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CME Diagnostic accuracy of trigeminal reflex testing in trigeminal neuralgia

Abstract—The authors prospectively studied 120 consecutive patients with trigeminal neuralgia (TN) to identify the clinical and laboratory features that most accurately distinguished symptomatic from classic TN. After a standardized evaluation, they identified 24 patients with symptomatic TN. Age, sensory examination, and affected division were not useful in the differential diagnosis. In contrast, electrophysiologic testing of trigeminal reflexes accurately distinguished symptomatic from classic TN (sensitivity 96%, specificity 93%).

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According to the International Headache Society (IHS) classification, trigeminal neuralgia (TN) may either be secondary to neurologic disease (symptomatic TN [STN]) or have no apparent cause other than neurovascular contact¹ (classic TN [CTN]). An age at onset of younger than 50 years, involvement of the ophthalmic division and the presence of sensory loss are classic indicators of symptomatic TN.^{2,3}

We prospectively studied patients with TN to identify the clinical and laboratory characteristics that distinguish STN from CTN. Characteristics assessed included age at symptom onset, the trigeminal divisions affected, and neurophysiologic testing of trigeminal reflexes.

Methods. We studied 120 consecutive patients (from February 2002 to May 2005) who fulfilled the IHS diagnostic criteria for TN. We excluded patients who had undergone surgical intervention. The local ethics committee approved the study. All patients gave written informed consent.

All subjects underwent prospective, standardized evaluation that included a neurologic history and examination, a complete study of trigeminal reflexes, and brain MRI. Facial sensitivity was examined with standard bedside methods: cotton wools for touch, wooden cocktail sticks for pinprick, and thermorollers for cold and warmth. Testing of trigeminal reflexes included the blink reflex after stimulation of the supraorbital nerve (V1) and the masseter inhibitory reflex after stimulation of the infraorbital (V2) and mental (V3) nerves. These responses are elicited by electrical stimuli with an intensity of about three times the reflex threshold on the unaffected side and recorded through surface electrodes with standard EMG apparatus. Figure 1 shows the stimulation and recording sites. A few trials are sufficient to measure the latency and its difference between sides, the most sensitive and reliable parameter. Methods and normal values from a group of 100 normal subjects were described in an earlier study.⁴ Neurophysiologists were unaware of the results of clinical evaluation and brain MRIs. A neuroradiologist, unaware of the results of the clinical examination or neurophysiologic testing, interpreted all brain MRIs.

The reference standard for the diagnosis of CTN or STN was the IHS diagnostic criteria: we diagnosed STN when a causative

lesion, other than vascular compression, was demonstrated by unequivocal sensory abnormalities in the distribution of the trigeminal nerve by brain MRI or laboratory tests, e.g., CSF examination, multimodal evoked potentials, or nerve biopsy.

The significance of the differences between CTN and STN patients in sex, affected side, affected trigeminal division, and abnormal reflexes were evaluated with Fisher's exact test, with calculation of sensitivity and specificity when significant. Differences between parametric data having a normal distribution were evaluated with Student's *t* test.

Results. We determined that 96 of 120 patients had CTN and 24 had STN: 16 MS, six had cerebellopontine-angle tumors, and two had isolated symmetric trigeminal neuropathy⁵ (table 1).

The mean age at onset of neuralgic pain was older in CTN than STN ($p < 0.0001$). The patients with STN, however, were largely intermingled with the younger patients with CTN (figure 2). For this reason, the diagnostic accuracy of a young age at onset (<50 years) for STN was poor: sensitivity 42% (95% CI: 24 to 61) and specificity 87% (95% CI: 82 to 94).

In the total TN population, the second trigeminal division was the most frequently affected and the first division the least frequently affected. Pain involved the first division in 38% of STN and 29% of patients with CTN and was restricted to it in 8.3% of patients with STN and 5.2% of patients with CTN. These differences were not significant.

Only two patients with TN had facial sensory loss. In both cases, the sensory loss was manifested by perioral hypoesthesia to touch and pin, with sparing of cold-warm discrimination. Both of these patients were classified as having STN after supraorbital nerve biopsy confirmed the presence of a trigeminal neuropathy.

Reflex testing. Abnormal trigeminal reflexes were strongly associated with STN (relative risk of STN 31, 95% CI: 8 to 124). Either the early blink reflex (R1) or the early masseter inhibitory reflex (SP1), or both, depending on the affected divisions, were abnormal in all but one patient with STN and normal in most patients with CTN. Thus, the diagnostic accuracy of the trigeminal reflex was high with a sensitivity of 96% (95% CI: 80 to 99) and a specificity of 93% (95% CI: 86 to 96), and positive and negative predictive values of 0.77 and 0.99, respectively. The evaluation did not cause adverse events in any patient.

MRI. Within this cohort, 38% of the MRIs demonstrated abnormalities: subtentorial lesions that were judged to be unrelated to TN (because the trigeminal system was not involved) in four patients, a neurovascular contact in 20 (both groups were diagnosed with CTN), and

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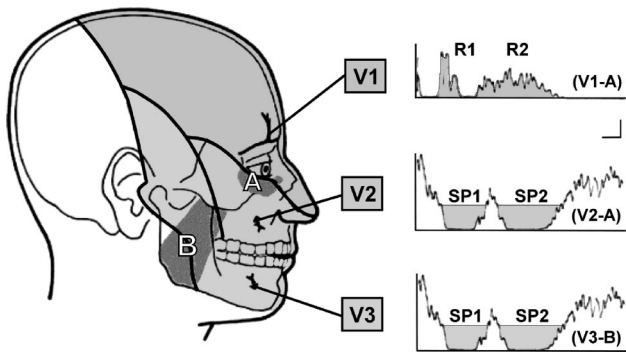


Figure 1. (Left) Schematic drawing of the three trigeminal divisions, stimulation sites at the supraorbital (V1), infraorbital (V2), and mental (V3) nerves and recording sites from the orbicularis oculi (A) and masseter (B) muscles. (Right) Early (R1) and late (R2) blink reflex (V1-A), and early (SP1) and late (SP2) masseter inhibitory reflex (V2-B and V3-B). Calibration: 10 ms/100 μ V.

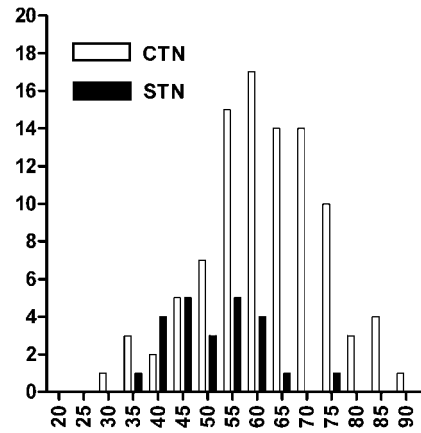


Figure 2. Frequency distribution of onset age in 120 patients with classic ($n = 96$) and symptomatic ($n = 24$) trigeminal neuralgia. y axis = number of patients; x axis = years.

lesions that were judged to be causally related to TN in 22 (18%) (these patients were diagnosed with STN). MRI did not detect any abnormality in the two cases of isolated trigeminal neuropathy diagnosed by supraorbital nerve biopsy.

Discussion. In a large cohort of patients with TN, we found that age at onset, sensory examination, and affected division were not sufficient to differentiate symptomatic from CTN. However, abnormal electrophysiologic testing of trigeminal reflexes accurately identified patients who were ultimately determined to have STN.

Whereas age at onset and affected division are not helpful because of too much overlapping between CTN and STN groups, the finding of sensory abnormalities is certainly a predictor of STN. But the prevalence of sensory abnormalities in patients with STN (8%) is too low for a normal sensory examination to exclude STN.

The relative uncommonness of sensory abnormalities is explained by the pathogenic mechanism of TN. When a disease process damages a sufficiently

large number of trigeminal nerve fibers to produce sensory loss, patients usually report dysesthesias or constant pain rather than the typical paroxysmal attacks of trigeminal neuralgia. Thus, brainstem infarctions or invasive tumors rarely give rise to neuralgic pain. Isolated symmetric trigeminal neuropathy⁵ constitutes the main exception to this rule. These patients have manifest sensory deficits, and some also report paroxysmal pain. In our STN group, only the two patients with trigeminal neuropathy had both sensory loss and neuralgic pain.

Quantitative sensory testing (QST) provides a far more precise sensory assessment; because there are reports of differences in mean sensory thresholds between patient groups with STN and CTN,³ QST might also be able to detect STN in individual patients.

Results of trigeminal reflex testing confirm uncontrolled studies from independent investigators. Combining the findings of this study with those of previous studies on trigeminal reflex testing in patients with TN, amounting to a total of 337, yields a sensitivity of 92% and specificity of 95%.⁶⁻⁸

Table Demographic, clinical, neurophysiologic, and neuroimaging results in 120 patients with classic or symptomatic trigeminal neuralgia

Condition (n)	Sex, F/M	Affected side, R/L	Age, y, <50/50+	Onset age, mean \pm SD (range)	Affected division				
					V1	V2	V3	Reflex, A/N	MRI, A/N
CTN (96)	60/36	56/40	10/86	62 \pm 12 (31–89)	28	73	43	7/89	24/72*
STN (24)	13/11	17/7	10/14	51 \pm 10 (35–75)	9	19	14	23/1	22/2†
<i>p</i>	NS‡	NS‡	<0.001‡	<0.001§		NS¶		<0.0001‡	<0.0001‡

* Four patients had an abnormal MRI because of subtentorial lesions that were not considered responsible for trigeminal neuralgia and 20 patients had MRI-documented neurovascular contact.

† Two patients with normal MRI had trigeminal neuropathy documented by supraorbital nerve biopsy.

‡ Fisher's exact test.

§ *t* test.

¶ Frequency of V1 vs V2/V3 divisions.

A/N = abnormal/normal.

In previous studies as well, the short-latency, A β fiber-mediated, oligosynaptic reflexes (R1 and SP1) were far more sensitive than the long-latency responses. It is indeed sufficient to test these short-latency responses on the affected division because either R1 or SP1 or both were abnormal in all our patients with abnormal reflex testing. The high sensitivity of the short-latency, A β fiber-mediated reflexes is explained by a great stability and narrow normal range and by the greater susceptibility of large myelinated fibers to compression and demyelination.^{9,10}

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