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Trigeminal Nerve Reflexes in Chronic Pain Syndromes

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Summary

Brainstem interneurons are suggested to play a key role in pain modulation and in nociceptive transmission in migraine, in tension type and in cluster headaches and according to the current understanding the primary headache disorders are caused by trigeminocervical pain dysfunction. Brainstem reflexes might be useful in patients with chronic pain syndromes, such as primary headaches and fibromyalgia in order to evaluate the possible pathophysiological mechanism. Patiets with chronic tension-type headache, depression, fibromyalgia and control group were examinated. The blink reflex was induced by surface electrostimulation with stimulus duration of 0,5 ms. The reflex activity was recorded bilaterally at the midline of the lower lid and the back of the nose with surface electrodes. The results of this neurophysiological study of trigeminal reflexes support the concept of primary brainstem dysfunction and central hyperexcitability of the trigeminal sensory pathways in patients with various types of chronic pain syndromes such as fibromyalgia and chronic tension-type headache.

Key words: Blink reflex; Pain syndromes

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Introduction

The pathophysiological mechanisms in primary headache are not completely understood. Brainstem interneurons are suggested to play a key role in pain modulation and in nociceptive transmission in migraine, in tension type and in cluster headaches and according to the current understanding the primary headache disorders are caused by trigeminocervical pain dysfunction [1]. There is evidence that pain symptoms in fibromyalgia may be due to alterations in central processing of sensory input, along with aberrations in the endogenous inhibition of pain and that in fibromyalgia the brainstem function is altered [2,3].

Various brain stem inhibitory and excitatory reflexes are used in neurophysiology to explore the excitability of the neural pathways involved in nociceptive transmission and in sensitization phenomena at brainstem trigeminal level, which are inaccessible by other research methods [4]. Brainstem reflexes might be useful in patients with chronic pain syndromes, such as primary headaches and fibromyalgia in order to evaluate the possible pathophysiological mechanisms [5-8]. The neurophysiological data in headache and in pain syndromes are controversial – some of the studies confirm the brainstem interneurons dysfunction, but others do not.

Depending on the afferent and efferent components and the level of reflex arcs formation the brain stem reflexes are trigemino-trigeminal, trigemino-facial and trigemino-cervical. The most frequently used reflexes are trigemino-facial (blink reflex) and trigemino-trigeminal (mandibular reflex and exteroceptive suppression of the masseter activity or the so-called masseter inhibitory reflex). Their different pathways and neural connections in the brain stem remain the basis of their topographic analysis diagnostic value in prominent clinical or subclinical organ damages.

The aim of this clinical study is to evaluate the involvement of the brain stem structures in chronic pain syndromes by examining the trigeminal reflexes.

Patients and Methods

A control group of twenty healthy volunteers (5 males and 15 females, mean age of 32, 02 ± 6, 6 years) was used for comparison in blink reflex, masseter inhibitory reflex and trigemino-facial reflex studies [9].

Fifty patients with chronic tension-type headache (CTH) in pain free period were studied (36 females and 14 males, mean age

of 42, 02 ± 13, 39 years). The headache was bilateral (in 21 patients) or bilateral with predominant side (in 29 patients). Ten patients (10 females, mean age of 48, 33 ± 13, 07 years) with fibromyalgia and 14 patients (11 females and 3 males, mean age of 45, 5 ± 14, 9 years) with mild and moderate anxiety and depression according to Zung Depression Scale were also studied.

Patients with chronic tension-type headache (CTH) and accompanying depressive syndrome were excluded from the study in order to prevent any comorbidity, which would compromise the neurophysiological results.

Methods

The blink reflex was induced by surface electrostimulation with stimulus duration of 0,5 ms. The stimuli were delivered at a distance of 2 cm from the exit of supraorbital nerve of the skull surface. Ten consecutive stimuli were delivered at the predominant pain or right side in patients with bilateral chronic tension-type headache, on the right side in healthy controls, in patients with fibromyalgia and in patients with depression. The reflex activity was recorded bilaterally at the midline of the lower lid and the back of the nose with surface electrodes. For preventing of habituation the separate stimuli were delivered at intervals of at least 40 seconds. The reflex was recorded at stimulus intensity 1, 5 times above reflex threshold. The signal was averaged, amplified and rectified. Latency parameters (ms) and R1 and R2 area (mV*ms) were calculated.

The masseter inhibitory reflex was recorded from masseter muscles bilaterally with surface electrodes. The patients were instructed to clench their teeth as much as possible until reaching a full electromyographic interference pattern. Ten consecutive stimuli were delivered. Electrostimulation with stimulus duration of 0,2 ms was performed on commissura labialis with surface electrodes unilaterally at the predominant pain or right side in patients with bilateral chronic tension-type headache, on the right side in healthy controls, in patients with fibromyalgia and in patients with depression. Stimulus intensity was 2, 5 times above the reflex threshold. Latency and duration of the two exteroceptive suppression periods (ES1 and ES2) were measured from the intersection point of the rectified and averaged signal and the line showing 80% of the basal activity. The following parameters were evaluated: latency and duration of both suppressor periods in ms.

The trigemino-cervical reflex was recorded bilaterally by resting sternocleidomastoid muscles using surface electrodes placed at 3 cm distance along the length of the muscle. Electrostimulation with 0, 2 ms duration was delivered on both sides of the supraorbital nerve. The stimulation intensity was 1, 5 times above the reflex threshold and was perceived by the studied patients as intense but not painful (about 40-60 mA). The following parameters were assessed: latency (ms), duration (ms), area (mV*ms) and peak-to-peak amplitude (mV).

Statistical Methods: The statistical data processing was made by means of SPSS 13.0 for Windows. Parametric (ANOVA and Paired Sample T-Test), as well as nonparametric (Man-Whitley U, Kruskal-Wallis or Wilcoxon) analyses were used. $P < 0.05$ was considered as a threshold value of level of statistical significance, unless otherwise specified.

Results

Trigemino-facial (blink) reflex

The neurophysiological data are shown in **Table 1**. In all studied subjects the R1 and R2 components of the blink reflex were obtained. No statistically significant differences were found in the parameters of the blink reflex between both sides of the body and between the patient groups.

Trigemino-trigeminal (masseter inhibitory) reflex

The neurophysiological data are shown in **Table 2**. Right-sided electrical stimulation of comissura labialis provoked a bilateral reflex response in all healthy controls.

In patients with chronic tension-type headache (CTH) the latency of ES1 was prolonged bilaterally. It was statistically significant in patients with a predominant headache side as compared to the control group. Regarding the ES2 a number of changes were established: in 3 patients ES2 was missing, in the other subjects it was reduced bilaterally. In the subgroup of patients with a predominant headache side the reported reduction was statistically significant on the painful side, as compared to the controls. In patients with bilateral headache without predominant side the reduction of ES2 was bilateral and statistically significant.

In patients with fibromyalgia the ES1 latency was prolonged and the duration of ES2 was shortened bilaterally. The abnormal changes were more pronounced than in the group with tension-type headache.

In patients with depression ES1 and ES2 parameters did not differ from the control group.

No significant differences were found in the other ES1 and ES2 parameters between the both sides of the body and between the groups.

Trigemo-cervical reflex in patients with primary headache disorders

The neurophysiological data are shown in **Table 3**. After electrical stimulation of the supraorbital nerve a bilateral response was induced in all normal controls.

Table 1 Neurophysiological parameters of Trigemino-facial (blink) reflex (*p<0.05).

Groups	Latency R1 (ms)	Latency R2 (ms)	Area R2 (mV*ms)
Control group (right side)	10,4	**32,0**	**2,01**
SD	0,7	3,9	0,6
Depression (right side)	10,35	32,35	2,51
SD	1,01	3,43	0,54
Fibromyalgia (right side)	10,05	34,77	2,42
SD	0,8	3,7	0,56
Chronic tension-type headache	10,02	31,4	1,9
SD	0,92	2,45	1,88

Table 2 Neurophysiological parameters of Trigemino-trigeminal (masseter inhibitory) reflex.

	Side with pain**/right side				Side without pain**/left side			
	ES1		ES2		ES1		ES2	
	Latency (ms)	Time (ms)	Latency (ms)	Time (ms)	Latency (ms)	Time (ms)	Latency (ms)	Time (ms)
Control group (L=D)	11,84	19,44	47,78	32,9	10,52	20,38	47,5	33,46
SD	3,30	2,74	10,04	8,73	2,77	3,86	10,69	9,63
Depression	13,86	17,43	44,71	31,6	13,10	19,75	48,08	29,4
SD	4,54	7,05	14,78	10,84	3,236	9,40	14,38	6,9
Fibromyalgia	16,64*	18,21	52,49	13,78*	18,1*	18,8	52,05	16,13*
SD	6,90	6,45	21,47	8,43	7,49	6,42	16,77	6,89
CTH (L/D)	16,35*	18,24	48,33	22,59*	16,99*	16,80	45,42	30,94
SD	5,45	7,59	10,05	11,27	6,45	6,12	10,39	13,76
CTH (L=D)	14,01	15,20	49,04	22,50*	13,15	16,47	48,35	25,95*
SD	6,29	4,53	11,83	9,99	5,67	4,48	10,28	9,46

**The electric stimuli were applied to the symptomatic side in headache patients with a dominant side and to the right side in patients with bilateral pain, fibromyalgia, depression and in healthy subjects.

In the patients with predominantly unilateral chronic tension-type headache the response of the side with headache was with shortened latency. In the patients with bilateral chronic tension-type headache the reflex latency was shortened bilaterally.

In the patients with fibromyalgia the reflex latency was shortened bilaterally, compared to healthy controls.

In the patients with depression the trigemino-cervical reflex was normal in comparison with healthy controls.

No significant differences were found in the other parameters of response between both sides of the body and between the groups.

Discussion

Most of the recent neurophysiological studies in headache disorders are focussed on the pathways located on the rostral part of the brainstem and the connection between the spinal cord and medulla oblongata investigating trigemino-trigeminal, trigemino-facial and trigemino-cervical reflexes. While there are many studies of the conventional blink reflex and the exteroceptive suppression of temporal muscle activity, there are only few studies on the habituation phenomenon, masseter inhibitory and trigemino-cervical reflexes.

In primary headache the R2 and R3 components of the blink reflex are of a great interest as they reflect structures and functions involved in the pathogenesis of headache and because their nociceptive nature [10]. Until now many studies have been conducted in patients with tension-type headache and migraine and in most of them the latencies of the individual components at conventional electrical stimulation were normal.

Our neurophysiological study confirmed the absence of significant abnormalities of the parameters in conventional blink reflex in patients with headache, as well as in patients with fibromyalgia and with depression. However, the R3 the findings in literature are quite intriguing. In patients with migraine with or without aura the area of R3 was increased during a headache attack and the R3 threshold was lower between the attacks [5]. It was suggested that such increased trigeminal excitability is probably caused by central mechanisms, rather than by peripheral sensitization of meningeal receptors [5]. In our study we have no enough data for habituation of R2 and R3, so we cannot discuss it.

The results for the masseter inhibitory reflex in our study reveal reduced suppression of the second phase of muscle activity suppression-in all patients with tension-type headache the duration of ES2 was abnormal and shortened. The neurophysiological findings in patients with fibromyalgia were similar. It was accepted that the periods of chewing muscles exteroceptive suppression, in particular masseter inhibitory reflex, are regulated by the activity of the antinociceptive system and that the reflex changes reflect an abnormal antinociceptive function [4]. Schœnen et al. [11] first reported a reduction of ES2 in patients with chronic tension-type headache and suggested that this reflects a deficit of activation or excessive inhibition of ponto-bulbar inhibitory interneurons that are under altered limbic modulation. For the first time, using neurophysiological methods, a central mechanisms were found for a disease considered to be completely peripheral. Although some authors obtain normal data [12,13], the summary results show a reduction of ES2 in more than 80% of all studied patients with chronic tension-type headache [1,14].

Taking into consideration the fact that similar pathophysiological mechanisms were involved in tension-type headache disorders

Table 3 Neurophysiological parameters of Trigemo-cervical (After electrical stimulation of the right supraorbital nerve).

		Side with pain**/right side				Side without pain**/left side			
	PatientsN	Latency ms	Time ms	Amplitude mV	Area mV*ms	Latency ms	Time ms	Amplitude mV	Area mV*ms
Control group **L=D**	20	49,20	61,94	0,44	3,56	50,27	59,96	0,36	3,95
SD		4,529	2,54	0,25	2,08	5,03	23,49	0,21	1,46
Depression	14	49,63	48,5	0,86	2,39	52,48	50,24	0,84	2,76
SD		3,6	16,57	0,62	2,13	3,43	18,82	0,68	1,86
Fibromyalgia	10	46,48*	51,98	0,46	1,6	47,91*	45,65	0,278	1,66
SD		3,4	3,9	0,2	0,7	3,5	20,6	-	0,28
CTH L>D	29	46,33*	65,36	0,29	1,74	50,37	46,16	0,29	2,29
SD		2,73	2,57	0,18	1,18	2,59	20,79	0,10	1,89
CTH L=D	19	45,97*	45,88	0,32	2,20	47,32*	42,49	20,67	2,23
SD		2,26	1,79	0,24	0,60	2,47	6,86	2,87	0,64

and fibromyalgia, Schepelmann et al. found that ES2 of m. temporalis was abnormally shortened only in the group with headache, but not in patients with fibromyalgia. In the present study a shortening of the ES2 duration was established also in patients with fibromyalgia and the abnormal changes are expressed bilaterally. These data reveal common mechanisms possibly related to endogenous pain control in both pain conditions-chronic tension-type headache and fibromyalgia. Suggesting common pathophysiological brainstem mechanisms in both chronic pain conditions. Additional studies are needed to determine definitely whether ES2 in fibromyalgia differs substantially from the normal controls and whether these changes are associated with pain, as are the changes in chronic tension-type headache.

The trigemino-cervical reflex in the tested patients with headache was abnormal with a shortened latency when compared with healthy controls. Similar results were obtained in our previous study in different patient groups with headache [15]. Our findings confirmed the data reported by Nardone et al. [16,17], who found abnormalities in latency and amplitude of the response in patients with migraine [16] and in patients with chronic tension-type headache [17].

In patients with fibromyalgia the trigemino-cervical reflex showed no statistically significant changes compared with healthy control group [18]. In our study bilateral changes regarding an increased reflex excitability reflex were established in all patients with pain disorders. Moreover, these changes are more pronounced in the patients with fibromyalgia, than in the patients with chronic tension-type headache. The shortening of latency of the trigeminocervical reflex, as well as the reduced duration of ES2 of masseter inhibitory reflex suggest a reduction of inhibitory activity of brainstem interneurons or increased excitability of the brainstem excitatory neurons in primary headache disorders as well as in fibromyalgia.

There are few studies on trigeminal reflexes in psychiatric disorders. A shortening (or reduction) of ES2 of exteroceptive suppression of m. temporalis was reported in patients with generalized anxiety disorder, but not in patients with depression [19]. A reduction of habituation and early onset of R3 component of blink reflex was established in psychotic states, but not in non-psychotic depression [20]. In our patients with depression changes in neurophysiological parameters of trigeminal reflexes were not found. So, we may confirm the previous study results of the above-mentioned authors as well.

The similar neurophysiological abnormalities in the trigeminal reflexes in headache and in fibromyalgia possibly reflect common pain mechanisms in both diseases. It may be speculated, that these abnormalities, taken together with the normal trigeminal reflex findings in patients with depression reflect different pathophysiological mechanisms and possibly may be helpful in differential diagnosis in these disorders - fibromyalgia, chronic tension-type headache and depression. Confirmation of the reported results in a larger number of patients would help to reveal the brainstem pathophysiological mechanisms of the tree distinct nosological entities involved in the present study.

Conclusion

In conclusion the results of this neurophysiological study of trigeminal reflexes support the concept of primary brainstem dysfunction and central hyperexcitability of the trigeminal sensory pathways in patients with various types of chronic pain syndromes such as fibromyalgia and chronic tension-type headache.

References

1 Cecchini AP, Sandrini G, Fokin Iv, Moglia A, Nappi G (2003) Trigeminofacial reflexes in primary headaches. Cephalalgia 23: 33-41.

2 Bradley LA (2009) Pathophysiology of fibramyalgia. Am J Med S22-30.

3 Kofler M, Halder W (2013) Alterations in excitatory and inchibitory brainstem interneuronal circuit in fibromyalgia: Evidence of brainstem dysfunction. Clin Neurophysiol 2013: 1345-1388.

4 Ellrich J (2002) Trigeminal nociceptive reflexes. Mov Disord 17: 41-44.

5 *De Tommaso M, Guido M, Libro G, Sciruicchio V, Puca F (2000) Zolmitriptan reverses blink reflex changes induced during the migraine attack in humans. Neurosci Lett 289: 57-60.*

6 Di Clemente L, Coppola G, Magis D, Fumal A, De Pasqua V, (2007) Interictal habituation deficit of the nociceptive blink reflex: an endophenotypic marker for presymptomatic migraine? Brain 130: 765-770.

7 *Ebinger F (2006) Exteroceptive suppression of masseter muscle activity in juvenile migraineurs. Cephalalgia 26: 722-730.*

8 Headache Classification Subcommittee of the International Headache Society (2003). The International Classification of Headache Disorders. 2nd Edition. Cephalalgia 24: 1-136.

9 Serrao M, Perrotta A, Bartolo M (2005) Enhanced recovery cycle of trigemino-cervical-spinal reflexes in migraine during the pain-free period. Headache 45: 1061-1068.

10 *Katsarava Z, Giffin* N, Diener H, Kaube H (2003) Abnormal habituation of 'nociceptive' blink reflex in migraine--evidence for increased excitability of trigeminal nociception. Cephalalgia 23: 814-819.

11 Schoenen J, Jamart B, Gerard P, Lenarduzzi P, Delwaide PJ (1987) Exteroceptive suppression of temporalis activity in chronic headache. Neurology 37: 1834-1836.

12 Sand T, Zwart JA (1994) The blink reflex in chronic tension-type headache, migraine, and cervicogenic headache. Cephalalgia 14: 447-450.

13 Schepelmann K, Dannhausen M, Kötter I, Schabet M, Dichgans J (1998) Exteroceptive suppression of temporalis muscle activity in patients with fibromyalgia, tension-type headache, and normal controls. Electroencephalogr Clin Neurophysiol 107: 196-199

14 Zwart J, Sand T (1995) Exteroceptive suppression of temporalis muscle activity: a blind study of tension-type headache, migraine and cervicogenic headache. Headache 35: 338-343.

15 Milanov I, Bogdanova D (2003) Trigemino-cervical reflex in patients with headache. Cephalalgia 23: 35-38.

16 Nardone R, Tezzon F (2003) Short latency trigemino-sternocleidomastoid response in patients with migraine. J Neurol 250: 725-732.

17 Nardone R, Tezzon F (2003) The trigemino-cervical reflex in tension-type headache. Eur J Neurol 10: 307-312.

18 Yürüten B, Ozerbil OM (2003) Trigeminocervical reflex in fibromyalgia patients. Arch Phys Med Rehabil 84: 1087-1089.

19 Wang W, Fu X, Wang Y (2000) Temporalis exteroceptive suppression in generalized anxiety disorder and major depression. Psychiatry Res 96: 149-155.

20 Taiminen T, Jääskeläinen S, Ilonen T, Meyer H, Karlsson H, et al. (2000) Habituation of the blink reflex in first-episode schizophrenia, psychotic depression and non-psychotic depression. Schizophr Res 44: 69-79.