Clinical Neurophysiology 117 (2006) 1821–1825

www.elsevier.com/locate/clinph

Trigeminal sensory pathway function in patients with SUNCT

A. Truini [a,b,*], P. Barbanti [b], F. Galeotti [a,b], M. Leandri [c], G. Cruccu [a]

[a] Department of Neurological Sciences, University 'La Sapienza', Rome, Italy
[b] Department of Neurological, Sensorial and Motor Sciences, IRCCS San Raffaele, Rome, Italy
[c] Interuniversity Centre for Pain Neurophysiology and Department of Oncology, Biology and Genetics, University of Genova, Genova, Italy

Accepted 18 April 2006

Abstract

Objective: Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is a rare primary headache whose origins are unclear. To seek information on its pathophysiology, we studied the trigeminal Aβ and Aδ pathways by recording trigeminal reflexes and laser evoked potentials (LEPs) in patients with SUNCT.

Methods: Trigeminal reflexes and LEPs were recorded in 11 consecutive patients. Ten patients had neuroimaging evidence documenting idiopathic SUNCT and one had a posterior fossa tumour that compressed the trigeminal nerve thus causing symptomatic SUNCT.

Results: Whereas the patients with idiopathic SUNCT had normal trigeminal reflex and LEP responses, the patient with symptomatic SUNCT had abnormal responses.

Conclusions: Our neurophysiological findings show that idiopathic SUNCT spares the trigeminal sensory pathways whereas symptomatic SUNCT does not.

Significance: Neurophysiological testing can easily differentiate the idiopathic and symptomatic forms of SUNCT. It also suggests that the two forms are pathophysiologically distinct entities.

Keywords: SUNCT; Trigeminal system; Trigeminal reflexes; Laser evoked potentials

1. Introduction

SUNCT—short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing—is a rare form of headache (Headache Classification Subcommittee of the International Headache Society, 2004). Pain involves the orbital and periorbital areas, it is short lasting, stabbing or electric shock-like in quality, and varies in frequency from one attack per day to 30 attacks per hour (Goadsby and Lipton, 1997; Headache Classification Subcommittee of the International Headache Society, 2004). Attacks are typically accompanied by autonomic symptoms including ipsilateral conjunctival injection, lacrimation and nasal congestion or rhinorrhea (Goadsby and Lipton, 1997; Headache Classification Subcommittee of the International Headache Society, 2004).

The clinical features and functional imaging findings in SUNCT syndrome both suggest hypothalamic involvement (Goadsby and Lipton, 1997; May et al., 1999). However, because pain strikes the orbital and periorbital areas and one report showed that surgical decompression of the trigeminal nerve provides effective relief (Sprenger et al., 2005) some investigators hypothesized that the clinical manifestations of SUNCT reflect trigeminal sensory pathways dysfunction along with central nervous system involvement (Sprenger et al., 2005). Trigeminal dysfunction in SUNCT receives support from the clinical observation that SUNCT and trigeminal neuralgia, a pain disorder initiated by trigeminal primary afferent dysfunction (Cruccu et al., 2001), share many clinical features (Benoliel and Sharav, 1998; Goadsby et al., 2001).

The trigeminal sensory pathways are best assessed by recording trigeminal reflexes, and laser evoked potentials

* Corresponding author. Address: Department of Neurological Sciences, La Sapienza University, Viale Università 30, 00185 Roma, Italy. Tel.: +39 06 49914196; fax: +39 06 49914758.
E-mail address: andrea.truini@uniroma1.it (A. Truini).

1388-2457/$30.00
doi:10.1016/j.clinph.2006.04.007

(LEPs) (Cruccu and Deuschl, 2000; Teerijoki-Oksa et al., 2003; Teerijoki-Oksa et al., 2004; Truini et al., 2005). Trigeminal reflexes comprise a series of reflex responses that assess the function of large myelinated afferents (Aβ afferents) from all trigeminal territories, as well as the central circuits in the pons and medulla (Cruccu and Deuschl, 2000; Valls-Solé, 2005). LEPs are considered the best tool for assessing nociceptive pathway function (Bromm and Lorenz, 1998; Truini et al., 2005). Laser-generated radiant heat pulses selectively activate Aδ and C mechanothermal nociceptors, and by activating type II AMH mechanothermal nociceptors evoke pinprick sensations and brain potentials (Truini et al., 2005).

Although trigeminal reflex and LEP recordings disclose an array of neurophysiological abnormalities in patients with primary headache, data are lacking to confirm their diagnostic sensitivity and specificity (Sandrini et al., 2004; De Tommaso et al., 2005). To our knowledge, trigeminal function has never been systematically assessed in patients with SUNCT. Nor is it clear whether neurophysiological testing will distinguish the idiopathic and symptomatic forms of SUNCT.

To seek information on trigeminal sensory pathway function in the pathophysiology of SUNCT and find out whether neurophysiologic testing could distinguish the idiopathic and symptomatic forms of this rare headache, we studied the trigeminal Aβ and Aδ pathways by recording trigeminal reflexes and LEPs in patients with SUNCT.

2. Methods

Trigeminal reflexes and LEPs were recorded in 11 consecutive patients with SUNCT (4 women, 7 men), aged 28–70 years (mean 47 years). Participants gave their informed written consent and the experimental protocol was approved by the local ethical committee. Of the 11 patients, 10 fulfilled the diagnostic criteria for SUNCT (Goadsby and Lipton, 1997; Headache Classification Subcommittee of the International Headache Society, 2004) (Table 1), and 1 patient had atypical symptoms. This patient was a 56-year-old woman with right-sided facial pain involving the first and the second trigeminal divisions. She described bursts of shooting, electric-shock-like pain that lasted seconds. Pain attacks were accompanied by intense conjunctival injection and tearing of the right eye. This patient had up to 10 attacks per day. Neurological examination was normal in all patients. On magnetic resonance imaging (MRI) scans 10 patients had normal findings (idiopathic SUNCT), and the patient with atypical SUNCT pain had an MRI-documented cerebello-pontine angle tumour compressing the proximal portion of the trigeminal nerve (symptomatic SUNCT).

Neurophysiological testing of the trigeminal reflexes included the early and late blink reflex (R1 and R2) after electrical stimulation of the supraorbital nerve and early and late masseter inhibitory reflex (SP1 and SP2) after electrical stimulation of the mental nerve. Evaluation methods adhered to those indicated by the International Federation of Clinical Neurophysiology (IFCN) (Deuschl and Eisen, 1999). The blink reflex was evoked by electrical stimulation (0.1 ms, 15–40 mA) of the supraorbital nerve through surface electrodes. EMG signals were recorded from the orbicularis oculi through surface electrodes. Latency and duration of R1 and direct and crossed R2 responses after stimulation of each side were measured. The masseter inhibitory reflex was evoked by electrical stimulation (0.1 ms, 15–45 mA) of the mental nerve through surface electrodes, while the subjects were instructed to clench the teeth at maximum strength with the aid of auditory feedback. EMG signals were recorded through surface electrodes. Latency and duration of direct SP1 and crossed SP2 responses after stimulation of each side were measured. To study LEPs we used a previously reported technique (Truini et al., 2005); using a CO_2-laser stimulator we delivered brief radiant heat pulses (1.5–15 W, 10 ms, 2.5 mm beam diameter) to the supraorbital (V1) and perioral (V2 and V3) regions. Stimulus intensity was set at twice the perceptive threshold; LEPs were recorded through surface electrodes from the vertex (Cz) referenced to linked earlobes (A1–A2); electro-oculographic recordings monitored possible eye movements or blinks. We averaged

Table 1
Clinical characteristics of patients with idiopathic SUNCT

Patients	Gender	Age (years)	Frequency (attack per day)	Duration (s)	Side	Tearing	Eye redness	Rhinorrhea	Periodicity
1	M	37	10	10	L	+	+	−	Episodic
2	M	47	15	20	R	−	+	+	Episodic
3	M	65	8	60	R	+	+	−	Episodic
4	M	36	20	30	R	+	+	+	Episodic
5	M	43	10	100	L	+	+	+	Episodic
6	F	70	12	90	L	−	+	−	Episodic
7	M	32	5	120	R	+	+	−	Episodic
8	F	64	4	30	R	+	+	−	Episodic
9	M	28	15	15	L	+	+	−	Episodic
10	F	48	3	45	R	+	+	+	Episodic

R, right side; L, left side; +, present; −, absent.

10–20 artefact-free trials for each site of stimulation and measured latency and amplitude of the main N2–P2 components. Neurophysiological data were compared with the normal ranges previously found in a group of 100 healthy subjects (Cruccu and Deuschl, 2000; Truini et al., 2005). Differences in neurophysiological data between normal and affected sides were analyzed with the paired *t* test. All results are reported as mean ± SD.

3. Results

In patients with idiopathic SUNCT, no significant differences were found in latency or duration of trigeminal reflex responses between sides ($P > 0.20$) (Table 2). Responses from the affected side were within the reported normal range for healthy subjects (Cruccu and Deuschl, 2000). LEPs neither differed between sides ($P > 0.20$) nor came outside the normal range found in a group of 100 healthy subjects (Truini et al., 2005).

Conversely, in the patient with symptomatic SUNCT, trigeminal reflex testing showed a side-asymmetry of the blink reflex R1 (10 ms on the normal side vs 13.9 ms on the affected side) and masseter inhibitory reflex SP1 (11 ms on the normal side vs 14.2 ms on the affected side) (Fig. 1). LEPs were absent after stimulation of the affected supraorbital region, but normal after stimulation of the perioral regions (Fig. 1). This patient underwent surgery and the tumour was partially removed. Histological examination revealed a cholesteatoma. Her pain attacks persisted even after the operation.

4. Discussion

Neurophysiologic investigation of trigeminal sensory pathways in patients with SUNCT disclosed clear differences between the idiopathic and symptomatic forms of this rare headache disorder.

Both the IFCN define and EFNS (European Federation of Neurological Societies) recommend trigeminal reflex testing as the most useful and reliable procedure in the laboratory diagnosis of trigeminal pain (Cruccu et al., 2004; Deuschl and Eisen, 1999; Valls-Solé, 2005). Similarly, the EFNS recommends LEPs as the best tool for assessing the nociceptive Aδ pathway in patients with pain (Cruccu et al., 2004).

Using these procedures we found no trigeminal Aβ and Aδ afferent abnormalities thus suggesting that trigeminal sensory pathway function is spared in patients with idiopathic SUNCT; we support the view that the pathophysiology of SUNCT involves a central nervous system mechanism. Earlier evidence suggesting a central mechanism came from functional neuroimaging studies showing ipsilateral hypothalamic activation (May et al., 1999). The hypothalamus receives direct connections from the trigeminal system and probably modulates the nociceptive and autonomic pathways (Goadsby and Lipton, 1997; May et al., 1999). In SUNCT, a hypothalamic abnormality could therefore lead to trigeminovascular activation (May et al., 1999).

All of our patients with idiopathic SUNCT, like those with idiopathic trigeminal neuralgia (Cruccu and Deuschl, 2000), had normal trigeminal reflexes, and normal LEPs. However, in a previous study investigating LEPs in trigeminal neuralgia we found that 50% of patients with idiopathic trigeminal neuralgia and all of those with symptomatic trigeminal neuralgia had documentable trigeminal nerve dysfunction (Cruccu et al., 2001). Our new neurophysiological findings therefore argue against earlier proposals paralleling SUNCT to trigeminal neuralgia and despite similar clinical features, favour the concept of two separate disease entities (Goadsby et al., 2001).

In our series of patients with SUNCT, only one had a symptomatic form, related to a posterior fossa tumour compressing the trigeminal nerve. Several cases of symptomatic SUNCT have been reported (Goadsby and Lipton, 1997). Symptomatic SUNCT is often associated

Table 2
Trigeminal reflex and laser evoked potential data in 10 patients with idiopathic SUNCT (mean ± SD)

BR latency	Normal side			Affected side		
	R1 (ms)	R2d (ms)	R2c (ms)	R1 (ms)	R2d (ms)	R2c (ms)
	10.9 ± 0.6	33 ± 3.6	34.4 ± 3.9	11 ± 0.7	33.1 ± 3.8	34.3 ± 3.7

MIR latency	SP1		SP2		SP1		SP2	
	Onset (ms)	Duration (ms)	Onset (ms)	Duration (ms)	Onset (ms)	Duration (ms)	Onset (ms)	Duration (ms)
	11.6 ± 0.6	18.7 ± 2.2	46 ± 7.2	42.8 ± 10.1	11.5 ± 0.8	18.6 ± 2.8	46.6 ± 6.6	41.9 ± 9.2

LEPs	PTh (mJ/mm^2)	N latency (ms)	P latency (ms)	Amp (μV)	PTh (mJ/mm^2)	N latency (ms)	P latency (ms)	Amp (μV)
V1	4.7 ± 1.4	156.5 ± 14.1	241.5 ± 19.2	18.8 ± 8.7	4.6 ± 1.6	154.8 ± 14.8	240.3 ± 12.4	17.4 ± 9.6
V2/3	4.6 ± 1	158.8 ± 13.6	245.6 ± 21.8	22.3 ± 8	4.6 ± 1	158.4 ± 12.3	243.1 ± 25.2	21.2 ± 9.4

BR, blink reflex; R2d, direct R2 response; R2c, crossed R2 response; MIR, masseter inhibitory reflex; LEPs, laser evoked potentials; V1, supraorbital region; V2/3, perioral region; PTh, perception threshold; Amp, peak-to-peak.

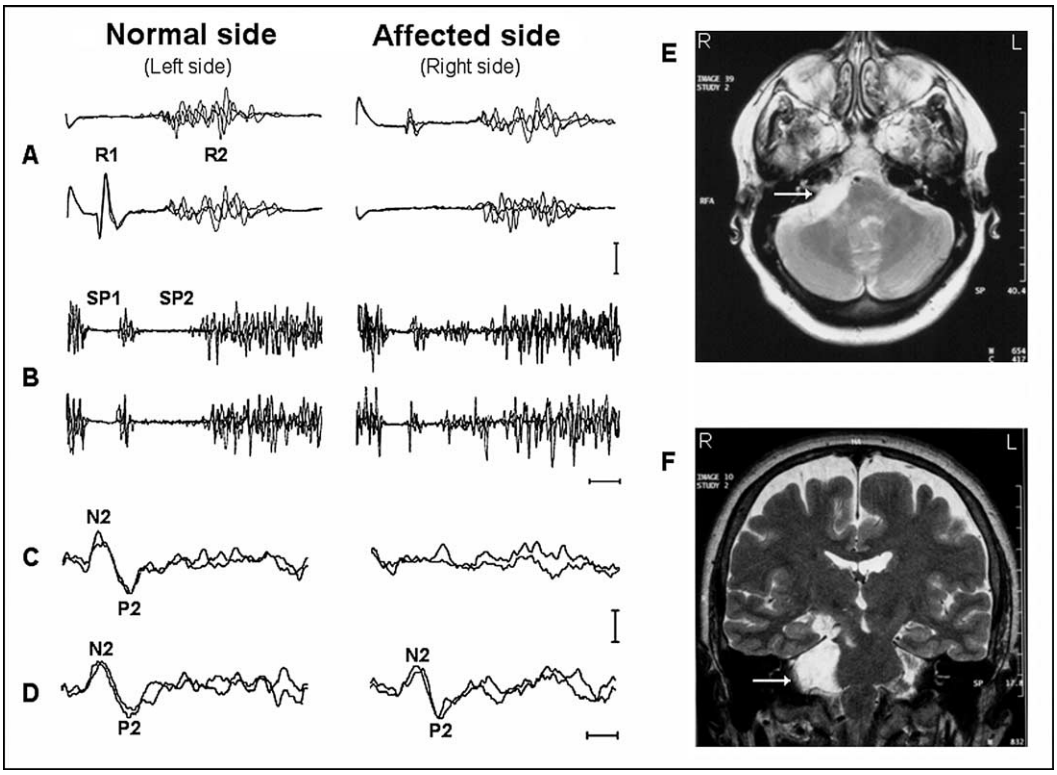

Fig. 1. Trigeminal reflexes, LEPs, and MRI scans in a patient with symptomatic SUNCT. Blink reflex recordings (A) after supraorbital stimulation and masseter inhibitory reflex (B) after mental nerve stimulation. Three trials superimposed. Calibration 10 ms/100 μV for A, 20 ms/100 μV for B. Note the asymmetry of R1 and SP1 latency between normal and affected side. Laser evoked potentials after supraorbital (C) and perioral (D) stimulation. Two averages of ten trials each superimposed. Calibration 100 ms/10 μV. Note the absence of the laser evoked potential after supraorbital stimulation of the affected side. Axial (E) and coronal (F) T2-weighted MRI scans showing the tumour in the right posterior fossa.

with benign lesions compressing the trigeminal nerve in the posterior fossa, suggesting ectopic activity and ephaptic transmission between primary trigeminal afferents (Bussone et al., 1991; Blattler et al., 2003). Patients with symptomatic SUNCT commonly present with atypical clinical manifestations. Pain often differs in duration or localization, and is sometimes accompanied by other symptoms not included in diagnostic criteria of SUNCT (Blattler et al., 2003; Goadsby and Lipton, 1997).

In conclusion, the abnormal trigeminal reflex and LEP responses—indicating trigeminal sensory pathway dysfunction—in patients with symptomatic SUNCT and the normal responses in patients with idiopathic SUNCT strongly suggest that the two forms of SUNCT arise through different pathophysiological mechanisms. Idiopathic SUNCT, as most investigators agree, arises through a central mechanism. Conversely, symptomatic SUNCT can also arise through a peripheral mechanism, for example when benign cerebello-pontine angle lesions compress the trigeminal nerve.

References

Benoliel R, Sharav Y. Trigeminal neuralgia with lacrimation or SUNCT syndrome? Cephalalgia 1998;18:85–90.

Blattler T, Capone Mori A, Boltshauser E, Bassetti C. Symptomatic SUNCT in an eleven-year-old girl. Neurology 2003;60:2012–203.

Bromm B, Lorenz J. Neurophysiological evaluation of pain. Electroencephalogr Clin Neurophysiol 1998;107:227–53.

Bussone G, Leone M, Dalla Volta G, Strada L, Gasparotti R, Di Monda V. Short-lasting unilateral neuralgiform headache attacks with tearing and conjunctival injection: the first 'symptomatic' case? Cephalalgia 1991;11(3):123–7.

Cruccu G, Deuschl G. The clinical use of brainstem reflexes and hand-muscle reflexes. Clin Neurophysiol 2000;111:371–87.

Cruccu G, Leandri M, Iannetti GD, Mascia A, Romaniello A, Truini A, Galeotti F, Manfredi M. Small-fiber dysfunction in trigeminal neuralgia. Carbamazepine effect on laser-evoked potentials. Neurology 2001;56:1722–6.

Cruccu G, Anand P, Attal N, Garcia-Larrea L, Haanpaa M, Jorum E, Serra J, Jensen TS. EFNS guidelines on neuropathic pain assessment. Eur J Neurol 2004;11:153–62.

De Tommaso M, Lo Sito L, Di Fruscolo O, Sardaro M, Pia Prudenzano M, Lamberti P, Livrea P. Lack of habituation of nociceptive evoked responses and pain sensitivity during migraine attack. Clin Neurophysiol 2005;116:1254–64.

Deuschl G, Eisen A. Long-latency reflexes following electrical nerve stimulation. The International Federation of Clinical Neurophysiology. Electroencephalogr Clin Neurophysiol Suppl 1999;52:263–8.

Goadsby PJ, Lipton RB. A review of paroxysmal hemicranias, SUNCT syndrome and other short-lasting headaches with autonomic feature, including new cases. Brain 1997;120:193–209.

Goadsby PJ, Matharu MS, Boes CJ. SUNCT syndrome or trigeminal neuralgia with lacrimation. Cephalalgia 2001;21:82–8.

Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders, (2nd ed). Cephalalgia 2004;24(Suppl. 1):1–160.

May A, Bahra A, Buchel C, Turner R, Goadsby PJ. Functional magnetic resonance imaging in spontaneous attacks of SUNCT: short-lasting neuralgiform headache with conjunctival injection and tearing. Ann Neurol 1999;46:791–4.

Sandrini G, Friberg L, Janig W, Jensen R, Russel D, Sanchez del Rio M, Sand T, Schoenen J, Buchem M, van Dijk JG. Neurophysiological tests and neuroimaging procedures in non-acute headache: guidelines and recommendations. Eur J Neurol 2004;11:217–24.

Sprenger T, Valet M, Platzer S, Pfaffenrath V, Steude U, Tolle TR. SUNCT: bilateral hypothalamic activation during headache attacks and resolving of symptoms after trigeminal decompression. Pain 2005;113:422–6.

Teerijoki-Oksa T, Jaaskelainen S, Forssell K, Virtanen A, Forssell H. An evaluation of clinical and electrophysiologic tests in nerve injury diagnosis after mandibular sagittal split osteotomy. Int J Oral Maxillofac Surg 2003;32:15–23.

Teerijoki-Oksa T, Jaaskelainen SK, Forssell K, Forssell H. Recovery of nerve injury after mandibular sagittal split osteotomy. Diagnostic value of clinical and electrophysiologic tests in the follow-up. Int J Oral Maxillofac Surg 2004;33:134–40.

Truini A, Galeotti F, Romaniello A, Virtuoso M, Iannetti GD, Cruccu G. Laser-evoked potentials: normative values. Clin Neurophysiol 2005; 116:821–6.

Valls-Sole J. Neurophysiological assessment of trigeminal nerve reflexes in disorders of central and peripheral nervous system. Clin Neurophysiol 2005;116(10):2255–65.