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Laser-evoked potentials in painful radiculopathy

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HIGHLIGHTS

- Laser-evoked potential (LEP)-latency shifts indicate pronounced nerve root damage, worsening of function, severity, and pain.
- Only full or nearly full abolishment of the N2/P2 amplitude indicates clinical relevance.
- LEPs help to differentiate between moderate and severe nerve root compression.

ABSTRACT

Objective: The aims of this exploratory study were (1) to develop a standardized objective electrophysiological technique with laser-evoked potentials to assess dorsal root damage quantitatively and (2) to correlate these LEP measures with clinical parameters and sensory abnormalities (QST) in the affected dermatome.
Methods: Thirty-eight patients with painful radiculopathy and 20 healthy subjects were investigated with LEP recorded from the affected dermatome and control areas as well as with quantitative sensory testing. Questionnaires evaluating severity and functionality were applied.
Results: On average, LEP amplitudes and latencies from the affected dermatomes did not differ from the contralateral control side. In patients with left L5 radiculopathy (more severely affected) the N2 latency was longer and the amplitudes reduced.
Conclusions: The N2P2 amplitude correlated with pinprick evoked sensations in QST. The N2 latency from the affected dermatome correlates with pain intensity, chronicity, clinical severity and with a decrease of physical function.
Significance: An increase in N2-latency indicates a more pronounced nerve root damage, which is associated with a decrease of function and an increase of severity and pain. LEP amplitudes are associated with the functional status of the nociceptive system and may distinguish between degeneration of neuronal systems and central sensitization processes.

1. Introduction

Painful radiculopathy is induced by pathology of the nerve root or its ganglion and is perceived along the length of the lower limb most frequently in the L5/S1 dermatomal distribution. The current pathophysiological concepts of dorsal root damage differentiate between biochemical and mechanical processes. Mechanical compression can lead to fibrosis and total functional loss of the affected nerve fibers, which is often accompanied by a reduced number of axons. The compression might reduce neuronal impulse synchronization or induce a complete conduction block (Yoshii et al., 2010). An alternative relevant factor of radiculopathy is a local inflammatory effect on nerve roots by substances leaking from the degenerated intervertebral discs. One major experimental electrophysiological finding in inflammatory radiculopathy was a decrease in conduction velocity fibers in the nerve root, which could be antagonized by anti-inflammatory substances (Dilley and Bove, 2008a, 2008b).

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Laser-evoked potentials (LEP) reliably measure the integrity of small fiber primary afferent nociceptors and the spinothalamic tract by assessing latencies (N1, N2, P2) and amplitudes (N1, N2/P2) in the EEG after stimulation of the affected skin with laser heat impulses. So far, only very few studies used LEP recordings to examine neurophysiological changes in painful radiculopathy (Lorenz et al., 1996; Quante et al., 2007). These authors described a reduction or loss of LEP amplitudes and latency shifts as the most likely correlate of mechanical dorsal root compression. Based on the animal experimental findings described above, however, it is very compelling that a predominant inflammatory lesion of the root will lead to prolonged LEP latencies rather than amplitude reductions consistent with a decrease in nerve conduction velocity.

The degree of neuronal damage in the nerve root of patients with chronic painful radiculopathy is an important factor that might guide conservative or surgical treatment strategies. This is in particular true if pain is the leading complaint of the patient and motor deficits are absent. Thus, an objective tool to assess the function and integrity of nociceptive pathways in radiculopathy could improve treatment decisions.

The aims of this exploratory study were:

1. To develop a standardized objective electrophysiological LEP technique to assess dorsal root damage quantitatively,
2. To correlate these LEP measures with clinical parameters and sensory abnormalities (QST) in the affected dermatome,
3. To identify objective measures to differentiate between inflammatory and mechanical mechanisms of root lesion.

2. Methods

Thirty-eight patients suffering from painful radiculopathy and 20 healthy age and height matched healthy subjects participated in the study. Radiculopathy patients were recruited within the department of neurosurgery (patients were mainly admitted by the emergency department and the neurosurgical outpatient clinic). MRI was performed during pre-surgical diagnostics. In patients, laser-evoked potentials (latency and amplitude) were recorded after stimulation of the affected dermatome (either S1 or L5) and after stimulation in different control areas (contralateral, S1 and L5; ipsilateral; S1 or L5). The same dermatomes (L5, S1 on both sides) were tested in healthy controls.

The study complied with the Declaration of Helsinki and the ethics committee of the University Hospital of Kiel approved the experimental procedure. All participants gave their written informed consent to participate in the study.

2.1. Inclusion and exclusion criteria

Inclusion criteria:

(1) At least one of the following abnormal findings in the neurological examination:
   - Abnormal straight leg test
   - Hypoesthesia in the affected dermatome
   - Thermal hypoesthesia in the affected dermatome
   - Foot elevation and/or lowering paresis

(2) Low back pain with radiation into the foot

(3) Diagnosis of painful radiculopathy by a neurologist (consultant status)

Exclusion criteria:

- Age < 18 years
- History of other neurological or psychiatric disorder
- Pregnancy
- Therapy with WHO III opioids at the day of testing
- Reduced communication skills

2.1.1. Differentiation between compression or inflammatory radiculopathy

If a one-sided compression of the L5 or S1 root in the MRI (confirmed by a radiologist or neuro-radiologist) was present, a compression radiculopathy was diagnosed (MR+). If the above inclusion criteria were fulfilled and no nerve root compression was demonstrated in the MRI (confirmed by a radiologist or neuro-radiologist) an inflammatory radiculopathy was suspected (MR−).

2.2. LEP recording

The methodological approach, which aimed to elicit A-delta fiber mediated laser evoked potentials, was published earlier (Hullemann et al., 2013, 2015, 2016): "Nd:YAP 1340 Stimul Laser (neodymium:yttrium-aluminum-perovskite, DEKA Lasertechnologie GmbH, Mainburg) with a beam diameter of 5 mm and a stimulus duration of 5 ms was used. The subject's detection threshold was determined by up-regulating the energy stepwise (beginning with 0.5 J and then stepwise by 0.5-J increases) until a sensation was felt. Beginning from the detection threshold, the energy was increased further until the subjects reported a distinct pinprick pain sensation between 3 and 6 on the numerical pain rating scale, which should be equal to a twofold detection threshold of the laser energy density" (Hullemann et al., 2013, 2016). In order to avoid receptor fatigue (Greffrath et al., 2007) or sensitization (Price et al., 1977), the hand piece of the laser stimulator was moved slightly within the testing area.

Stimuli were given in blocks of 25 (5 min). The inter-stimulus intervals were randomized from 8 to 12 s (mean 10 s). In healthy subjects stimuli were applied to identical dermatomes of both legs. In patients stimuli were applied to the affected and to the corresponding contralateral dermatome.

The choice of EEG-electrodes, recording of LEP and documentation of the individual pain rating was published earlier (Hullemann et al., 2013, 2015, 2016): "The following EEG electrodes were attached according to the international 10–20 system: Fz, Cz, PZ, C3, C4 with linked earlobes as reference for the recording of the N2/P2 component; T3 and T4 with Fz as reference (Cruccu and Truini, 2010). An EOG was attached for detection of artifacts, and a wrist band for grounding.

The subjects reported the pain intensity of the perceived laser stimuli on a numerical rating scale (0 = no pain, 10 = most imaginable pain) after hearing the ping tone.

The EEG was recorded with Brain vision recorder 1.2 using the BrainAmp MR plus EEG amplifier (Brain products GmbH, Gilching Germany) and analyzed with Brain Vision Analyzer 2.0 (Brain Products GmbH; Gilching, Germany, Version 2.0.3.6367). All frames which contained artifacts 0.5 s before the laser stimulus and 2 s afterwards due to movement or blinking were excluded from analysis during visual inspection. The EEG was band-pass filtered with 0.3–35 Hz; the sampling rate was 1000 Hz.

The N2/P2 amplitude was measured from the most negative to the most positive peak. The N1 amplitude was measured from baseline to the N1 peak (baseline correction was performed using a −500 ms to 0 ms pre-stimulus interval). The latency of each A-delta component was measured from the stimulus onset (0 ms) to the peak of the averaged potentials (N2 latency)" (Hullemann et al., 2013, 2016).

2.3. Quantitative sensory testing

QST was performed according to the DFNS-protocol (Rolke et al., 2006; Maier et al., 2010; Vollert et al., 2016) at the mediodorsal area of the foot (L5 dermatome) or the lateral area of the foot (S1 dermatome), depending on the damaged nerve root. QST