

Trigeminal small-fibre function assessed with cold evoked potentials (CEPs) in humans

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To investigate whether cold thermal cutaneous stimulation evokes reproducible CEPs from the trigeminal territory and may prove a reliable diagnostic tool in facial neuropathic pain. A novel micro-Peltier element device able to cool the skin at -300°C/s was used to record CEPs from the trigeminal territory (V1 and V2–V3) in 15 healthy participants and compared them to LEPs from the same sites. To assess the clinical usefulness, we performed LEPs and CEPs in three patients suffering from facial neuropathic pain due to different conditions (PHN, TISN and CPSP). CEPs were observed in all healthy subjects from both sites of stimulation, with a biphasic complex maximal at the vertex (Cz), peaking 170–290 ms after stimulus onset, preceded by a negative wave over temporal areas contralateral to the stimulated site. Unlike LEPs, perioral cold stimulation did not yield shorter latency and larger amplitude CEPs than supraorbital stimulation. The patient with CPSP had suppressed CEPs and partially spared LEPs from the affected side. No significant differences were found in the other clinical conditions. Cold thermal cutaneous stimulation elicits clear CEPs. The latencies and magnitudes of CEPs response seem not to be function of the site of facial stimulation. CEPs are a useful diagnostic tool to disclose the cold pathway impairment in patients with cold allodynia.

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Non-invasive vagus nerve stimulation: effects on trigeminal laser evoked potentials

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A portable transcutaneous non-invasive device that stimulates the cervical portion of the vagus nerve has been developed (GammaCore®) for the treatment of migraine. Cervical nVNS was shown to rapidly inhibit cortical spreading depression in rodents, providing important insights into the mode of action of nVNS. We aimed to test the effects of cervical nVNS on cortical responses and Gamma Band Oscillations (GBO) induced by painful laser stimuli delivered to the right and left forehead and hands in a cohort of twenty-eight migraine patients. Patients were selected and randomly assigned to active or sham nVNS stimulation on the neck bilaterally with GammaCore®. We recorded Laser evoked responses (LEPs) by stimulating bilaterally the hand and the forehead, in basal condition, during nVNS and sham stimulation and two minutes after stimulation.

We observed a significant reduction of amplitude of the P2 wave from the forehead during active nVNS, as compared to basal and sham stimulation. However LEPs amplitude immediately recovered after stimulation session. The sham device induced an evident reduction of LEP amplitude, though not significant in respect to active device. Active nVNS seems to have a transitory effect on the transmission of trigeminal pain, which can contribute to induce changes of trigeminal function improving migraine.

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Impairment of the endogenous pain-inhibitory control in patients with pain due to EhlerDanlos disease

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We aimed at verifying whether widespread pain due to Ehlers Danlos syndrome, hypermobile type (hEDS) is associated with deficit of the endogenous pain-inhibitory control. In 22 patients with pain due to hEDS and in 22 healthy participants, matched for age and sex, we investigated function of the endogenous pain-inhibitory control using the Conditioned Pain Modulation (CPM) protocol. CPM protocol consisted of two heat painful stimuli, i.e. a test stimulus and a conditioning stimulus; no change or an increase in the test stimulus rating during conditioning stimulation is compatible with a deficit in the descending inhibitory pain control. In healthy participants the CPM protocol showed that the test stimulus rating was significantly reduced during conditioning ($P < 0.01$); conversely in patients with pain due to hEDS the test stimulus rating increased during conditioning ($P < 0.001$). We did not find any correlation between CPM variables and duration of disease, pain intensity and the widespread pain index. Our study showing that patients with pain due to hEDS have abnormal CPM protocol suggests that in this condition pain is associated with a deficit of the endogenous pain-inhibitory control. This finding is probably relevant to pharmacological treatment of pain due to hEDS, supporting the use of antidepressants.

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The incidental finding of elevated anti GQ1B antibodies in a patient with selective small fiber neuropathy

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Small fiber neuropathy occurs in several autoimmune diseases and autoantibodies against neuronal proteins may play a role in SFN pathophysiology.^{1–2} Antigangliosides antibodies anti-GQ1b have not previously associated to SFN. We describe a 45-year-old woman complaining of a two-year history of tingling and/or burning pain sensation in the arms and legs, with nocturnal exacerbation. The anamnesis revealed a ten-year history of an autoimmune disorder including HLA-B27 negative psoriatic arthritis, complement C3 deficiency membrano-proliferative glomerulonephritis and sicca syndrome. Neurological examination did not disclose ophthalmoplegia, signs of central nervous dysfunctions or peripheral large nerve fiber abnormalities. Laboratory screening disclosed IgM antiganglioside antibodies anti-GQ1b (high titer) and anti-GD1b (low titer). Skin biopsies from distal leg and thigh revealed decreased epidermal nerve fiber density, whereas autonomic innervation of dermal annexes was preserved. Motor and sensory nerve conduction studies were normal excluding a large nerve fiber involvement. SFN likely explained the sensory dysfunctions complained of by the patient. A trial with adalimumab resulted in long-term pain relief. This is the first report of SFN associated with antigangliosides antibodies anti-GQ1b. Further studies will clarify a possible pathogenetic role of these antibodies in SFN. Moreover, their recognition of in SFN may be an indicator of patients who would potentially benefit from immunotherapy.

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