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# CNS Involvement in Chronic Inflammatory Demyelinating Polyneuropathy: A Visual Evoked Potential Study

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## Abstract

The visual evoked potentials (VEPs) of 10 patients with chronic inflammatory demyelinating polyneuropathy (CIDP) and 25 normal subjects were studied to identify possible evidence of central nervous system (CNS) demyelination. VEPs were performed in each patient before and 1 month after treatment with intravenous immunoglobulins (IVIg). Prolonged P100 latency (≥mean±2SD of normal subjects) in 3 patients (30%) in at least one eye before IVIg treatment was improved in both eye stimulations after treatment. They also showed recovery of motor function after IVIg administration. MRI showed no lesions suggestive of CNS demyelination in any patients. Our findings suggest the existence of combined central and peripheral demyelinating lesions in CIDP and emphasize the possibility of a common pathogenic mechanism for both lesions.

**Keywords:** Chronic inflammatory demyelinating polyneuropathy (CIDP); Visual evoked potentials (VEPs); Intravenous immunoglobulins (IVIg); Central nervous system (CNS) involvement

## Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is considered to be an autoimmune disorder of the peripheral nervous system. Central nervous system (CNS) involvement has been clinically observed in 5% [1] and 8% [2] of patients and in many cases of CIDP, there is accompanying CNS demyelination with the presence of subclinical electrophysiological and magnetic resonance imaging (MRI) abnormalities [3-5]. In an attempt to investigate the possible existence of CNS demyelinating lesions in CIDP patients, we prospectively studied visual evoked potentials (VEPs) in 10 patients.

## Patients and Methods

Ten patients (61.1±16.9 years, mean±SD) with CIDP, fulfilling the diagnostic criteria outlined by the Joint Task Force of the EFNS and the PNS [6] and 25 normal subjects (66.6±9.5 years) participated in this study. The clinical features of the patients are described in (Table 1). Age at examination ranged from 38 to 77 years (61.1±16.9 years) and duration of illness ranged from 4 months to 10 years. None of the patients had a history of CNS involvement. Clinical course was chronic progressive in 5 patients and relapsing-remitting in the remaining 5. Electrophysiological data were consistent with a demyelinating polyneuropathy and the etiology of the neuropathy was unknown. Patients with paraneoplastic disorders, monoclonal gammopathy, HIV, metabolic disorders, sarcoidosis, lupus erythematous, or angiitis were excluded. All patients underwent an ophthalmological examination to rule out refractive error and retinal lesions which may affect the VEP study. All patients had corrected visual acuity beyond 0.7 in each eye. CSF protein level was normal in 2 patients (20%) but over 40 mg/dl in 8 patients (range 45–135 mg/dl) without oligoclonal bands.

VEP studies were performed in all patients before and 2 and 4 weeks after treatment with intravenous immunoglobulins (IVIg). To record the VEPs, Ag/AgCl electrodes were placed at O1, Oz and O2, referred to as Fpz in the international 10/20 system. Pattern reversal VEPs were elicited using a black and white checkerboard pattern on a TV screen. The screen was subtended at an angle of 17° at the eyes and each check was subtended an angle of 1°. The mean luminance of the checkerboard was 50 cd/mm$^2$ with high contrast (60%). Monocular stimuli were delivered at a frequency of 1 Hz. The responses were amplified and potentials to 100 stimulations were averaged with the Neuropack MEB-2208 measurement system (Nihon-Koden, Japan). The filter window was 1–100Hz and the analysis time was 200 ms. P100 responses to independent left and right eye stimulations were recorded at O1, O2 and Oz. The P100 latency referred to the interval between the stimulus and the peak of the major positive components and the P100 amplitude referred to the peak-to-peak amplitude between N75 and P100 responses. The P100 latency and amplitude at Oz in response to left and right eye stimulation were used for comparison. Informed consent was obtained from all study participants.

## Results

In the normal subjects, mean P100 latency and amplitude of the VEPs were 102.5±9.2 ms and 7.4±2.8 μV, respectively. More than 120.9 ms (mean+2SD) in P100 latency and less than 1.8 μV (mean+2SD) in amplitude were considered to be abnormal. The results for P100 latency and amplitude of the VEPs for the 10 subjects are summarized in (Table 2). Compared with the controls, 3 patients (Nos. 2, 4 and 10) had increased P100 latency preoperatively in at least one eye, which was shortened (Figure 1) in both eyes after treatment with IVIg (Table 2). After the IVIg administration, muscle weakness and cranial nerve palsy improved in all 3 patients. On the other hand, in the other 7 patients (Nos. 1, 3, 5, 6, 7, 8 and 9) P100 latency was within normal range and remained unchanged after treatment with IVIg.

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| Clinical Symptoms | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Patient No. | Sex | Age at onset (year) | Age at exam. (year) | Duration (months or years) | CSF cells / protein / ul ( /ul, mg/ dl) | Clinical course | Response to IVIg | Predominant symptoms | Clinical type | Other symptoms |
| 1 | M | 35 | 38 | 3y | 1/135 | R | + | motor > sensory | typical CIDP | double vision, dysarthria |
| 2 | M | 39 | 43 | 4y | 2/45 | R | + | motor ≥ sensory | typical CIDP | - |
| 3 | F | 33 | 43 | 10y | 2/19 | R | + | motor >> sensory | MADSAM | - |
| 4 | F | 74 | 75 | 8m | 7/70 | CP | + | motor > sensory | typical CIDP | - |
| 5 | F | 76 | 77 | 1y | 2/66 | CP | + | motor ≥ sensory | typical CIDP | double vision, ptosisb |
| 6 | F | 67 | 71 | 4y | 1/29 | CP | + | motor = sensory | typical CIDP | numbness of face |
| 7 | M | 75 | 76 | 4m | 0/46 | R | + | motor > sensory | MADSAM | - |
| 8 | F | 42 | 42 | 5m | 5/65 | R | + | motor > sensory | MADSAM | double vision, dysarthria ptosis |
| 9 | M | 74 | 75 | 5m | 1/49 | CP | + | motor >> sensory | typical CIDP | - |
| 10 | M | 65 | 70 | 5 | 1/129 | CP | ± | motor = sensory | typical CIDP | - |

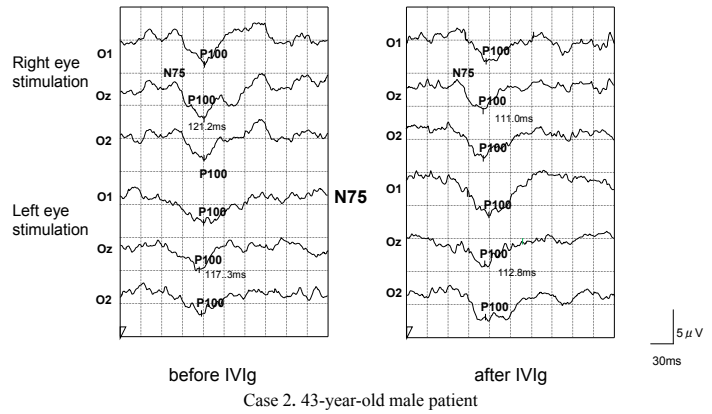
CP: chronic progressive R: relapsing-remitting
MADSAM: multifocal acquired demyelinating sensory and motor

**Table 1:** Clinical characteristics of patients with CIDP.

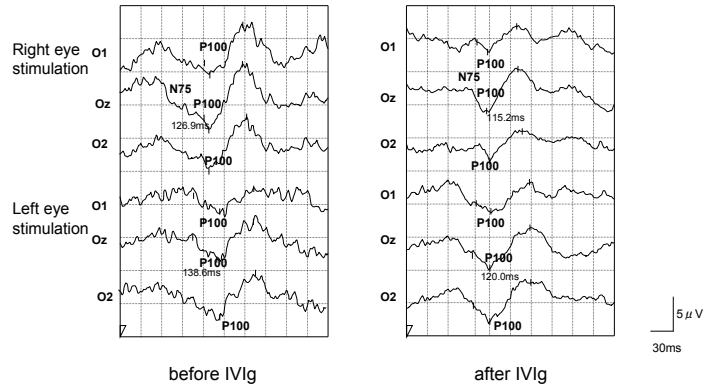
| Patient No. | latency (ms) (R/L) | | amplitude (μv) (R/L) | |
|---|---|---|---|---|
| | before IVIg | after IVIg | before IVIg | after IVIg |
| 1 | 98.7/101.4 | 86.4/90.5 | 1.9/2.5 | 2.8/2.9 |
| 2 | 121.2*/117.3 | 111.0/112.8 | 3.9/4.5 | 4.5/3.5 |
| 3 | 94.8/98.2 | 98.7/95.2 | 6.6/9.5 | 4.1/8.2 |
| 4 | 147.9*/146.7* | 127.8*/125.7* | 4.1/4.8 | 10.3/10.2 |
| 5 | 97.5/101.7 | 98.0/99.2 | 3.4/2.6 | 5.6/2.5 |
| 6 | 94.2/98.1 | 94.8/99.3 | 8.0/10.9 | 10.4/11.0 |
| 7 | 106.5/103.8 | 103.5/98.7 | 5.2/2.3 | 5.1/4.5 |
| 8 | 95.4/95.1 | 91.8/93.0 | 8.3/11.6 | 11.8/9.8 |
| 9 | 96.0/95.7 | 98.1/99.0 | 4.5/7.3 | 10.3/8.9 |
| 10 | 126.9*/138.6* | 115.2/120.0 | 7.6/6.5 | 6.5/6.3 |

R: right eye stimulation, L: left eye stimulation
*abnormal value

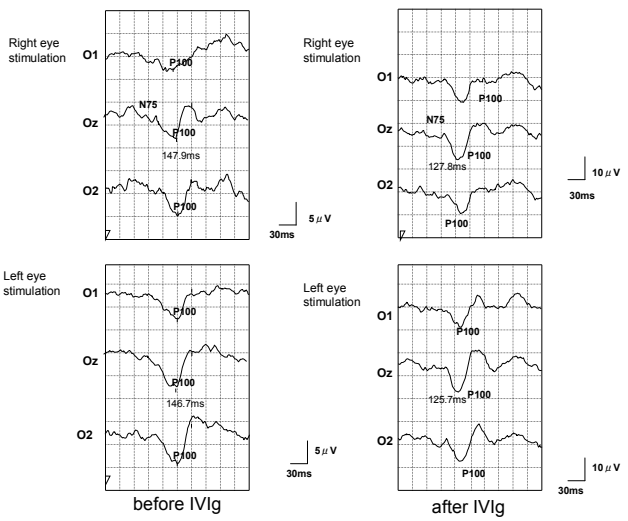
**Table 2:** P100 latency and amplitude in patients with CIDP and normal controls.




Case 2. 43-year-old male patient




Case 4. 74-year-old female patient




Case 10. 69-year-old male patient

**Figure 1:** VEPs of 3 cases with prolonged P100 latency before and after IVIg treatment. Prolonged P100 latency showed a trend to normal values in all 3 patients after IVIg treatment.

## Discussion

CIDP is an acquired, immune-mediated disease that targets the myelin sheaths of peripheral nerves. CIDP involves both demyelination and axonal degeneration, with the balance being determined by disease duration and severity [7]. Electrophysiological data of our CIDP patients were consistent with a demyelinating polyneuropathy. The present study revealed subclinical CNS involvement suggestive of demyelination in patients with CIDP by electrophysiological study. Our results are compatible with those of Pineda et al. [4], who indicated such subclinical CNS demyelination-involved CIDP patients more responsive to immunotherapies. Subclinical visual pathway abnormalities were demonstrated in 30% of our CIDP patients. Other authors have also demonstrated VEP abnormalities in CIDP patients, but at higher rates of 50% [8] or 85% [9]. Stojkovic et al. [10] studied 8 patients with CIDP who had increased VEP latency, although VEP results were not significantly modified after treatment with either steroid or IVIg. They concluded that the measurement of VEPs was a useful technique for the diagnosis of visual pathway involvement, but was of no value for monitoring the effect of treatment in CIDP patients. We concur with this finding, as CIDP patients with prolonged P100 latency in the present study had shorter VEP latency in both eyes after treatment with IVIg. Moreover, the VEP parameters in patients with CIDP showed overall improvement with IVIg therapy, further supporting that its administration may be effective even for CNS lesions in CIDP.

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