Contact Heat Evoked Potential (CHEP) – Description of method and recordings from healthy subjects

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BACKGROUND

Clinical diagnosis of peripheral small fibre neuropathy (PNP) is based on findings of sensory loss or abnormal gain within thermal and nociceptive sensory modalities. Clinical examination is rather insensitive, though, and several quantitative methods have been developed for more accurate diagnosis of small fibre system disorders or dysfunction. Contact heat evoked potential (CHEP) recording is one of these recent developments that can be used to diagnose small fibre PNP and neuropathic pain.

Sensory fibres are divided according to their conduction velocity and anatomy into large myelinated Aα and Aβ fibres, and small myelinated Aδ, and unmyelinated C fibres. Warm sensation and slow heat pain are mediated by unmyelinated C fibres. Small myelinated Aδ fibres mediate fast heat pain (first pain) and cold sensations.

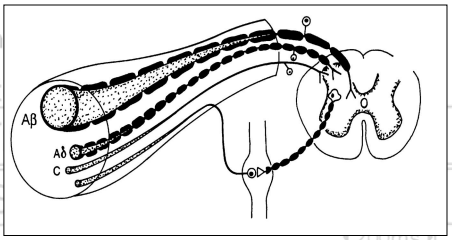

Figure 1. Peripheral nerve

With a specially constructed thermode, CHEP-device enables specific stimulation of the intraepithelial small fibre endings that transmit cool, warm, and thermal pain sensations. Neuropathic pain has been associated particularly with lesions of the small fibre system either within the peripheral (PNS) or central nervous system (CNS).

The thermal evoked brain potentials can be recorded from the scalp with EEG electrodes, with a maximum at the vertex. Main components of the Aδ fibre mediated CHEP responses are N200 and P400, named after their mean latencies and polarity. Their sources are located within the anterior cingulum and insula/opercular cortex bilaterally. When stimulating the facial area, the latencies are approximately 200 ms and 400 ms, in the extremities 250-300 ms and 500-600 ms. Peak-to-peak N-P amplitude is also measured from the recordings, and is considered the most useful parameter for diagnostic use. Very-late CHEP component may be recorded from Pz (P1000) at 800-1000 ms associated with function of C fibres.

Decrease in amplitude of the N200-P400 component, prolonged latencies of N200 and P400 components, or even absence of CHEP responses can occur in small fibre PNP and neuropathic pain conditions. CHEP recording evaluates the whole small fibre mediated pathway from the skin receptors via anterolateral spinal cord pathway to the cerebral cortex, so the abnormal responses do not reveal topographic level of abnormalities. However, in comparison with subjective psychophysical testing of the small fibre system with thermal quantitative sensory testing (QST), CHEP provides a completely objective and quantitative measurement tool. In addition, CHEP evaluates the same fibre tracts and central nervous system structures as laser evoked potential (LEP) that has been considered "the best diagnostic tool for neuropathic pain".

DEVICES

In this study, Viking Select™ (CareFusion, USA) and ATS/Pathway (Medoc Ltd, Israel) -devices were used to perform CHEP.

CHEP-stimulator thermode has a circular contact area of 27 mm in diameter (572,5 mm²). Stimulators in two layers are working together. The external layer consists of a heating foil. The heating thermofoil (Minco Products, Minneapolis, MN) is covered with a 25 µm layer of thermo-conductive plastic (Kapton®). Two thermocouples are embedded within this conductive coating directly contacting the skin and providing an estimate of the skin temperature at the thermode surface.

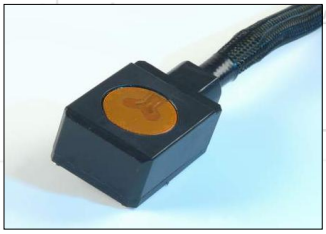

Figure 3. Contact Heat Evoked Potential stimulator (CHEPs)

Figure 2. ATS/Pathway (Medoc Ltd, Israel) -device

The lower layer is a Peltier element with two electronic thermal sensors. The external thermofoil permits a very rapid heating rate, up to 70 °C/s, and the lower layer Peltier allows fast cooling; up to 40 °C/s. Return to baseline begins immediately after the thermode reaches its target stimulus temperature based on the algorithms provided by the manufacturer. The baseline temperature was 32°C, target temperature was set at 54°C. Interstimulus interval (ISI) varied randomly from 10 to 15 sec when stimulating the facial skin and from 12 to 20 sec in the arm and leg.

METHOD

19 healthy subjects participated in the study (with 7 males and 12 females, ages 21-57, mean age 31 years (SD 8,7).

During the examination the subjects were in a half-sitting position on an examination chair with their eyes open. We asked the subjects to fix their eyes in one target to minimize blinking.

Triangular heat pulses were applied to the face at the infraorbital distribution of the trigeminal nerve, to the lateral and medial cutaneous nerve distributions in the forearm, 7-10 cm proximal to the wrist, and to the superficial peroneal nerve distribution in the distal leg, 10 cm proximal to the lateral malleolus. Contact of the thermode must be firm, without excessive pressure.

Cortical evoked potentials were recorded from three midline EEG-electrode locations (Fz, Cz and Pz) and the reference electrode was placed at Fpz' of the international 10-20 system. For control of artefacts, we monitored also the electro-oculogram. The impedances were checked. The evoked potentials were filtered with a bandpass from 0.2 Hz to 30 Hz. Recording was triggered by the onset of each stimulus, and the time window was 2000 ms. To avoid interference by the startle elicited often by the first heat stimulus, the first evoked potential was not included in the average. 5-15 trials were averaged twice to ensure repeatability of the waveforms.

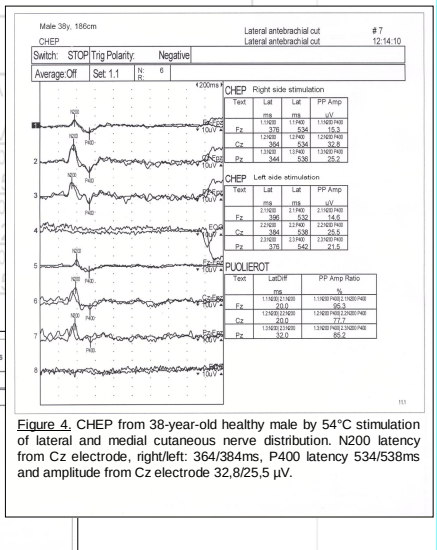

Figure 4. CHEP from 38-year-old healthy male by 54°C stimulation of lateral and medial cutaneous nerve distribution. N200 latency from Cz electrode, right/left: 364/384ms, P400 latency 534/538ms and amplitude from Cz electrode 32,8/25,5 µV.

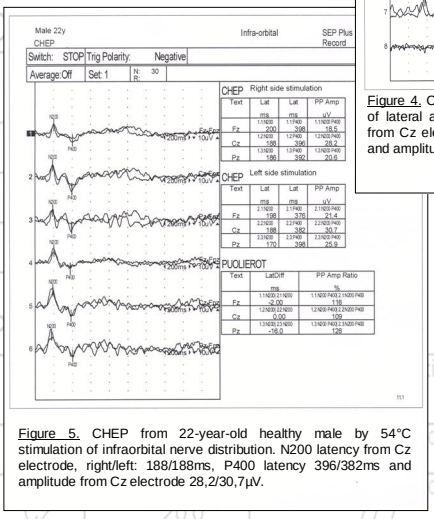

Figure 5. CHEP from 22-year-old healthy male by 54°C stimulation of infraorbital nerve distribution. N200 latency from Cz electrode, right/left: 188/188ms, P400 latency 396/382ms and amplitude from Cz electrode 28,2/30,7µV.

RESULTS AND CONCLUSIONS

We found that young healthy subjects had distinct and reproducible N200-P400 response when stimulating the facial area, and the extremities. If the stimulus was not experienced painful, the amplitude was smaller. Vigilance seemed to affect latencies and amplitudes: drowsiness resulted in smaller responses and longer latencies. Also if the subjects kept their eyes closed, the amplitudes were lower.

By moving the thermode slightly in-between the stimuli we tried to avoid habituation, especially at the extremities. In addition, the ISI seemed to influence habituation. At the facial skin, tendency to CHEP amplitude diminishment between consecutive responses was less pronounced than in the limbs, which allows the use of shorter ISI within the trigeminal distribution.

With numerical rating scale (NRS) reflecting the intensity of perceived pain (0 = no pain at all; 10 = worst pain imaginable), we tried to control for the effects of variability in the subjective experience of stimulus intensity. Besides the NRS, we asked the patient if the stimulus got stronger / stayed same / got weaker during the recording session. Possible after sensations and other qualitative sensory alterations during testing were also documented.

CHEP recording seems to be a feasible method for the study of small fibre system but several factors (including ISI, site of stimulation, and subjective pain rating) affecting the tendency to response habituation have to be taken into account when collecting reference values and performing patient diagnostics. In addition, medications with CNS effects may change the CHEP waveforms because of alterations in vigilance or habituation.