

Francesca Galeotti
Andrea Truini
Giorgio Cruccu

Neurophysiological assessment of craniofacial pain

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F. Galeotti · A. Truini · G. Cruccu (✉)
Department of Neurological Sciences,
University of Rome “La Sapienza”,
Viale Università 30,
I-00185 Rome, Italy
e-mail: cruccu@uniroma1.it
Tel.: +39-06-49694209
Fax: +39-06-49914758

Abstract This review deals with the diagnostic usefulness of neurophysiological testing in patients with craniofacial pain.

Neurophysiological testing of trigeminal nerve function relies on trigeminal reflexes and laser-evoked potentials (LEPs). This review briefly describes the physiology of trigeminal reflexes and LEPs, reports normal values and highlights the neurophysiological abnormalities in the main clinical conditions.

Key words Trigeminal nerve · Pain · Trigeminal reflexes · Laser-evoked potentials

Introduction

Neuropathic facial pain syndromes, such as trigeminal neuralgia, postherpetic neuralgia, trigeminal neuropathy and Wallenberg syndrome, are due to a peripheral or central lesion of the trigeminal system [1–3]. A trigeminal system dysfunction (with no evidence of lesion) may contribute also to several craniofacial pains of uncertain origins (temporomandibular disorders or persistent idiopathic facial pain) [1–3].

The trigeminal nerve and the trigeminal nuclei may be involved by a wide variety of lesions. Trigeminal lesions usually produce sensory disturbances (sensory loss, paraesthesia and possibly neuropathic pain) occasionally accompanied by motor dysfunction (i.e., weakness of the masticatory

muscles). Because neuroradiological studies sometimes yield negative findings in patients with trigeminal symptoms [1], or may occasionally show clinically irrelevant abnormalities, neurophysiological tests have gained wide acceptance as a method for assessing the functions and dysfunctions of the trigeminal nerve and nuclei [4, 5].

In this review we discuss the clinical applications of neurophysiological testing of the trigeminal nerve.

Neurophysiological testing of the trigeminal nerve

For several reasons, standard neurophysiological techniques (such as cortical evoked potentials and nerve conduction studies) cannot be applied in the trigeminal territory. Not

only are the nerve branches in a deep position but the superficial nerve terminals are very short and intermingle with those of the facial motor nerves. Stimulation to the trigeminal area unavoidably elicits several reflex responses that contaminate or hide the genuine neural signals [6–8].

A study in curarised subjects showed that trigeminal scalp potentials elicited by surface electrical stimuli delivered to the face consist only of myogenic artefacts [9]. The only reliable trigeminal evoked potentials are the very early waves of the scalp potentials – described by Leandri and associates [10] – obtained by needle stimulation of the infraorbital nerve. Although this method is excellent for guiding thermal rhizotomy, it has the limitation of being invasive and technically difficult.

For these reasons, neurophysiological testing of the trigeminal territory relies mainly on trigeminal reflexes (blink reflex, masseter inhibitory reflex and jaw jerk) and on trigeminal laser-evoked potentials [1–3, 5].

Blink reflex

The blink reflex is the surface electromyographic (EMG) recording from the orbicularis oculi muscle of the reflex evoked by electrical stimulation of the supraorbital region. It comprises two responses: the first or early reflex, R1, is a short EMG response (not visible clinically) that occurs at a 10 ms latency ipsilateral to the side of the stimulation. The second or late response, R2, has a 30-ms latency, is bilateral and more prolonged.

The afferent impulses for the R1 response of the blink reflex are conducted by large myelinated fibres (A β fibres) [11, 12] and relayed to the facial motoneurons through an oligosynaptic circuit. The whole circuit lies in the pons. The afferent impulses for the R2 response of the blink reflex are also conducted by A β fibres but are relayed to the facial motoneurons through a polysynaptic circuit, lying in the dorsolateral region of the pons and medulla. The brainstem interneurons that mediate blinking are extremely sensitive to sensory inputs of all types.

In clinical neurological practice, R1 is studied to investigate the afferents from the supraorbital region and the pons. R1 is a stable response and is uninfluenced by suprasegmental dysfunction, such as supratentorial lesions, disorders of consciousness and cognitive factors [6]. The R1 response is regarded as delayed if its latency exceeds 13.0 ms; a latency difference between the two sides exceeding 1.5 ms is also abnormal [13].

Possibly because it relays through a large number of synapses, R2 is a relatively unstable response and is strongly modulated by suprasegmental influences. Although R2 is less reliable than R1 in disclosing extra-axial lesions, it is crucial in diagnosing medullary lesions. The simultaneous

recording of the bilateral R2 is useful in differentiating an afferent (trigeminal) and efferent (facial) pattern of lesion.

Masseter inhibitory reflex

Electrical stimulation of the infraorbital and mental nerves evokes a reflex inhibition of the jaw-closing muscles, the masseter (or temporalis) inhibitory reflex. On surface EMG recordings from contracted jaw-closers, this reflex inhibition appears as an early and a late phase of suppression (or silent periods, SP1 and SP2). Most investigators consider that SP1 and SP2 are both mediated by A β fibres [12, 14]. The short-latency SP1 response (11–12 ms latency) is probably mediated by a single inhibitory interneuron that is located close to the ipsilateral trigeminal motor nucleus and projects onto jaw-closing motoneurons bilaterally. The whole circuit lies in the mid-pons. A latency difference between the ipsilateral and contralateral responses exceeding 2 ms is considered abnormal [1, 6]. The SP2 response (40–50 ms latency) is mediated by a polysynaptic chain of excitatory interneurons, probably located in the medullary lateral reticular formation; the last interneuron of the chain is inhibitory and gives rise to ipsilateral and contralateral collaterals that connect with the jaw-closing motoneurons in the masticatory nuclei [15].

Jaw jerk

Taps to the chin evoke a jaw jerk, also termed jaw reflex, mandibular reflex or masseter reflex. The reflex afferents are Ia fibres from muscle spindles of the jaw-closing muscles. Unique among the primary sensory neurons, these afferents have their cell body in the central nervous system (the trigeminal mesencephalic nucleus) rather than in the ganglion; short collaterals connect monosynaptically with synergistic jaw-closing motoneurons in the pontine trigeminal motor nucleus; no collaterals cross the midline. Although mechanical stimuli excite receptors on both sides, this anatomical organisation permits disclosure of side-to-side asymmetries. The response recorded from the masseter or temporalis muscles has a 6–8 ms latency and may jitter considerably [1]. Because dental occlusion, position of the mandible and the level of central motoneuronal excitability strongly affect its amplitude and even its latency, the jaw jerk is often absent bilaterally in elderly people. Although the jaw jerk is useful only for disclosing unilateral lesions, it is most sensitive to focal extra-axial compressions, probably because it is supplied by a relatively small number of afferents, and pressure damages the largest fibres first [1, 8].

Laser-evoked potentials

Laser-generated radiant heat pulses selectively excite free nerve endings in the superficial skin layers and activate A δ and C nociceptors [16]. Low-intensity pulses directed to the hairy skin evoke pinprick sensations and brain potentials (LEPs), both related to the activation of type II AMH mechanothermal nociceptors; the afferent volley is conducted along small myelinated (A δ) primary sensory neurons, and relayed to spinothalamic neurons and brain [17]. The main LEP signal that is usually measured in a clinical setting is a widespread negative-positive complex (N2P2) that reaches its maximum amplitude at the vertex [18]. This complex is mostly generated by the anterior cingulate gyrus, with a possible contribution from the bilateral insular regions [19, 20]. LEPs are widely used in patients with peripheral and central nervous system lesions [21–23], and they have been acknowledged by the European Federation of Neurological Societies as the most reliable laboratory tool for assessing pain pathways [5].

Because of the short conduction distance and high receptor density, the trigeminal territory is particularly advantageous for LEP recording. Trigeminal LEPs are of higher amplitude and are recorded more easily than LEPs after limb stimulation [24].

Findings in facial neuropathic pain

In all patients with trigeminal pain secondary to a documented disease trigeminal reflexes objectively document dysfunction, even when pain is unaccompanied by other signs [8, 25]. Reflex responses are more extensively and markedly affected in patients with constant pain than in

those with paroxysmal pain. This finding agrees with the classic notion that a dysfunction of a few fibres provokes paroxysmal pain, whereas severe damage does not.

Useful pathophysiologic information in facial pain syndromes also comes from trigeminal LEPs, currently the most reliable and agreed method of investigating small fibre function [5, 25, 26].

Trigeminal neuralgia

Trigeminal neuralgia (TN) may be classified as *classical* TN (with no apparent cause other than vascular compression) and *symptomatic* TN (pain indistinguishable from that of *classical* TN but caused by a demonstrable structural lesion other than vascular compression) [27]. TN is a rare disease and secondary TN accounts only for about 1%–2% of cases [28]. Even though vascular compression remains the most studied and supported hypothesis for *classical* TN, several factors may contribute to its development. Indirect evidence that vascular compression may not be the only cause is that microvascular decompression often fails to provide complete and persistent pain relief.

In patients with *classical* TN, trigeminal reflex testing yields normal responses or, occasionally, mild reflex abnormalities [14, 25, 29, 30]. Conversely, in patients with symptomatic TN, trigeminal reflex testing constantly discloses abnormal responses [1, 30]. Posterior fossa tumours producing mechanical damage to the proximal portion of the trigeminal root, or a demyelinating plaque affecting the intrapontine presynaptic primary afferents near the root entry zone in patients with multiple sclerosis, typically lead to abnormalities of all responses [25, 30, 31] (Fig. 1). The short-latency, oligosynaptic reflexes

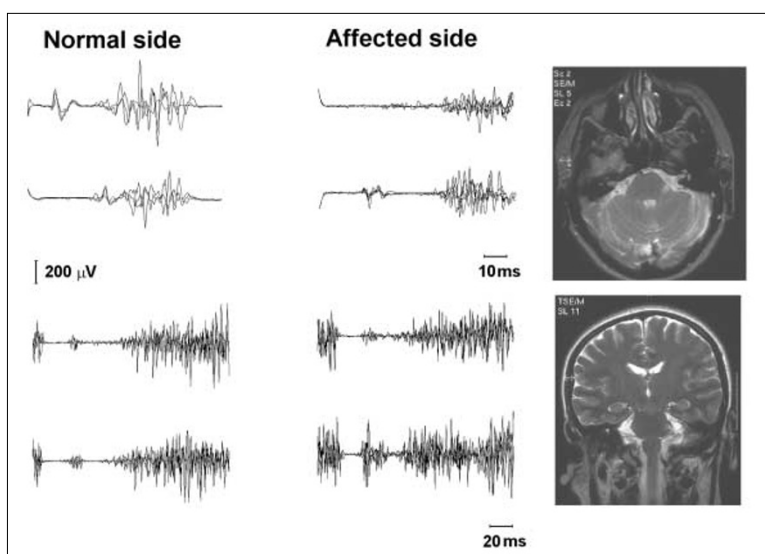


Fig. 1 MRI and neurophysiological findings in a patient with trigeminal neuralgia due to a demyelinating plaque in the trigeminal root entry zone. In the right panels: T2-weighted MRI scans showing the small demyelinating lesion in the left pons. In the left panels: blink reflex (upper panel) and masseter inhibitory reflex (lower panel) after stimulation of the normal and affected sides. Three trials superimposed. On the affected side R1 and SP1 were delayed

(R1, SP1 and JJ) are more sensitive than the long-latency, polysynaptic reflexes (R2 and SP2) in detecting abnormalities in symptomatic TN [14, 29, 32, 33].

In patients with TN who have undergone trigeminal reflex testing, LEPs can often provide useful complementary diagnostic information. Patients with symptomatic TN and about 50% of those with classical TN have abnormal LEPs [34]. Hence LEPs may indicate trigeminal dysfunction also in patients with normal trigeminal reflexes and no evidence of structural lesions involving the trigeminal system. Possibly because LEPs are mediated by a small number of afferents, they are diagnostically more sensitive than trigeminal reflex testing. Obviously the finding of normal LEPs by no means excludes the diagnosis of idiopathic TN, which relies only on the clinical description of the paroxysmal pain [8].

Trigeminal neuropathy

Involvement of trigeminal nerve branches or roots

For diagnosing extra-axial trigeminal nerve lesions, the short latency responses (R1 of the blink reflex, SP1 of the masseter inhibitory reflex and jaw jerk) are far more sensitive than the long-latency responses (R2 of the blink reflex and SP2 of the masseter inhibitory reflex). One reason is that they are supplied by fewer reflex afferents. In addition, they exhibit less variability and have a smaller normal range than do polysynaptic responses [1].

One way of localising the site of the lesion is to study trigeminal reflexes evoked from all three divisions [1, 6, 8]. Abnormalities in all divisions of the trigeminal nerve indicate a trigeminal root lesion in the middle or posterior cranial fossa (e.g., ponto-cerebellar angle tumours). An abnormality in one division alone suggests a more peripherally located lesion. The blink reflex can be abnormal in lesions of the supraorbital nerve branch or, more proximally, in lesions of the ophthalmic division of the trigeminal nerve. For example, postherpetic neuralgia (PHN) affecting the first division of the trigeminal nerve typically delays or abolishes the blink reflex R1 while leaving the masseter inhibitory reflex and jaw jerk unchanged [25]. In PHN, LEPs constantly disclose damage to small-size trigeminal afferents [23].

In lesions of the infraorbital nerve or, more proximal, of the maxillary root, infraorbital stimulation may elicit an abnormal masseter inhibitory reflex. Damage to the mental nerve or the trigeminal mandibular root may also cause masseter inhibitory reflex abnormalities. In many patients, the only response affected is the jaw jerk, because Ia afferents are extremely sensitive to compression. An abnormal jaw-jerk caused by dental malocclusion should first be

excluded by testing whether the reflex abnormality disappears in various mandibular positions or during clenching [35, 36]. If not, the extracranial and intracranial pathways must be carefully examined with magnetic resonance imaging (MRI).

Bone tumours may affect the trigeminal nerve branches as they exit from the cranial cavity or maxillary bones. Some tumours may involve the Gasserian ganglia, thereby affecting the three trigeminal branches. Other conditions, such as the so-called numb-chin syndrome, damage the mental nerve alone, either at the base of the skull or at the mandible [37]. Iatrogenic damage after dental or maxillo-facial surgery are frequent causes of maxillary and mandibular nerve involvement. A previous study, which investigated LEPs and masseter inhibitory reflex in a patient with a iatrogenic lesion of the inferior alveolar nerve, suggested that LEPs after perioral stimulation are diagnostically more sensitive than the masseter inhibitory reflex [24].

Involvement of the Gasserian ganglion

Neurophysiological studies can differentiate a dysfunction involving the Gasserian ganglia neurons from a dysfunction involving the trigeminal branches. A lesion involving the third trigeminal branch is usually demonstrated by finding neurophysiological deficits in reflexes relayed through afferents from that specific branch. If the lesion lies in the neurons of the Gasserian ganglia, but not in the nerve fibres, neurophysiological testing will still show abnormalities in reflexes elicited by the cutaneous afferents carried by the mandibular branch, but the jaw jerk will remain completely normal [38], because the cell bodies of neurons subserving the reflex are located not in the Gasserian ganglia but in the mesencephalic nucleus.

A pain syndrome that can cause abnormal cutaneous trigeminal reflexes but spare the jaw jerk is isolated symmetrical trigeminal neuropathy (ISTN). Trigeminal nerve dysfunction caused by peripheral neuropathies is usually clinically unimportant and rarely painful [39]. ISTN (i.e., not associated with systemic neuropathy) is a rare clinical condition [40]. Several studies described an association between chronic trigeminal sensory neuropathy and connective tissue diseases [41]. In patients with ISTN, sensory loss develops gradually; first, it is usually localised in the perioral region on one side and then extends, over a period of months or a few years, to the other side, the intraoral mucosa and the tongue, and subsequently the whole face. Pain is a relatively common symptom; it is more often constant, and usually described as burning or aching [40, 41]. In the earlier stage of disease, whereas the masseter inhibitory reflex may be abnormal, the blink reflex may be normal. In the later stage of disease all brainstem reflexes are markedly abnormal, often com-

pletely absent. Only the jaw jerk is constantly normal. A unique case report described LEP recordings in a patient with ISTN. In this patient, LEPs mediated by $A\delta$ fibres were absent, whereas C-fibre-related LEPs were normal [39] (Fig. 2). The neurophysiological findings in this patient receive support from supraorbital biopsy studies, indicating that this neuropathy predominantly affects the $A\beta$ afferents and spares C fibres. This is an unexpected

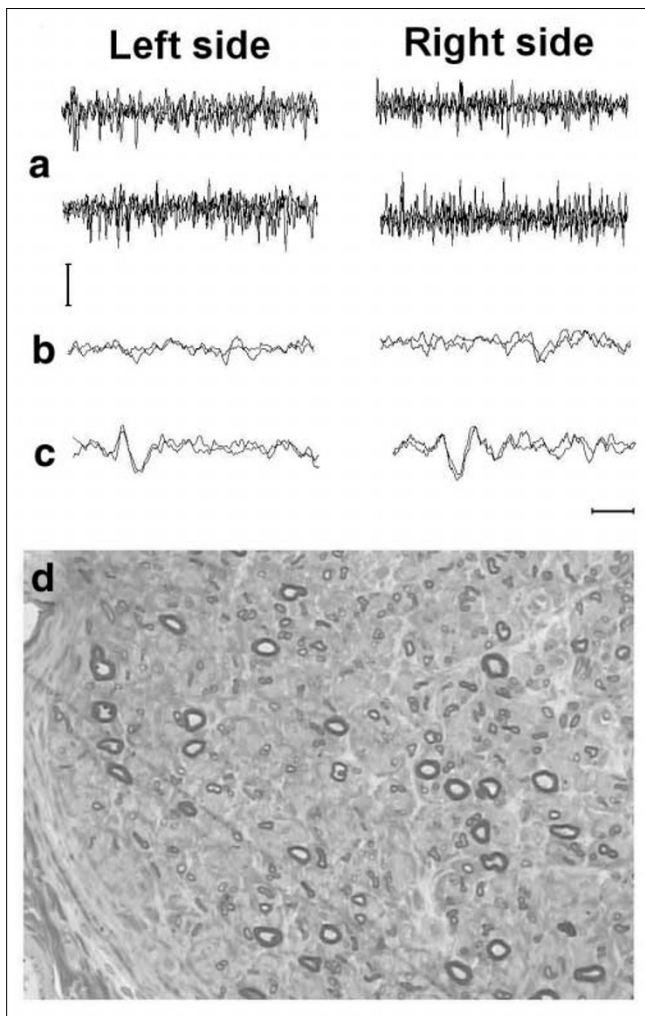


Fig. 2 Histological and neurophysiological findings in a patient with isolated symmetrical trigeminal neuropathy. **a** Electrical stimulation of the infraorbital nerve failed to evoke a masseter inhibitory reflex during voluntary contraction. Three trials superimposed. **b** High-intensity laser pulses eliciting pin-prick sensation failed to evoke an $A\delta$ -fiber-related LEP. Two averages of 10 trials each superimposed. **c** Laser pulses set for C-fiber activation elicited warm sensations and C-fiber-related LEPs. Two averages of 10 trials each superimposed. Stimulation of left and right sides. Vertical calibration: 200 μ V in **a**; and 10 μ V in **b** and **c**. Horizontal calibration: 20 ms for **a**, 200 ms for **b** and **c**. **d** Optic microscopy of a supraorbital nerve fascicle shows severe loss of myelinated fibres (magnification 40x)

finding because these patients typically complain of constant burning pain, a symptom that in limb pains is usually attributed to C-fibre deafferentation [42].

Intra-axial lesions

Because the trigeminal sensory nuclei and reflex circuits extend from the mesencephalon to the spinal cord, they are rarely spared in vascular or compressive brain stem syndromes [1, 2, 6, 8,]. Peripheral lesions are more likely to affect both blink reflex components to a similar degree, or affect R1 more clearly than R2. Conversely, intra-axial lesions often affect R1 or R2 separately [1, 2, 6, 8].

The finding of an abnormal jaw-jerk with normal masseter EMG features may disclose a midbrain lesion involving structures adjacent to the aqueduct [6, 33]. Combined features of denervation and reinnervation in masseter EMG point to impairment of the trigeminal motor nucleus in the dorsolateral region of the mid-pons [6, 8].

Pontine lesions, regardless of their aetiology, may produce various trigeminal reflex abnormalities, according to the precise site of the lesion. Very discrete lesions limited to the upper pons may cause a delay in, or absence of, the R1 component without accompanying R2 response abnormalities [32]. In general, ventral lesions involving the trigeminal afferents before they divide towards their respective circuits (R1 and R2) may induce abnormalities of all responses.

Wallenberg syndrome is provoked by infarction of the lateral tegmentum of the medulla due to thrombosis of the posterior inferior cerebellar artery or one of its branches supplying the lower portion of the brainstem. Wallenberg syndrome manifests with thermal-pain hypoaesthesia on the ipsilateral face and contralateral body, ipsilateral Bernard-Horner syndrome, dysphagia, dysphonia, dysarthria and ipsilateral, contralateral or bilateral ataxia.

Wallenberg syndrome has an overall good prognosis. Residual sensory disturbances are frequent. They include thermal-pain hypoaesthesia and pain on the face and body. Pain is both spontaneous and provoked (generally allodynia to light mechanical stimuli) [39]. Pain correlates with the degree of clinical sensory loss but not with the size of infarction seen on MRI. Studies testing brainstem reflexes in patients with Wallenberg syndrome have described various abnormalities [15, 43]; the neurophysiological heterogeneity of this syndrome correlates with the anatomical extension of the ischaemic area. The most common finding is an abnormality of the R2 blink reflex, whereas R1 is spared [1, 44–46] (Fig. 3). This abnormal blink-reflex pattern reflects the block of afferent impulses travelling through the descending trigeminal spinal tract. Stimulation of the intact side elicits bilaterally normal responses. A study that correlated clinical, radiological and neurophysiological findings in patients with Wallenberg syndrome [47] suggested that facial pain after medullary infarction is due to lesions of the lower spinal

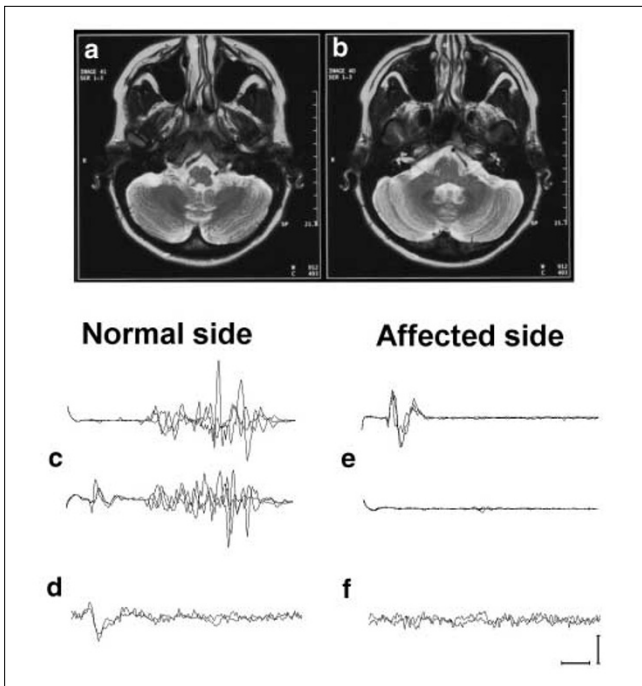


Fig. 3 MRI and neurophysiological findings in a patient with neuropathic pain localised in the supraorbital region due to Wallenberg syndrome. **a, b** T2-weighted MRI scans showed a small infarction in the left dorsal-lateral medulla. **c** Blink reflex recordings showing the R2 absence after stimulation of the affected side. Three trials superimposed. **d** Laser stimuli directed to the affected region failed to evoke LEPs, whereas those directed to the contralateral face evoked normal A δ -fibre-related LEPs. Two averages of 10 trials each superimposed. Verical calibration: 200 μ V for **c** and **e**, 20 μ V for **d** and **f**. Horizontal calibration: 10 ms for **c** and **e**, 200 ms for **d** and **e**

trigeminal tract (axons of primary afferent neurons), leading to deafferentation of spinal trigeminal nucleus neurons. Patients whose MRI showed infarcts in the upper or middle portion of the medulla invariably had abnormal masseter inhibitory reflex responses, suggesting that afferent fibres mediating the masseter inhibitory reflex actually descend as far as the upper portion of the medulla [15]. Previous studies investigating LEPs in patients with neuropathic pain due to a lateral medullary infarction reported the abnormality of both A-related and C-related LEPs [24, 39]. Further studies are needed to correlate blink reflex and LEP abnormalities and the presence of pain and neurophysiological abnormalities.

Findings in facial pain of uncertain aetiology

Burning mouth

The International Association for the Study of Pain (IASP) definition of burning mouth syndrome (BMS) is

“glossodynia and sore mouth, also known as burning tongue or oral dysaesthesias, as burning pain in the tongue or other oral mucous membranes”. Several studies used quantitative sensory testing, electrophysiological methods and functional neuroimaging to assess trigeminal sensory function in patients with BMS: some investigators demonstrated abnormalities of trigeminal pathway function, thus indicating a possible neuropathic aetiology of BMS [48, 49]. In a recent study, Lauria and coworkers [50] investigated innervation of the epithelium of the tongue in superficial biopsies from 12 patients who had a 6-month history of clinically definite BMS and healthy persons. The epithelial nerve-fibre density was significantly lower in patients than in controls, with a trend towards a correlation with the duration of symptoms. This finding led the investigators to conclude that BMS is caused by a trigeminal small-fibre sensory neuropathy. The selective involvement of small fibres seems to be confirmed by our unpublished observation that blink reflex and the masseter inhibitory reflex after tongue stimulation (both mediated by A β fibres) are invariably normal in patients with BMS. We have seen only two patients, who had abnormal responses and presented with clinical symptoms resembling BMS, in whom the full clinical manifestations of ISTN ultimately developed.

Atypical facial pain

Atypical facial pain (AFP) is a diagnosis of exclusion used to describe a chronic facial pain that has none of the characteristics of cranial neuralgias and no identifiable associated lesions affecting the trigeminal system or the facial tissues. This diagnosis is not accepted by the IASP and no agreement has been reached on diagnostic criteria. In a study investigating the blink reflex and jaw jerk in 17 patients with atypical facial pain who also underwent MRI, Jaaskelainen and coworkers [51] identified, trigeminal dysfunctions that had no corresponding MRI changes. They therefore proposed that atypical facial pain should be considered as a neuropathic pain.

Temporomandibular disorders

Temporomandibular disorder or dysfunction (TMD) is a condition characterised by spontaneous pain and tenderness in the masticatory muscles and temporomandibular joint, and other symptoms related to the masticatory apparatus. The cause of the disease is still controversial. Most investigators agree on a multifactorial origin, the key

mechanisms being muscle hyperactivity and changes in the peripheral input from periodontal mechanoreceptors and muscle spindles.

Reports over the years have described an array of neurophysiological abnormalities in patients with TMD. The conflicting results of the different studies probably reflect the wide intra-individual variability and various technical problems (see references in [52] and [53]). The masseter inhibitory reflex recovery cycle overcomes some of these technical problems by measuring the excitability of the interneurons alone. The masseter inhibitory reflex recovers normally in patients with TMD. Hence the lack of facilitation in these patients' responses excludes central hyperactivity as the primary cause of their masticatory dysfunction and pain [36].

Testing of the jaw jerk and masseter silent periods currently has uncertain diagnostic value in TMD and may yield a false-positive diagnosis. In clinical practice the finding of a jaw-jerk asymmetry in a given patient by no means leads to a diagnosis of TMD. Jaw-jerk amplitudes and side asymmetries vary widely even in normal subjects, and the jaw-jerk can be unilaterally absent in patients with TMD. A useful diagnostic point to remember is that in a patient with no other trigeminal abnormality, a unilaterally absent jaw-jerk can be caused by a functional impairment. It does not necessarily imply damage to the nerve fibres or brainstem, and should warrant – besides an MRI study – stomatognathic investigations [36].

In patients with TMD, trigeminal LEPs are significantly attenuated [54].

Findings in headaches

Several studies have dealt with trigeminal reflex and trigeminal LEPs testing in patients with headache. Reports over the years have described an array of neurophysiological abnormalities [1, 55, 56]. Some studies reported that the R2 blink reflex is delayed and reduced in amplitude in migraine [57], however others did not con-

firm these findings [58]. In cluster headache the blink reflex has been found to be suppressed on the painful side [59], whereas the corneal reflex had a lowered threshold [60]. In patients with chronic paroxysmal hemicrania or hemicrania continua the blink reflex is normal; in chronic paroxysmal hemicrania the corneal reflex threshold, however, is significantly reduced bilaterally [61].

The SP2 recorded from the temporalis muscle (or ES2 as commonly used in the literature on headache) was found to be shortened in tension-type headache, though not in migraine [62]. Several studies confirmed this finding [63, 64] while others did not [65, 66]. The shortening of ES2 is probably related to the duration of illness, thus being more common in patients suffering from chronic rather than episodic headache [65, 66]. A study measuring ES1 and ES2 and their recovery cycle in 20 patients with migraine and with tension-type headache found that whereas latency and duration of all responses did not differ from control values, the ES2 recovery cycle was significantly slowed in patients with tension-type headache [58].

A previous study [56] reported a reduced habituation of LEP, possibly reflecting an abnormal excitability of the cortical areas involved in pain processing in patients with migraine.

Because studies investigating trigeminal electrophysiological testing in headache aimed at understanding the pathophysiology of headache rather than assessing the diagnostic value of these tests, the diagnostic specificity and sensitivity of trigeminal reflexes and LEPs in primary headaches remain unclear [56, 67].

It is worth mentioning that several studies reported that trigeminal autonomic cephalalgias, such as cluster headache and SUNCT, may be due to posterior fossa lesions or brainstem infarction, involving the trigeminal system [68, 69]. While in primary headaches trigeminal reflex and LEP abnormalities may be documented only by statistical analysis in large series of patients, in the rare cases of headaches secondary to trigeminal sensory pathway lesions, trigeminal reflexes and LEPs constantly show abnormalities [1].

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