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Research paper

# Unilateral suppression of P/N13′ potential amplitude in young patients with persistent numbness due to cervical monoradiculopathy. A case-control study

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ABSTRACT

*Objective:* The utility of Dermatomal Somatosensory Evoked Potentials (DSEPs) in the diagnostic workup of suspected cervical monoradiculopathy has been limited by significant overlap between measurements obtained from affected versus unaffected roots. In a case-control study, we explored whether, under certain conditions, asymmetry in DSEP parameters may offer significant help in the diagnosis of monoradiculopathy.

*Methods:* DSEPs were obtained bilaterally from patients with persistent (age range 33–55, $n = 10$) or intermittent (age range 31–55, $n = 7$) unilateral sensory symptoms of less than one month duration due to MRI-confirmed cervical monoradiculopathy. DSEPs were also obtained bilaterally from age-matched asymptomatic volunteers (age range 31–54, $n = 8$) and older asymptomatic volunteers (age range 57–77, $n = 8$). Amplitude and latency of the P/N13′ potential (negative peak at 13 ms) were measured.

*Results:* In all ten patients with persistent symptoms, the P/N13′ amplitude ratio, defined as P/N13′ amplitude on the symptomatic side divided by P/N13′ amplitude on the contralateral asymptomatic side, ranged between 0.0 and 0.50 (unilateral suppression). In all seven patients with intermittent symptoms, P/N13′ amplitude ratios ranged between 0.60 and 1.00. In all age-matched asymptomatic controls, P/N13′ amplitude ratio (side with lower divided by side with higher amplitude) was always at least 0.80. Among older asymptomatic subjects, DSEPs had inconsistent characteristics.

*Conclusions:* Cervical monoradiculopathy with persistent numbness in young patients (aged up to 55 years) is very strongly associated with unilateral suppression of P/N13′ DSEP amplitude. No significant asymmetry is observed in cases of monoradiculopathy with intermittent numbness.

*Significance:* In young patients with unilateral upper extremity persistent sensory complaints, DSEP amplitude asymmetry, as quantified by the P/N13′ ratio, may offer significant help in the diagnosis of monoradiculopathy.



## 1. Introduction

Cervical radiculopathy is a leading cause of patient referral to a neurophysiology department. In the acute phase, EMG findings are usually confined to a reduced interference pattern if motor fibers are impinged by the herniated disk, whereas they are usually uninformative if the patient presents with sensory symptoms only. In these cases, somatosensory potentials evoked by electrical stimulation of the skin sensory fibers in the area of a given dermatome (Dermatomal Somatosensory Evoked Potentials – DSEPs) may give valuable information if the prolapsed disk disrupts sensory volley propagation at the cervical level. A number of studies have employed DSEPs in the assessment of cervical radiculopathy, while stimulating skin regions corresponding to single dermatomes and recording from both cervical and cerebral electrodes on each subject (Piade et al., 1984; Schmid et al., 1988; Le Pera et al., 1998; Talavera-Carbajal et al., 2003; Kwast-Rabben et al., 2008), but no firm diagnostic guidelines have emerged.

*Abbreviations:* DSEP, Dermatomal Somatosensory Evoked Potentials; P/N13′, negative peak at 13 ms.

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Several potentials are recorded at the rostro-caudal neuraxis after electrical stimulation of sensory fibers. Among them, P/N13′ is a stationary complex postsynaptic potential that is thought to be generated by cervical cord gray matter interneurons as well as by cuneate nucleus neurons and medial lemniscus (Evoked potentials in clinical medicine, Chiappa, third edition) (Sonoo et al., 1990). In one study, the latency of the P/N13′ or the N9′-P/N13′ segment is increased at the side of radiculopathy (Talavera-Carbajal et al., 2003). Other studies assessed the amplitude of P/N13′ stimulating sensory nerves (Eisen et al., 1983; Tataroglu and Bicer, 2003) or dermatomes (Piade et al., 1984; Le Pera et al., 1998; Kwast-Rabben et al., 2008) and found that it is reduced in the symptomatic side or bilaterally in about 50% of cases, suggesting that the method has a variable degree of sensitivity. Another study questioned the validity of DSEPs in the diagnostic workup of cervical radiculopathy, arguing that all potential diagnostic criteria assessed, based mainly on latency but also on amplitude, show low specificity and/or sensitivity (Schmid et al., 1988). Even classical textbooks claim that DSEPs can be abnormal bilaterally even in cases of clearly defined unilateral disease suggesting that this test has high sensitivity but low specificity (Dumitru, 2000).

Based on our clinical neurophysiological experience, we suspected that certain DSEP parameters, especially P/N13′ DSEP amplitude asymmetry, may, under certain clinical conditions, serve as a reliable marker for presence of monoradiculopathy. We chose to focus on three such conditions. First, analyses were limited to patients with exclusively sensory symptoms. Second, we subdivided our patients according to whether symptoms were persistent or intermittent, expecting that the former group is more likely to yield abnormal DSEP values. The third condition examined was patients' age, since older ages are known to be generally associated with degenerative burden at the cervical spine possibly leading to DSEP lower amplitudes and longer latencies.

## 2. Methods

### 2.1. Subjects

Four subject groups were studied in a case-control design (Tables 1 and 2). In brief: *Intermittent symptoms (IS) group*: Cervical monoradiculopathy patients aged up to 55 years with intermittent unilateral sensory symptoms. *Persistent symptoms (PS) group*: Cervical monoradiculopathy patients aged up to 55 years with persistent unilateral sensory symptoms. *Age-matched asymptomatic group*: Aged-matched (up to 55 years) asymptomatic volunteers. *Older asymptomatic group*: Older (aged >55 years) asymptomatic volunteers.

In more detail, patient inclusion criteria were: Presentation at Iatropolis Medical Group from January 2014 to July 2015, age less than or equal to 55 years, acute unilateral upper extremity sensory symptoms (duration <1 month), lack of motor symptoms, free medical history, MRI-confirmed cervical radiculopathy and non-diagnostic nerve conduction and EMG studies. The 17 patients who fulfilled the criteria were separated into two groups (Tables 1 and 2). The IS group ($n = 7$) consisted of patients with intermittent symptoms of unilateral pain or numbness. The PS group ($n = 10$) consisted of patients with persistent numbness confined to a dermatome region. In order to be included in the study, a patient should have MRI of the cervical spine showing a single unilateral disk prolapse compressing a corresponding cervical root, as well as nerve conduction and EMG studies with negative results. All patients satisfying the above criteria were included.

We use DSEPs as part of the routine diagnostic workup in patients suspected of having radiculopathy, based on recommendations of some previous studies, as well as on the fact that they are non-invasive and carry little risk of complications. All patients gave verbal consent to the diagnostic procedure, but it was impractical to obtain formal written informed consent retrospectively for this report.

A group of asymptomatic age-matched subjects (aged 31–54 years, $n = 8$) with normal MRI of the spine and Nerve Conduction Velocity studies and free medical history served as a control group. We further conducted DSEPs studies in a group of older subjects, aged 57–77 years ($n = 8$), asymptomatic at the time of study, with MRI findings of chronic degenerative disk changes (not a disk protrusion) which can be considered as 'normal' for their age.

Asymptomatic subjects of both age groups were volunteers acquainted to the authors, mostly health care professionals already familiar with electrophysiology and MR imaging. They signed informed consent before undergoing the study.

All procedures on patients and healthy controls were approved by Iatropolis Medical Group.

### 2.2. Electrodiagnosis

Experiments were carried out with Nihon–Kohden instrument (MEB 9400 model). Stimuli were delivered with ring electrodes to the finger corresponding to the sensory deficit (thumb for C6, middle finger for C7 and little finger for C8 radiculopathy). In control subjects (young or aged), stimulation was applied to the thumb. We chose to stimulate this dermatome because the majority of patients had radiculopathy corresponding to that finger and it has been shown that both the amplitude and latency of DSEPs is similar under stimulation of either dermatome in control subjects (Sohn et al., 2012).

Recordings were made by needle subdermal electrodes, with active electrode over C2 and reference electrode over Fpz' (recordings referenced to Fpz' and also, for comparison, to NC from a young asymptomatic subject are shown in Appendix Fig. A1). The active electrode was placed at C2 level, rather than the more frequently used C6 level, because P/N13′ may have higher amplitude at C2 (recordings from C2 and C6 levels from a young asymptomatic subject are shown in Appendix Fig. A2) (Sonoo et al., 1990; Kwast-Rabben et al., 2008). Considerations and recommendations for Median nerve DSEPs recording described in a standard textbook (Dumitru, 2000) were taken into account. Care was taken to always have impedance values below 5 kOhm.

To limit high-frequency noise, the bandwidth was restricted to 0.5–200 Hz (Appendix Fig. A3), as used by Eisen and colleagues (Eisen et al., 1979; Eisen and Elleker, 1980) and discussed by Dumitru (2000).

Two trains of 500 stimuli (3 Hz, with intensity x3 above sensory threshold, 9–11 mA) were delivered to each arm tested. The average of the two waveforms obtained under the above conditions was calculated (Fig. 1). The trough preceding P/N13′ was taken as baseline. Two parameters were measured: The latency of P/N13′ to the peak of the negative wave and the amplitude from the zero line to the peak of the negative wave (Fig. 1). Measurements were taken from both arms of all subjects.

In the two groups suffering from unilateral monoradiculopathy (intermittent or persistent), ratio of the P/N13′ amplitudes was defined as P/N13′ amplitude on the symptomatic side divided by P/N13′ amplitude on the asymptomatic side. In the two asymptomatic groups (younger and older), ratio was defined as P/N13′ amplitude on the side where it was lower divided by P/N13′ amplitude on the side where it was higher.

**Table 1**
Characteristics of indvidual subjects.

| id | Group | Sex | Age | rootLevel | AMPasym_hi | AMPsym_lo | AMPratio | LATasym_hi | LATsym_lo |
|---|---|---|---|---|---|---|---|---|---|
| 11 | Persist | M | 45 | C6 | 0.46 | 0.16 | 0.34 | 18.5 | 18.7 |
| 12 | Persist | M | 47 | C7 | 0.49 | 0.13 | 0.28 | 15.4 | 16.3 |
| 13 | Persist | F | 43 | C6 | 0.88 | 0.32 | 0.37 | 16.5 | 17.4 |
| 14 | Persist | F | 55 | C6 | 0.56 | 0.05 | 0.09 | 18.2 | 19.0 |
| 15 | Persist | F | 42 | C6 | 0.40 | 0.20 | 0.50 | 17.1 | 17.3 |
| 16 | Persist | M | 41 | C8 | 0.58 | 0.21 | 0.37 | 16.9 | 19.7 |
| 17 | Persist | F | 33 | C6 | 0.75 | 0.22 | 0.30 | 16.6 | 17.3 |
| 18 | Persist | F | 37 | C6 | 0.65 | 0.00 | 0.00 | 16.9 | |
| 19 | Persist | F | 37 | C7 | 0.75 | 0.00 | 0.00 | 17.5 | |
| 20 | Persist | F | 36 | C6 | 0.55 | 0.00 | 0.00 | 17.2 | |
| 21 | Interm | M | 46 | C6 | 0.91 | 0.57 | 0.62 | 17.1 | 18.3 |
| 22 | Interm | F | 33 | C7 | 0.67 | 0.42 | 0.63 | 16.4 | 16.1 |
| 23 | Interm | F | 49 | C6 | 0.66 | 0.64 | 0.97 | 21.6 | 20.2 |
| 24 | Interm | F | 31 | C6 | 0.61 | 0.65 | 1.07 | 17.1 | 17.0 |
| 25 | Interm | F | 46 | C7 | 0.71 | 0.93 | 1.30 | 16.4 | 15.4 |
| 26 | Interm | M | 55 | C6 | 0.60 | 0.54 | 0.91 | 18.4 | 19.0 |
| 27 | Interm | F | 35 | C6 | 0.96 | 0.79 | 0.82 | 16.7 | 15.6 |
| 31 | AsymYng | M | 31 | C6 | 0.83 | 0.67 | 0.80 | 16.1 | 16.6 |
| 32 | AsymYng | M | 37 | C6 | 1.04 | 0.97 | 0.93 | 18.6 | 18.7 |
| 33 | AsymYng | F | 54 | C6 | 0.96 | 0.79 | 0.82 | 17.5 | 18.0 |
| 34 | AsymYng | M | 52 | C6 | 1.20 | 1.02 | 0.85 | 16.9 | 17.3 |
| 35 | AsymYng | F | 36 | C6 | 0.90 | 0.80 | 0.89 | 15.0 | 15.4 |
| 36 | AsymYng | F | 34 | C6 | 1.25 | 1.19 | 0.95 | 15.4 | 15.8 |
| 37 | AsymYng | F | 31 | C6 | 0.95 | 0.89 | 0.93 | 15.4 | 16.0 |
| 38 | AsymYng | F | 40 | C6 | 0.61 | 0.59 | 0.97 | 16.2 | 16.6 |
| 41 | AsymOld | M | 65 | C6 | 0.29 | 0.00 | 0.00 | 18.7 | |
| 42 | AsymOld | F | 57 | C6 | 0.75 | 0.40 | 0.53 | 17.5 | 17.3 |
| 43 | AsymOld | M | 77 | C6 | 0.75 | 0.47 | 0.62 | 16.2 | 17.1 |
| 44 | AsymOld | F | 66 | C6 | 0.40 | 0.20 | 0.50 | 16.5 | 15.4 |
| 45 | AsymOld | F | 71 | C6 | 0.44 | 0.00 | 0.00 | 15.6 | |
| 46 | AsymOld | F | 58 | C6 | 1.01 | 0.80 | 0.79 | 17.8 | 15.9 |
| 47 | AsymOld | M | 57 | C6 | 0.00 | 0.00 | | | |
| 48 | AsymOld | M | 68 | C6 | 0.00 | 0.00 | | | |

**PS**: persistent symptom of unilateral numbness.
**IS**: intermittent symptom of unilateral numbness.
**AsymYng**: asymptomatic, age-matched (31–54 years) subjects.
**AsymOld**: asymptomatic, older (57–77 years) subjects.
**AMPasym_hi**: P/N13′ DSEP amplitude of asymptomatic side (in patients) or of higher amplitude side (in asymptomatic controls).
**AMPsym_lo**: P/N13′ DSEP amplitude of symptomatic side (in patients) or of lower amplitude side (in asymptomatic controls).
**AMPratio**: P/N13′ DSEP amplitude ratio of symptomatic/asymptomatic side (in patients) or of lower/higher amplitude side (in asymptomatic controls).
**LATasym_hi**: P/N13′ DSEP latency of asymptomatic side (in patients) or of higher amplitude side (in asymptomatic controls).
**LATsym_lo**: P/N13′ DSEP latency of symptomatic side (in patients) or of lower amplitude side (in asymptomatic controls).

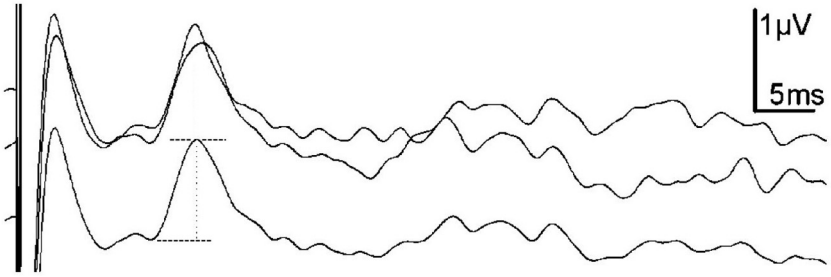


**Fig. 1.** Example of typical Dermatomal Somatosensory Evoked Potentials (DSEP) recording in a normal subject. Stimulation of the right thumb. Recording at level of the second cervical vertebra (C2). Filter band at 0.5–200 Hz. Each of the two upper traces represents the average response to a train of 500 stimuli. The bottom third trace represents the average of the above two traces. The prominent upward (negative) peak is the P/N13′ complex.

### 2.3. Statistical analysis

For analyses with one categorical predictor (subject group) and a quantitative outcome (amplitude, amplitude ratio or latency), independent student *t*-test was used. For analyses with the side (left versus right) as predictor and a quantitative outcome (amplitude or latency), paired student *t*-test was used. Since all p-values which we declare as «significant» are extremely small, no multiple comparison correction was applied. For additional exploratory analyses with multiple predictors (sex, age, etc), linear regression was used.

Results for amplitude and latency are reported as mean ± SEM. Statistical calculations were performed in Origin software.

## 3. Results

### 3.1. Age-matched asymptomatic group

The group consisted of eight subjects aged 31–54 years (Table 1 & Table 2). P/N13′ was reproducible in every arm tested ($n = 16$). The latency of P/N13′ was 16.6 ± 0.3 ms and the amplitude 0.92 ± 0.05 μV ($n = 16$) (Fig. 2). The amplitude ratio between sides

(lower to higher amplitude) was 0.89 ± 0.02 (minimum 0.80) (Fig. 3).

### 3.2. Intermittent unilateral symptoms (IS) group

The group consisted of seven patients aged 31–55 years (Tables 1 and 2). P/N13′ was reproducible in every arm tested ($n$ = 14). The latency of P/N13′ was shorter on the symptomatic side only in two patients. Therefore, overall, the latency of P/N13′ was usually shorter on the healthy side (17.35 ± 0.39 ms vs 17.64 ± 0.7 ms) but not significantly so (paired $t$-test, $p$ = 0.44).

The amplitude of P/N13′ was smaller on the symptomatic side in five out of seven patients. Overall, in all patients of this group, P/N13′ had smaller amplitude on the symptomatic side (0.64 ± 0.06 μV) than the normal side (0.73 ± 0.05 μV) but not significantly so (paired $t$-test, $p$ = 0.28) (Fig. 3). The ratio of P/N13′ amplitudes (symptomatic to asymptomatic side) was never less than 0.62 (0.90 ± 0.09) (Fig. 3).

In comparison with the asymptomatic age-matched group, P/N13′ amplitudes of the symptomatic side in the IS group were significantly lower (independent $t$-test, $p$ = 0.001, Fig. 2).

### 3.3. Persistent unilateral symptoms (PS) group

The group consisted of ten patients aged 33–55 years (Tables 1 and 2). P/N13′ was reproducible in the symptomatic side in only seven of them. Latency of P/N13′ was always shorter on the asymptomatic side ($n$ = 7, 17.1 ± 0.3 ms vs 17.9 ± 0.4 ms, paired $t$-test, $p$ = 0.034). Latency of P/N13′ on the symptomatic side was not statistically significantly longer than the control group (independent $t$-test, $p$ = 0.065). Amplitude of P/N13′ was always smaller on the symptomatic side.

The ratio of the amplitude of P/N13′ (symptomatic to asymptomatic side) was 0.22 ± 0.06 ($n$ = 10, 0.13 ± 0.04 μV vs 0.61 ± 0.05 μV, paired $t$-test, $p$ = 0.0002, Fig. 2) and always 0.50 or less (Fig. 3).

In comparison with the asymptomatic age-matched group, P/N13′ amplitudes of all symptomatic limbs in the PS group were lower than all amplitudes obtained from asymptomatic subjects (independent $t$-test, $p = 3.4 * 10^{-9}$, Fig. 2). Notably, P/N13′ amplitudes on the asymptomatic side in the PS group were also significantly lower than amplitudes obtained from asymptomatic subjects (independent $t$-test, $p$ = 0.0002, Fig. 2).

### 3.4. Older asymptomatic group

The group consisted of eight subjects aged 57–77 years (Table 1 & Table 2). In two of them, P/N13′ could not be elicited in both sides and in another two P/N13′ could not be elicited in one side. Therefore, P/N13′ was reproducible in 10 arms (10/16). The latency of P/N13′ was 16.8 ± 0.3 ms ($n$ = 12) and the amplitude 0.34 ± 0.08 μV ($n$ = 16) (Fig. 2). The ratio of the amplitude between sides was 0.4 ± 0.13 (range 0.0–0.79).

The amplitude of P/N13′ was statistically lower than the younger asymptomatic group (independent $t$-test, $p$ = 0.00005, Fig. 2).

### 3.5. Potential predictors of within-group variability in amplitude or latency

A number of parameters that might affect amplitudes and latencies within each group were tested. These included sex, age, height, weight, handedness, side of sensory symptoms, affected dermatome and duration of symptoms (within the maximum 2-month requirement). None of these parameters was significantly associated with amplitude or latency within any group. Nevertheless, because of the low number of patients, a negative result could represent a type II error. Higher numbers would be needed for a more reliable assessment.

## 4. Discussion

The main finding of the present study was that in all of ten young (aged up to 55 years) cervical monoradiculopathy patients with persistent numbness, the P/N13′ amplitude ratio of the symptomatic to the asymptomatic side was 0.5 or less ('unilateral suppression'). On the other hand, all seven monoradiculopathy patients with intermittent sensory symptoms had ratios 0.6 or higher, largely overlapping with the age-matched asymptomatic control group.

For use as a diagnostic marker of unilateral disease, the amplitude ratio has certain advantages over absolute amplitude value. SEP amplitude is highly variable among subjects. It is also dependent on electrode placement and stimulus intensity. Calculation of amplitude ratio between DSEPs from the arms of the same subject significantly reduces both the inter-subject variability and the variability in electrophysiological methodology. This is apparent in the young asymptomatic group, where amplitude ratio had a value of 0.91 ± 0.03 ($n$ = 8) and never below 0.8.

**Table 2**
Characteristics of the four population groups: number of subjects in each group ($n$), ages, latencies and amplitudes of N13′ Dermatomal Somatosensory Evoked Potentials (DSEPs).

| | $n$ | Age (years) | | Latency (ms) | Amplitude (μV) | Amplitude ratio |
|---|---|---|---|---|---|---|
| | | Mean (range) | | Mean ± sem (range) | Mean ± SEM (range) | Mean ± SEM (range) |
| Young asymptomatic | 8 | 39.4 (31–54) | Both sides ($n$ = 16) | 16.6 ± 0.3 (15.0–18.7) | 0.92 ± 0.05 (0.59–1.25) | 0.89 ± 0.02 ^ (0.80–0.97) |
| Young – intermittent unilateral symptoms (IS) | 7 | 42.1 (31–55) | Symptomatic side | 17.4 ± 0.7 (15.4–20.2) | 0.65 ± 0.06 (0.42–0.93) | 0.90 ± 0.09 † (0.62–1.30) |
| | | | Asymptomatic side | 17.6 ± 0.7 (16.4–21.6) | 0.73 ± 0.06 (0.60–0.96) | |
| Young – persistent unilateral symptoms (PS) | 10 | 41.6 (33–45) | Symptomatic side | 17.9 ± 0.4 (16.3–19.7) | 0.13 ± 0.04 (0.00–0.32) | 0.22 ± 0.06 † (0.00–0.50) |
| | | | Asymptomatic side | 17.1 ± 0.3 (15.4–18.5) | 0.61 ± 0.05 (0.40–0.88) | |
| >55 years asymptomatic | 8 | 64.9 (57–77) | Both sides ($n$ = 16) | 16.8 ± 0.3 (15.4–18.7) | 0.34 ± 0.08 (0.00–1.01) | 0.41 ± 0.14 ^ (0.00–0.79) |

^ Ratio of lower to higher amplitude.
† Ratio of amplitude at symptomatic to amplitude at asymptomatic side.

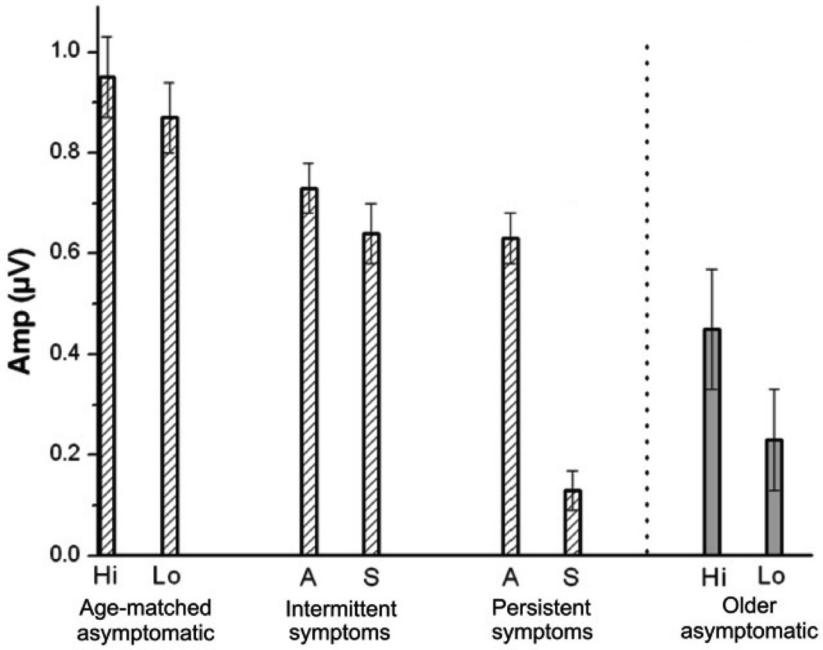


**Fig. 2.** Histogram showing P/N13′ amplitude (mean ± SEM) in every side and in every group studied. Patient groups: Intermittent unilateral sensory symptoms (ages 31–55, $n = 7$). Persistent unilateral sensory symptoms (ages 33–55, $n = 10$). A: asymptomatic side, S: symptomatic side. Asymptomatic groups: Age-matched (ages 31–54, $n = 8$). Older (ages 57–77, $n = 8$). Hi: Side with higher amplitude, Lo: Side with lower amplitude.

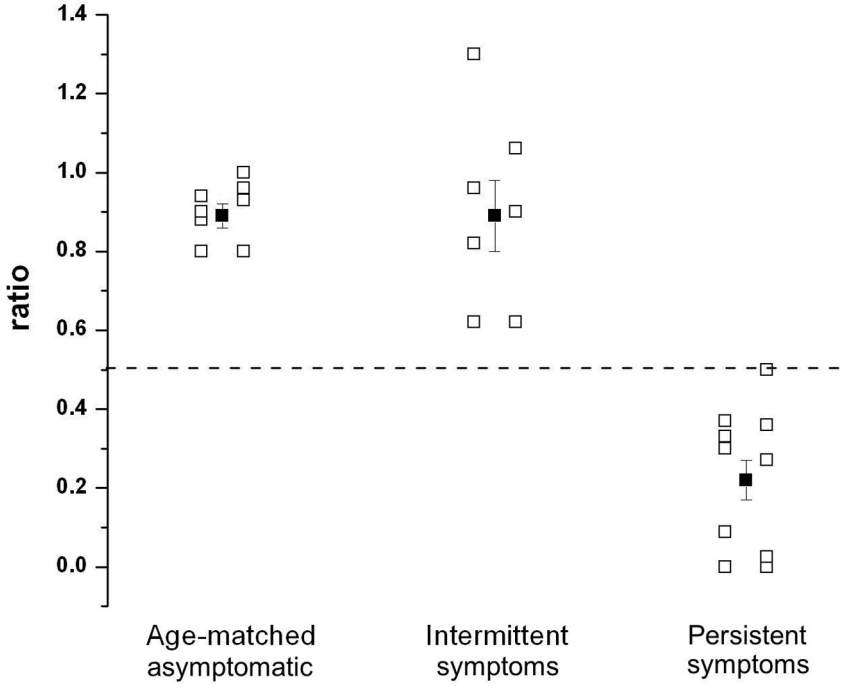


**Fig. 3.** Scatterplot showing ratios of P/N13′ amplitudes between sides in every subject of the three age-matched groups. In the intermittent ($n = 7$) and the persistent ($n = 10$) unilateral sensory symptom groups, ratio = symptomatic divided by asymptomatic side. In the asymptomatic age-matched group ($n = 8$), ratio = lower amplitude divided by higher amplitude. Ratios of 0.5 or less were observed in all patients with persistent symptoms.

Previous studies have shown that in cases of cervical radiculopathy the amplitude of P/N13′ potential may be reduced unilaterally (Eisen et al., 1983; Tataroglu and Bicer, 2003) or bilaterally (Caccia et al., 1976; Piade et al., 1984). However, the specificity and/or sensitivity of DSEP-based diagnostic criteria for radiculopathy have been questioned (Schmid et al., 1988). It is generally accepted that DSEP abnormalities are usually present in cases of confirmed unilateral disease, but they tend to be bilateral, without prominent asymmetry, a fact that may often hinder rather than help reach a correct diagnosis (Dumitru, 2000). In line with this general consensus, we did observe bilateral decreases in DSEP amplitude in monoradiculopathy cases, but the lack of prominent asymmetry was strictly limited to patients with intermittent sensory symptoms. On the contrary, in all 10 patients younger than

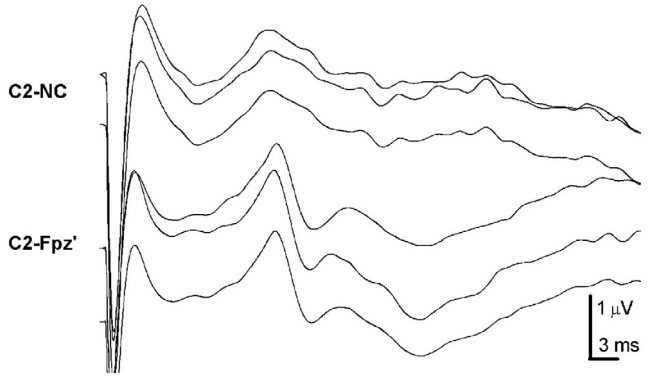


**Fig. A1.** Choice of reference electrode. Simultaneous recording of N13′ complex in a normal subject using a non-cephalic (NC, contralateral shoulder) reference electrode (upper three traces, where the third trace stands for the average of the first two) and the Fpz' as a reference electrode (bottom three traces). The signal of interest can be more prominently seen in the second case. We preferred a cephalic reference electrode (although it contaminates signal with P13/P14 far field potential) because a non-cephalic one records the desired signal with a significantly lower amplitude. Furthermore, the vast majority of studies using DSEPs have been conducted using a cephalic reference electrode.

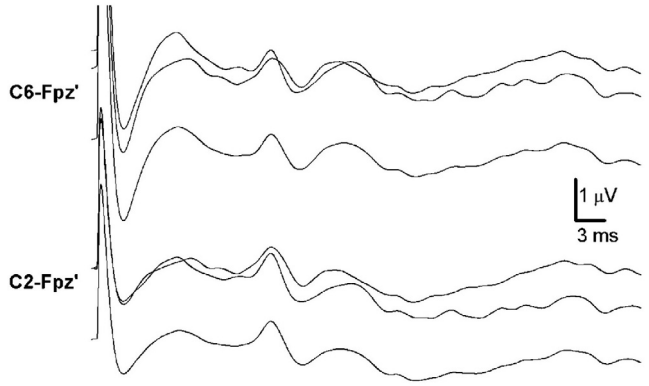


**Fig. A2.** Choice of active electrode site. Simultaneous recording of P/N13′ complex in a normal subject using the derivation more commonly used with the active electrode over C6 (upper three traces, the third trace being the average of the first two) and the derivation employed in the present study (bottom three traces) where the active electrode is placed over C2. With this montage P/N13′ complex potential has a somewhat higher amplitude. When positioning the active electrode at C2 level, P/N13′ had a somewhat higher amplitude in previous studies as well (Sonoo et al., 1990), (Kwast-Rabben et al., 2008). See also recommendations for Median nerve DSEPs in textbook by Dumitru (2000), pp. 388–389.

55 years of age with persistent unilateral sensory symptoms due to MRI-confirmed monoradiculopathy, the symptomatic to asymptomatic P/N13′ amplitude ratio was always 0.50 or less. Therefore, in this patient subgroup the DSEP amplitude ratio threshold of 0.50 may serve as a highly sensitive diagnostic marker of unilateral radiculopathy.

It may be useful to discuss our findings in the light of certain important previous studies which have derived moderate degrees of sensitivity of DSEPs in the study of cervical radiculopathy. In the study of Eisen et al. (1983), the overall sensitivity of the DSEPs study was 57%. The investigators pointed out that the severity of the sensory symptoms was correlated with the degree of DSEP abnormalities. In the present study, if we merge the two groups with sensory symptoms (intermittent $n = 7$, persistent $n = 10$), the amplitude of P/N13′ is unilaterally suppressed in 10 out of 17 patients (58%). Therefore the two studies have many qualitative and qualitative similarities, with the exception that the distinguishing criterion we offer (intermittent vs persistent symptoms)

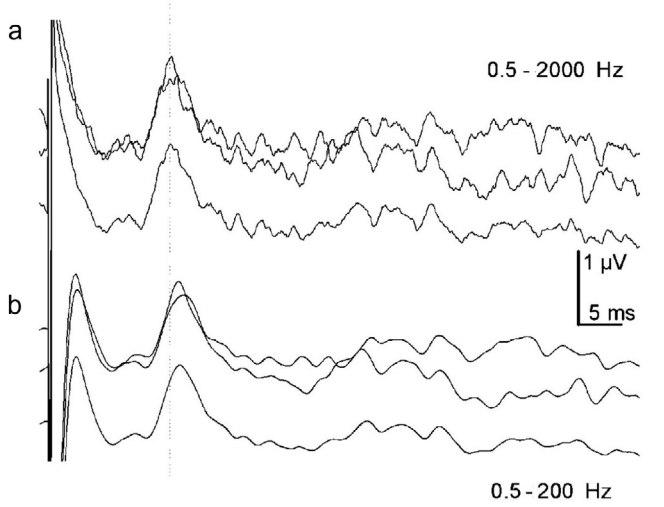


**Fig. A3.** The effect of the narrow band filter (low-pass filter at 200 Hz) on N13′ complex morphology. Simultaneous recording of N13′ complex in a young asymptomatic subject using the more frequently applied filter band of 0.5–2000 Hz (a) and the more restricted filter band applied in the present study (0.5–200 Hz) (b). In each panel (a, b) the bottom third trace represents the average of the above two traces (2 × 500 stimuli). With the 200 Hz low-pass filter, there appears to be less contamination by high frequency noise. A disadvantage of the narrow filter range is an artifactual phase shift of N13′ complex, resulting in a longer latency measurement.

is simple, easily assessable and, furthermore, highly predictive of amplitude asymmetry.

Discussion is also merited to another previous study arguing that DSEPs have serious limitations in the diagnosis of sensory radiculopathy because of many false positive and false negative results (Schmid et al., 1988). In that work, the P/N13′ could not be reliably recorded in every patient or control subjects (possibly due to technical factors or to the age of patients), and the investigators focused primarily on alterations in latency of P/N13′ or N9-P/N13′ segment. In the figure presented in that study as a representative of a false negative result (as per criteria adopted in that study) it can be seen that indeed, the amplitude of P/N13′ is suppressed on the symptomatic side (although presented at a different scale). Furthermore, in this particular study the laterality of the lesion was not confirmed by imaging. This is important when examining side to side differences, especially when an apparently unilateral lesion reduces P/N13′ amplitude bilaterally as we and others have shown.

The reduction of the amplitude of P/N13′ could be attributed to the blockade of neural pulse propagation proximally by the compression of nerve fibers by the herniated disk. If this is the case, then why the amplitude also decreases in the asymptomatic side? Previous investigators have hypothesized that although the symptoms are unilateral, the disease involves subclinically both sides (Ganes, 1980). In our study this was not the case, since we carefully enrolled patients with unilateral symptoms and MRI findings of unilateral disease.

Concerning the effect of age, in the present work we included a group of asymptomatic subjects older than 55 years mainly in order to test our previous empirical impression that, in contrast to younger individuals, DSEP variability (including failure to elicit any DSEP) renders standard DSEP methodology unlikely to offer reliable diagnostic markers of unilateral monoradiculopathy. We chose apparently healthy subjects with no symptoms or signs of radicular disease and MRI of the spine that can be considered normal for their age. In some of them P/N13′ potential could not be reliably elicited in both sides, while in others we observed a

unilateral suppression of P/N13′ and overall the amplitude of P/N13′ was smaller compared to the control group of the younger subjects. The latter observation could be easily explained by the physiological neurodegeneration of cervical spine, where the generator of P/N13′ is located, leading to smaller potentials (Desmedt and Cheron, 1980). We could also state that if P/N13′ amplitude is sensitive to intermittent radiculopathy, then previous and possibly forgotten relapses of radiculopathy could have influenced P/N13′ potential negatively. Whatever the case, we show that age higher than 55 years is associated with significantly and often asymmetrically reduced P/N13′ amplitudes in asymptomatic controls and, therefore, standard DSEP methodology is unlikely to be very sensitive in the diagnosis of monoradiculopathy in this population.

Technical factors may be important for the recording of P/N13′ potential more reliably. In the present study two of them were given particular attention. First of all, filter settings were set to 0.5–200 Hz; the high frequency border of 200 Hz is lower than the setting often used. This setting reduces contamination by high frequency artifacts without undue distortion (Eisen and Elleker, 1980). Secondly, the active electrode was higher (over C2) than the site more often used (C6S). By this placement, P/N13 is more clearly defined because of less contamination by N9 ((el-Negamy and Sedgwick, 1978) and Fig. 1 therein) and may have somewhat higher amplitude ((Sonoo et al., 1990) and Fig. 3 therein, also (Dumitru (2000))).

Concerning latency measurements, some previous studies have also shown that the latency of P/N13 is delayed on the symptomatic side (Caccia et al., 1976; Talavera-Carbajal et al., 2003). We also observed that P/N13′ was in all cases delayed on the symptomatic side of patients with persistence of symptoms but the difference was not significant compared to the other groups studied limiting its diagnostic utility (specificity).

The aim of the present study was to reevaluate the role of DSEP asymmetry in the diagnosis of cervical monoradiculopathy and make practical suggestions that can possibly increase the diagnostic yield of the method. We suggest that unilateral suppression of the amplitude of P/N13′ be sought for in younger patients with new onset unilateral disease and persistent sensory symptoms.

The main limitations of the study are its relatively small number of subjects, especially for roots C7 and C8 (four and one patients respectively). An additional limitation is its strict set of inclusion requirements, which leave many patients with cervical radiculopathy excluded. Nevertheless, we think that the proposed diagnostic criteria can increase the yield of correct diagnosis of cervical radiculopathy in a sizeable subgroup of patients with unilateral sensory symptoms.

## Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

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## Appendix A. Electrodes position and filtering

The three Appendix figures, while not essential for continuity of reading, are provided because they address certain important methodological choices made in this work, namely: (1) reference electrode site, (2) active electrode site, (3) low-pass filter frequency.

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