth motion stimuli were restricted either to central 8° of the visual field (macular stimulation) or to periphery outside the central 20° (peripheral stimulation) of the expanding/contracting circle stimulus. All moving stimuli had the same timing – 200 ms of motion was followed by 1 s interstimulus interval (stationary pattern).

The stimuli were generated using our own software (Kremlacek et al 2004) on a 21” Iiyama monitor (stimulus field 37 x 28 deg) with a 105 Hz frame frequency and mean luminance of 17

1 cd/m<sup>2</sup>. Forty single sweeps (440 ms epochs, 20 000 times amplified in the frequency band of 0.1 –  
2 45 Hz with sampling frequency of 500 Hz) were averaged. Viewing distance was 0.6 m, and  
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4 correct fixation of the stimulus field centre was monitored via near infrared CCD camera.  
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### 6 *Recordings*

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8 We recorded monocular VEPs from six unipolar derivations using the right ear lobe as a  
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10 reference. Four derivations from the midline (Oz, Pz, Cz, and Fz) and two lateral derivations (OL  
11 and OR, 5 cm to the left and right from the Oz position) were used to cover areas with maximum  
12  
13 amplitudes both for pattern-reversal and motion-onset VEPs (for distribution of motion-onset  
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15 VEPs see Kuba, Kubová et al. 2007). Parameters of the pattern-reversal VEPs (latencies and inter-  
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17 peak amplitudes of the P100 peak) were always evaluated in the Oz derivation. Due to  
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19 interindividual differences in topography of motion-onset VEPs, their parameters (latencies and  
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21 inter-peak amplitudes of the N2 motion-onset specific peak) were read from one of the lateral  
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23 occipital or Pz lead. We selected the lead with maximum VEP amplitude. Our latency norms are  
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25 from testing of 70 normal subjects, respecting significant age-dependent changes in the function  
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27 of the motion processing system (Langrova et al 2006). Two examples of upper limits of the  
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29 latency are displayed in Table 3.  
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40 Insert Tab 3 about here  
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## 45 **RESULTS**

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47 30 cooperating subjects displaying a VEP pathology in their first examination were divided  
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49 into two groups: 1.with optic neuritis and 2.without optic neuritis.  
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### 52 **Monocular or binocular VEP changes**

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54 The number of patients with monocular VEP changes was 2 out of 6 patients with optic  
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56 neuritis (ON) and 2 out of 24 remaining LNB patients. In all remaining 26 patients prolonged  
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58 VEP latencies in both eyes were found.  
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### **LNB patients with optic neuritis**

Six out of 30 patients were diagnosed as having isolated, recurrent or binocular ON. Two patients had a picture of a single episode of monocular optic neuritis with VEPs recovery to normal during months. Two patients experienced new symptoms of ON in the fellow eye 1 and 3 years after the first ON attack. Tendency to total VEPs recovery in recurrent ON was only in the case depicted in Fig. 1.

Last two patients showed binocular optic neuritis without VEP improvement during monitoring (follow-up period 7 and 15 months).

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Insert Fig 1 about here

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### **LNB patients without ON**

In the group of 24 LNB patients without ON, 14 patients displayed prolonged latencies only to motion stimuli (either to all motion variants or at least to one of them) and 10 patients had abnormal VEPs latencies in both to reversal and motion-onset (Tab. 4). During the follow-up period, 7 patients with initially delayed latencies displayed progressive shortening to normal latency during treatment courses (Fig. 2) (mean follow-up period 45 months).

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Insert Fig 2 about here

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VEPs latencies in 5 patients showed a tendency to normalize only partially (mean follow-up period 36 months). Treatment efficacy of the remaining 12 patients was not accompanied by the improvement of VEPs. Nine of 12 patients had a permanent prolongation of VEPs (mean



1 follow-up period 29 months) and 2 patients displayed gradual deterioration (mean follow-up  
2 period 50 months). Furthermore, one LNB patient had a positive clinical response with  
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follow-up period 29 months) and 2 patients displayed gradual deterioration (mean follow-up period 50 months). Furthermore, one LNB patient had a positive clinical response with antibiotherapy together with VEPs recovery to normal parameters within one year and subsequent VEP re-deterioration after ten months with return of clinical symptoms (Fig. 3). Two patients without ON who were examined six times in more than five years period displayed recovery to near-normal VEPs. One patient had a positive response to the first antibiotherapy together with significant improvement of all VEP latencies, and during subsequent years he had only discreet VEP prolongation in only one eye. The second of these patients had permanent prolongation of motion-onset VEPs for four years followed by improving VEPs only after the fourth antibiotherapy.

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Insert Fig 3 about here

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### ***Comparison of the used VEP types results***

Five out of six patients with ON displayed prolonged latencies in both reversal and motion-onset VEPs (twice to all motion variants, three times at least to one of them). In one patient only abnormal pattern-reversal VEPs were present.

In the group without ON, we found occurrence of delayed VEP latencies in both the pattern-reversal R40' and R20' in 6 cases and another 5 patients displayed prolongation only in pattern-reversal R20'. Motion-onset VEP latencies in translation motion were prolonged in 20 patients, motion-onset VEPs to peripheral stimulation were delayed in 18 patients, 13 patients had abnormal expanding/contracting full-field motion VEP and macular stimulation of the visual field displayed pathology in 14 cases (Tab. 4).

### ***Overlap with other neurological diseases***

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2 There was only one such a case in the selected group of 30 patients. A 53 year-old female  
3  
4 suffering from headache, blurred vision, diffuse arthralgia, paresthesia and fatigue displayed  
5  
6 prolonged latencies in three types of motion-onset VEPs (translation motion, m 20° and c 8°).  
7  
8 Specific intrathecal AI and PCR were positive. The patient had a favorable clinical outcome  
9  
10 after 3 weeks treatment course with intravenous penicillin G. Afterwards, brain MRI showed  
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12 multiple periventricular lesions corresponding to McDonald's criteria (McDonald et al 2001).  
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14 Presence of oligoclonal IgG bands confirmed Multiple sclerosis (MS) 7 months after  
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16 antibiotherapy. Treatment with penicillin in this case was not accompanied by any  
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18 improvement of VEPs and permanent prolongation of VEPs to motion stimuli was observed  
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20 throughout the whole 22-month period of monitoring.  
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### ***MRI***

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29 Non-specific progression-free small white-matter abnormalities in brain MRI were found in 16  
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31 out of 30 patients.  
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35 The described patient with MS displayed multiple periventricular lesions.  
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### **DISCUSSION**

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47 Our previous study revealed abnormal VEPs latencies in 33 out of 81 LNB patients, and the visual  
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49 pathway involvement was found predominantly in the magnocellular system/dorsal stream  
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51 (Kubova et al 2006).  
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55 The goal of this study was to evaluate objectively the long-term development of the visual  
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57 pathway involvement in LNB patients during treatment courses of LNB. In one half of the cases  
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1 the latencies prolongation recovered to normal or near-normal latency. However, in some  
2 cases the VEPs systematically deteriorated and VEP latencies were not reacting to therapies at  
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4 all.  
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7 Our main conclusion from this observation is that the changes of VEPs latencies can be used  
8  
9 as a measure for objective evaluation of functions of the parvocellular system/ventral stream and  
10  
11 magnocellular system/dorsal stream during treatment courses of LNB. Our data demonstrate a  
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13 long time course of latency changes in most cases with no relation to subjective neurological  
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15 symptoms. Nevertheless, a similar discrepancy between clinical symptoms and VEP findings is  
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17 quite common also in Multiple sclerosis and in the recovery phase of acute ON (Jones 1993;  
18  
19 Matthews & Small 1983).  
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22  
23 *Borrelia burgdorferi* can persist in the brain and may initiate and sustain chronic inflammation and  
24  
25 neural tissue damage. The persistence of more resistant spirochete forms including cystic forms,  
26  
27 and their intracellular location in neurons and glial cells, may explain the long course and need re-  
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29 treatment (Miklossy et al 2008). On the other hand, reinfection is possible after another tick bite  
30  
31 as we have seen it in one case. The effect of treatment is usually judged according to clinical  
32  
33 manifestations rather than to the laboratory findings. Therapeutic effect need not be permanent  
34  
35 (Oksi et al 1999; Stricker 2007; Vrethem et al 2002) as it was as in 20/30 of patients in our group.  
36  
37 Four patients recovered to normal or near-normal VEP latencies after the first 3weeks ATB  
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39 treatment and 11 re-treated patients in the time period after the second or subsequent  
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41 treatment courses.  
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47 Thus we suggest that VEP latencies might be an objective indicator of functional changes of the  
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49 nervous system in LNB patients in whom visual pathway dysfunction developed during the  
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51 disease. Possibly it could also reflect a treatment efficacy.  
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55 Six cases of ON in our group support previous reports of its existence in LNB patients, although it  
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57 seems to be a rare manifestation of LNB (Blanc et al 2010; Jacobson 2003; Krim et al 2007;  
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59 Rothermel et al 2001; Sibony et al 2005).  
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The utility of brain MR imaging for confirmation of suspected chronic LNB and monitoring of  
disease development is very limited due to the overlap with age-related basal ganglionic and  
subcortical white matter lesions and their persistence subsequent to successful treatment of LNB  
(Hildenbrand et al 2009; Morgen et al 2001). In agreement with it, 16 out of 30 patients in our  
group had non-specific progression-free small white-matter abnormalities on brain MRI and  
whilst recovery to normal or near-normal latency VEPs was found in 9 out of these 16  
patients, the MRI changes persisted in all of them. We might conclude that VEPs seem to be  
more sensitive to positive CNS changes in LNB that could indicate also an effect of ATB  
therapy.

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Lyme disease can mimic a lot of other neurologic diseases. The disorder that can be most  
frequently confused with LNB is Multiple sclerosis. Because the VEP prolongation is non-  
specific in LNB and MS, it is not possible to differentiate these diseases completely on the basis  
of VEP examination. However, in MS mainly pattern-reversal VEP latency is prolonged, which  
signals dominating parvocellular system/ventral stream involvement (Szanyi et al 2007), while  
in LNB motion-onset VEPs pathology (representing predominant magnocellular system/dorsal  
stream dysfunction) is much more frequent (Kubova et al 2006).

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Optic neuritis is often initial clinical manifestation of MS and may occur at any time in the course  
of disease (Agarwal & Sze 2009; Bednarova et al 2005; Halperin et al 1989; Chen & Gordon  
2005; Karussis et al 1999). Six cases of ON in our group were not related to MS. The overlap of  
LNB with MS was detected only once and it was without concurrent ON presence. This MS patient  
displayed binocular permanent motion-onset VEPs prolongation only, rather typical for LNB which  
was diagnosed one year earlier.

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1 magnocellular system/dorsal stream function changes (motion-onset VEPs prolongation) with  
2 relatively long time course of latency shortening in half of these cases. Thus, ON in LNB  
3 represents also, as well as in MS, predominantly parvocellular/ventral stream disorder.  
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9 Shortcoming of this study is certainly the lack of consistent timing of VEP testing and treatment  
10 courses. The problem arose from interindividual differences in the disease process, not fully  
11 uniform clinical strategy of the ATB therapy and the fact that VEP testing could not be stated as  
12 an obligatory part of treatment and it was dependent on patient's willingness to co-operate.  
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20 We believe that the reported results of VEPs changes in LNB could be motivating for some more  
21 research in this field, which could help in difficult assessment of LNB treatment efficacy.  
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## 34 **References**

- 35  
36 Agarwal R, Sze G. 2009. Neuro-lyme disease: MR imaging findings. *Radiology* 253:167-73  
37 Bednarova J, Stourac P, Adam P. 2005. Relevance of immunological variables in  
38 neuroborreliosis and multiple sclerosis. *Acta Neurol Scand* 112:97-102  
39 Blanc F, Ballonzoli L, Marcel C, De Martino S, Jaulhac B, de Seze J. 2010. Lyme optic  
40 neuritis. *J Neurol Sci* 295:117-9  
41 Burgdorfer W, Barbour AG, Hayes SF, Benach JL, Grunwaldt E, Davis JP. 1982. Lyme  
42 disease-a tick-borne spirochetosis? *Science* 216:1317-9  
43 Halperin JJ, Luft BJ, Anand AK, Roque CT, Alvarez O, et al. 1989. Lyme neuroborreliosis:  
44 central nervous system manifestations. *Neurology* 39:753-9  
45 Hildenbrand P, Craven DE, Jones R, Nemeskal P. 2009. Lyme neuroborreliosis:  
46 manifestations of a rapidly emerging zoonosis. *AJNR Am J Neuroradiol* 30:1079-87  
47 Hollants-Gilhuijs MA, De Munck JC, Kubova Z, van Royen E, Spekreijse H. 2000. The  
48 development of hemispheric asymmetry in human motion VEPs. *Vision Res* 40:1-11  
49 Chen L, Gordon LK. 2005. Ocular manifestations of multiple sclerosis. *Curr Opin*  
50 *Ophthalmol* 16:315-20  
51 Jacobson DM. 2003. Lyme disease and optic neuritis: long-term follow-up of seropositive  
52 patients. *Neurology* 60:881-2  
53 Jones SJ. 1993. Visual evoked potentials after optic neuritis. Effect of time interval, age and  
54 disease dissemination. *J Neurol* 240:489-94  
55 Karussis D, Weiner HL, Abramsky O. 1999. Multiple sclerosis vs Lyme disease: a case  
56 presentation to a discussant and a review of the literature. *Mult Scler* 5:395-402  
57  
58  
59  
60  
61  
62  
63  
64  
65

- 1 Kremlacek J, Kuba M, Kubova Z, Chlubnova J. 2004. Motion-onset VEPs to translating,  
2 radial, rotating and spiral stimuli. *Doc Ophthalmol* 109:169-75
- 3 Krim E, Guehl D, Burbaud P, Lagueny A. 2007. Retrobulbar optic neuritis: a complication of  
4 Lyme disease? *J Neurol Neurosurg Psychiatry* 78:1409-10
- 5 Kuba M, Kubova Z. 1992. Visual evoked potentials specific for motion onset. *Doc*  
6 *Ophthalmol* 80:83-9
- 7 Kuba M, Kubova Z, Kremlacek J, Langrova J. 2007. Motion-onset VEPs: characteristics,  
8 methods, and diagnostic use. *Vision Res* 47:189-202
- 9 Kubova Z, Kuba M, Spekreijse H, Blakemore C. 1995. Contrast dependence of motion-onset  
10 and pattern-reversal evoked potentials. *Vision Res* 35:197-205
- 11 Kubova Z, Szanyi J, Langrova J, Kremlacek J, Kuba M, Honegr K. 2006. Motion-onset and  
12 pattern-reversal visual evoked potentials in diagnostics of neuroborreliosis. *J Clin*  
13 *Neurophysiol* 23:416-20
- 14 Langrova J, Kuba M, Kremlacek J, Kubova Z, Vit F. 2006. Motion-onset VEPs reflect long  
15 maturation and early aging of visual motion-processing system. *Vision Res* 46:536-44
- 16 Lesser RL. 1995. Ocular manifestations of Lyme disease. *Am J Med* 98:60S-2S
- 17 Matthews WB, Small M. 1983. Prolonged follow-up of abnormal visual evoked potentials in  
18 multiple sclerosis: evidence for delayed recovery. *J Neurol Neurosurg Psychiatry*  
19 46:639-42
- 20 McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, et al. 2001. Recommended  
21 diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the  
22 diagnosis of multiple sclerosis. *Ann Neurol* 50:121-7
- 23 Miklossy J, Kasas S, Zurn AD, McCall S, Yu S, McGeer PL. 2008. Persisting atypical and  
24 cystic forms of *Borrelia burgdorferi* and local inflammation in Lyme neuroborreliosis.  
25 *J Neuroinflammation* 5:40
- 26 Morgen K, Martin R, Stone RD, Grafman J, Kadom N, et al. 2001. FLAIR and magnetization  
27 transfer imaging of patients with post-treatment Lyme disease syndrome. *Neurology*  
28 57:1980-5
- 29 Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, et al. 2010. ISCEV standard for  
30 clinical visual evoked potentials (2009 update). *Doc Ophthalmol* 120:111-9
- 31 Oksi J, Marjamaki M, Nikoskelainen J, Viljanen MK. 1999. *Borrelia burgdorferi* detected by  
32 culture and PCR in clinical relapse of disseminated Lyme borreliosis. *Ann Med*  
33 31:225-32
- 34 Pachner AR, Steiner I. 2007. Lyme neuroborreliosis: infection, immunity, and inflammation.  
35 *Lancet Neurol* 6:544-52
- 36 Rothermel H, Hedges TR, 3rd, Steere AC. 2001. Optic neuropathy in children with Lyme  
37 disease. *Pediatrics* 108:477-81
- 38 Rupprecht TA, Koedel U, Fingerle V, Pfister HW. 2008. The pathogenesis of lyme  
39 neuroborreliosis: from infection to inflammation. *Mol Med* 14:205-12
- 40 Sibony P, Halperin J, Coyle PK, Patel K. 2005. Reactive Lyme serology in optic neuritis. *J*  
41 *Neuroophthalmol* 25:71-82
- 42 Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, et al. 2010. Lyme borreliosis:  
43 Clinical case definitions for diagnosis and management in Europe. *Clin Microbiol*  
44 *Infect*
- 45 Steere AC, Berardi VP, Weeks KE, Logigian EL, Ackermann R. 1990. Evaluation of the  
46 intrathecal antibody response to *Borrelia burgdorferi* as a diagnostic test for Lyme  
47 neuroborreliosis. *J Infect Dis* 161:1203-9
- 48 Stricker RB. 2007. Counterpoint: long-term antibiotic therapy improves persistent symptoms  
49 associated with lyme disease. *Clin Infect Dis* 45:149-57
- 50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1 Szanyi J, Kubová Z, Kuba M, Kremláček J, Langrová J, et al. 2007. Comparison of Visual  
2 Evoked Potentials in patients with Multiple Sclerosis and Neuroborreliosis. *Cs.*  
3 *Neurol. Neurochir.* 70:658-64  
4 Vrethem M, Hellblom L, Widlund M, Ahl M, Danielsson O, et al. 2002. Chronic symptoms  
5 are common in patients with neuroborreliosis -- a questionnaire follow-up study. *Acta*  
6 *Neurol Scand* 106:205-8  
7  
8  
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10  
11  
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**Tab. 1**

Organization of VEP examination and ATB treatment sorted by the number of treatment courses

Subject	Age (years)	Sex	ON	OCS	ATB	VEP	VEP	D	ATB	VEP	D	ATB	VEP	D	VEP	D	ATB	VEP	D	ATB	VEP	D	ATB	VEP	D
1	52	F	0	2002	10-02	10-02	4-06	1																	
2	34	F	1	2007	4-07	6-07	6-07	1		4-08	1														
3	50	F	0	2001	3-01	1-03	9-04	2																	
4	56	M	0	2002	3-03	9-03	3-09	3																	
5	57	F	1	2001	4-06	4-06	11-06	3																	
6	50	F	0	1997	5-02	6-02	4-03	3																	
7	39	F	0	2001	6-01	12-03	12-08	3																	
8	56	F	0	2007		1-08			2-08	11-08	3														
9	56	F	0	2003		9-03	4-04	3	4-04	4-05	3														
10	33	M	1	2005		6-05			1-06	5-06	2		12-06	2	2-08	3		12-08	4						
11	43	F	0	2007	10-07	11-07	1-08	2	2-09	3-09	1														
12	54	M	0	2006	11-06	1-07	10-07	3	11-07	9-08	1														
13	14	F	0	2001	2-01	12-02			4-05	6-06	1														
14	35	F	0	2000	2-04	2-04			5-07	3-09	1														
15	45	F	1	2002	11-03				4-05	4-05			6-07	1											
16	38	F	0	1993	2-98				11-01	10-03			2-10	1											
17	52	F	0	2000	1-02	2-03			2-03	5-03	2														
18	72	M	0	2004	6-04	6-04			4-05	4-05	2														
19	53	F	0	2003	3-04	3-04	5-04	3	1-06	1-06	3														
20	41	M	0	2001	5-01	10-02	7-03	4	9-04	10-06	3														
21	53	F	0	2003	4-03				9-03	9-03			5-04	3											
22	34	M	0	2004	1-05	5-05		1	11-05	5-06	4		3-07	3											
23	43	F	0	2001	11-02	4-03			5-06	10-07	4														
24	42	F	0	2005		4-05			6-05			12-05	5-06	1	3-07	4									
25	53	F	0	2000	4-03	4-03			5-05	5-05	3	2-08	2-08	1											
26	37	F	1	2003	8-04	11-04			1-05	4-05	4	4-05	2-07	1											
27	53	F	1	2001	5-01	3-03			5-03	11-03	3	6-04	6-04	3											
28	17	F	0	1997		9-02			12-02	2-04	4	6-04					4-05	6-06	4						
29	53	F	0	2003	3-03	3-03	9-03	4	11-03	5-04	3	6-05	6-05	3	3-06	3	4-07	4-07	2						
30	52	F	0	1999		4-99	1-00	2	1-01	1-01	2	4-02					2-05	2-05	2	1-06	1-06	2	1-07	1-07	2

F = female, M = male, ON = optic neuritis, OCS = onset of clinical symptoms  
 ATB = date of antibiotic treatment course, VEP = date of visual evoked potentials examination  
 D = development of VEP changes: 1. return to normal 2. partial improvement 3. permanent pathology 4. gradual deterioration



**Tab.2**

Demographic and clinical characteristics of the pursued patients

Characteristic	No of Patients
Gender (women/men)	24/6
Positive CSF-to-serum-antibody index	21
Positive polymerase chain reaction	10
CSF lymphocytic pleocytosis	4
Abnormal MRI of the brain	17
Erythema migrans	3

**Tab.3**

Examples of laboratory latency norms of the pattern-reversal and motion-onset VEPs for ages 18 and 60 years (from 70 normal subjects)

VEP type	Age 18 years	Age 60 years
	L [ms]	L [ms]
R 40°	125	126
R 20°	131	133
Translation motion	185	211
Radial motion	175	203
Radial motion - peripheral 20°	178	212
Radial motion - central 8°	184	211

The value of the mean + 2.5 SD represents the upper limit of the norm for each type of VEPs. The upper limit of VEPs interocular latency differences is 10 ms for the pattern-reversal VEPs and 20 ms for the motion-onset VEPs.

The systematic prolongation of motion-onset VEP latencies starts at age of 18 years and ranges between 0.6 – 0.8 ms every year, dependent on the particular variant of motion stimuli (Langrova et al 2006). The formula of the regression line for the mean of motion-onset VEP latencies (peripheral radial motion with the highest dependence on the age) is as follows: N2 Latency = 136.7 + 0.8 \*age.

**Tab.4**

Subject	Age (years)	Sex	ON	VEP					
				R40'	R20'	TM	E-C	M20°	C8°
1	52	F	0	0	0	1	1	1	1
2	34	F	1	1	1	0	0	0	1
3	50	F	0	0	0	1	0	1	0
4	56	M	0	0	0	1	0	1	0
5	57	F	1	1	1	1	0	0	1
6	50	F	0	0	0	1	0	1	1
7	39	F	0	0	0	1	1	1	0
8	56	F	0	0	1	1	0	1	0
9	56	F	0	1	1	1	1	0	1
10	33	M	1	1	1	1	1	1	1
11	43	F	0	0	0	1	0	0	0
12	54	M	0	1	1	0	1	1	1
13	14	F	0	0	0	0	1	1	0
14	35	F	0	0	0	0	1	0	1
15	45	F	1	1	1	0	0	0	0
16	38	F	0	0	0	0	1	0	1
17	52	F	0	0	1	1	0	1	0
18	72	M	0	0	1	1	0	1	0
19	53	F	0	0	0	1	0	1	1
20	41	M	0	0	1	1	0	1	1
21	53	F	0	0	0	1	1	1	0
22	34	M	0	1	1	1	1	1	1
23	43	F	0	0	0	1	1	1	0
24	42	F	0	0	1	1	1	1	1
25	53	F	0	1	1	1	0	0	1
26	37	F	1	1	1	1	1	1	1
27	53	F	1	0	1	1	0	0	0
28	17	F	0	1	1	1	0	1	1
29	53	F	0	0	0	1	1	1	1
30	52	F	0	1	1	1	1	0	0

F = female, M = male

1 = abnormal VEP, 0 = normal VEP

ON = optic neuritis

R40' = pattern-reversal VEP: element size 40'

R20' = pattern-reversal VEP: element size 20'

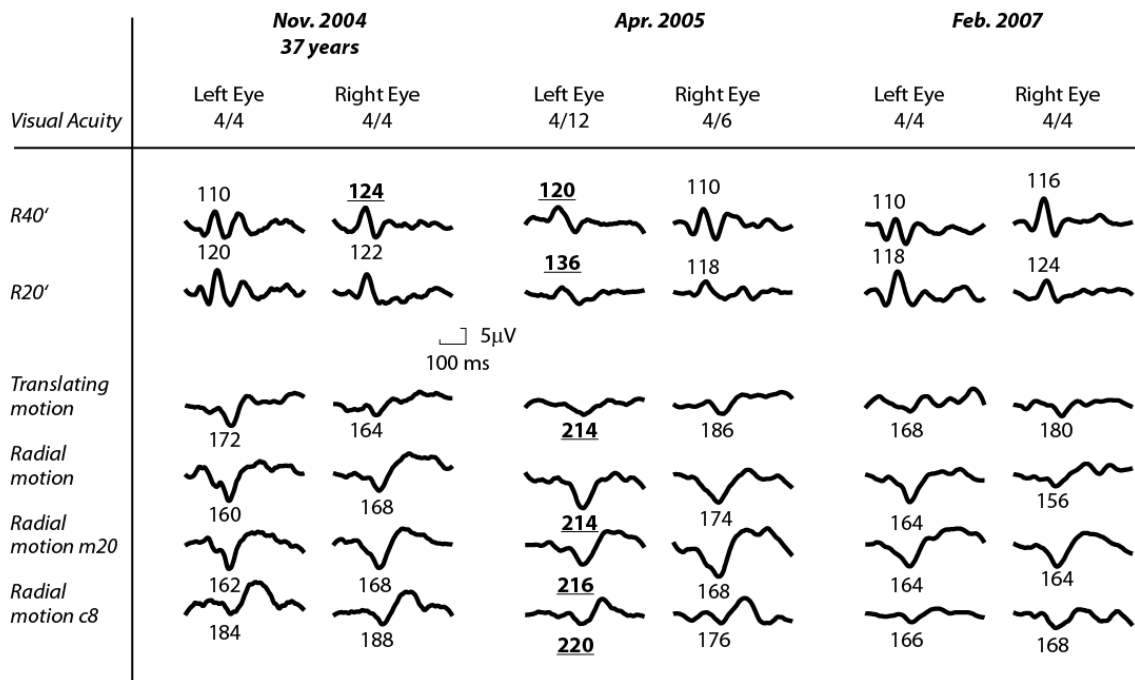
TM = motion-onset VEP: translating motion of low contrast checks

E-C = motion-onset VEP: expanding/contracting motion of low contrast circles

M20° = E-C outside the central 20° of the visual field

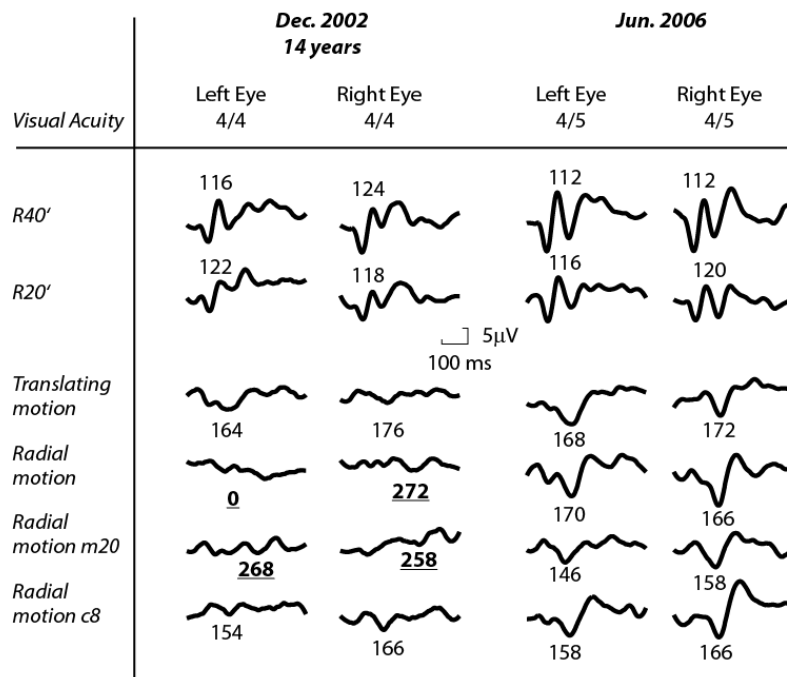
C8° = E-C in central 8° of the visual field

**Fig. 1**



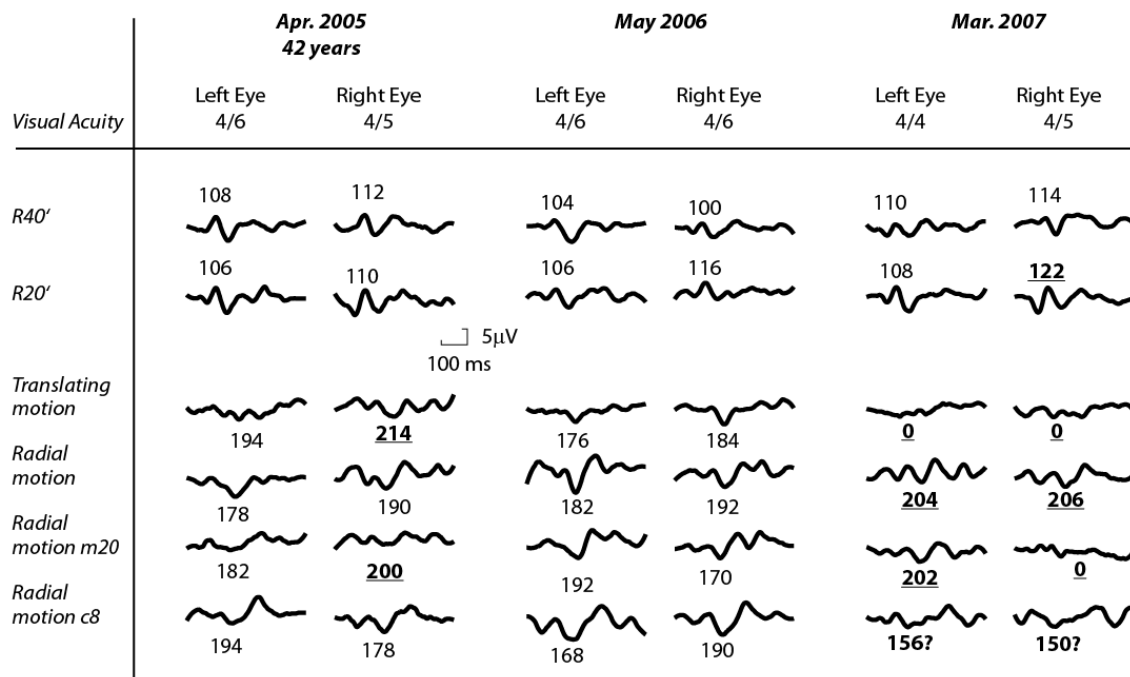
VEP findings in LNB patient No. 26 (woman, 37 years old) developed right ON in December 2003. She suffered from headache, diffuse arthralgia, motor nerve paresis and subfebrilia. Brain MRI showed three non-specific lesions. In April 2005 she developed left ON and displayed prolonged VEP latencies in both reversal and motion stimulation (underlined latency values). VEP return to normal latencies was within two years. Parenteral penicillin was used in August 2004, January and April 2005.

**Fig. 2**



An example of the typical VEP prolongation only to motion stimuli in 14 year-old female (patient No. 13) with LNB since 2001, headache, blurred vision and other „non-specific“ visual symptoms. VEP returned to normal latencies within five years. Patient was treated with intravenous penicillin in February 2001 and April 2005.

**Fig. 3**



A 42 year-old female (patient No. 24) with history of erythema migrans and positive PCR in June 2005. She had headache, episodes of visual impairment and pressure behind eyes. Positive clinical response after antibiotherapy in June and December 2005 was together with VEPs recovery to norm lasting approximately ten months. Subsequently return of clinical symptoms appeared together with prolongation of motion-onset VEPs.