Journal of Zhejiang University SCIENCE B
ISSN 1673-1581 (Print); ISSN 1862-1783 (Online)
www.zju.edu.cn/jzus; www.springerlink.com
E-mail: jzus@zju.edu.cn

Report:

Abnormalities of masseter inhibitory reflex in patients with episodic tension-type headache

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Received Aug. 15, 2008; Revision accepted Sept. 17, 2008; Crosschecked Dec. 1, 2008

Abstract: Objective: To investigate the masseter inhibitory reflex (MIR) and its eventual changes in patients with episodic tension-type headache (TTH). Methods: MIR was studied in 21 patients with episodic TTH and 30 healthy subjects, with age and sex matched to the study cohort. Median age of patients was 17.0 years (ranged 16~49 years), median duration of disease 12 months (1~5 years), and median frequency of headache 7.5 d per month. Results: The second period of suppression (S2) of MIR was reduced in intensity and duration in 10% of controls and 66.7% (confidence interval (*CI*)=45.3%~85%; $P<0.05$) of patients with episodic TTH ($\chi^2=74.9$; $P<0.001$). In 3 (14.3%) of patients with episodic TTH, S2 was completely absent. No significant correlation between the duration of disease and headache frequency was found. Conclusion: Our results confirm the link between episodic TTH and reduction or absence of S2. Teenage patients with episodic TTH may exhibit marked pathological changes in S2 in contrast to older individuals.

Key words: Tension-type headache (TTH), Temporalis muscle exteroceptive suppression, Masseter inhibitory reflex (MIR)
doi:10.1631/jzus.B0820249 **Document code:** A **CLC number:** R338

INTRODUCTION

Masseter inhibitory reflex (MIR), also known as jaw-opening reflex (jaw jerk reflex), temporalis muscle exteroceptive suppression, and masseter silent period, manifests in reflex inhibition of the voluntary contraction of the muscles of mastication in response to intensive mechanical or electrical stimulation of the oral mucosa, and the teeth and skin in the area innervated by the maxillary and mandibular nerves. It is considered mainly as protective reflex, but participates in the coordination of the mandibular movements in mastication and articulation as well (Schoenen, 1993).

From a neurophysiologic point of view, the phenomenon of MIR becomes apparent in the appearance of two periods of muscle silence: early (S1), with latent period of 10~15 ms and minimum duration of 10 ms, and late (S2), with latent period of 40~60 ms and minimum duration of 20 ms. These periods are separated by a short period of activity (Wallasch *et al*., 1993; Göbel and Dworschak, 1996), which is considered to be a transcortical analogue of the long-loop reflex of the limbs (Ongerboer de Visser *et al*., 1990).

Many researches clarify MIR to a great extent to be the anatomical background and the functional importance of the reflex (Yemm, 1972; Cruccu *et al*., 1989; Ongerboer de Visser *et al*., 1990). A commonly accepted opinion is that S1 represents oligosynaptic inhibitory reflex, mediated by A-beta afferent components of the trigeminal nerve, which complete a reflex arch via neurons exiting the rostral portion of the spinal trigeminal nucleus at the level of the middle third of the pons, and project bilaterally on the trigeminal motor nucleus. S2 causes greater contradictions and is considered as nociceptive reflex, proprioceptive period of silence, a pause evoked by the synchronization in the neuronal activity, and multisynaptic skin reflex (Ongerboer de Visser *et al*., 1990).

It has been clarified that S2 is also mediated by A-beta afferent fibers, which reach neurons of the spinal trigeminal nucleus located in the lowest caudal pons, from where projections extend polysynaptically via the lateral reticular formation and ascend to the motor nucleus bilaterally (Yemm, 1972). S2 is suppressed by nicotine, as this effect in turn is blocked by naloxon. The reason for this is that the inhibitory neurons, responsible for S2, are cholinergic and are included in a wider cholinergic inhibitory system, passing through the whole brain stem. This system is under intensive limbic control and participates in the structures connected with pain modulation (Yu *et al*., 1973; Woolf, 1991; Schoenen *et al*., 1991).

It has been reported that in patients with chronic tension-type headache (TTH) S2 of MIR is reduced in duration and intensity (Miles *et al*., 1987; Cruccu *et al*., 1989; Wang and Schoenen, 1994; Wang *et al*., 1995; Lipchik *et al*., 2000; Aktekin *et al*., 2001). The aim of the present study is to investigate the reflex and its eventual changes in patients with episodic TTH.

MATERIALS AND METHODS

Twenty-one patients (median age 17.0 years, ranged 16~49 years) with episodic TTH (median duration of disease 12 months (1~5 years), and median frequency of headache 7.5 d per month), who met the criteria of Headache Classification Subcommittee of the International Headache Society (2004), were studied in the period without headache after informed consent. Young patients, who are non-smokers, without personal and family history of migraine, any somatic diseases, or systematic acceptance of medication, were deliberately chosen. History and physical examination data are presented in Table 1.

To investigate the episode frequency, the patients were examined a month after the primary check up. The equipment used was “Medicor” with a computer system for electromyography “Pulse-Art” and “Toennies-Multilinear” (Jaeger/Toennies, Germany) machine. MIR was investigated according to the

Table 1 Clinical features of patients with episodic tension-type headache

Patient No.	Sex	Age (year)	Duration of disease	Incidence (day per month)	Duration of attacks (h)	Site	Clinical characteristics of the headache
1	M	16	2 years	4~8	1~2	b, f, t	Pressure, tightness
2	M	18	18 moths	4~8	1~2	b, f, t	Pressure, tightness
3	F	16	2 years	2~4	2~6	b, t	Tightness
4	F	39	6 months	10~15	1~4	b, f, t	Pressure
5	F	35	6 months	10	6~12	b, t	Tight band around head
6	F	46	1 year	5~10	4~6	f, b, t	Tightness
7	F	35	18 years	10~15	2~6	b, f, t	Pressure
8	M	49	5 months	5~10	4~6	b, f	Tightness
9	M	28	1 month	10	4~6	b, f, t	Tightness, pressure
10	F	18	1 year	5	≤24	b, f, t	Tightness
11	F	17	1 year	1~2	6~12	b, f, o	Tightness
12	F	17	6 month	10	2	b, t	Pressure, tightness
13	F	17	4 years	15	12	b, f, t	Tightness
14	M	17	6 months	10~15	1~2	b, t	Tightness
15	F	17	1 year	15	12	b, f, t	Pressure
16	F	17	1 year	15	2~4	b, f	Tightness
17	F	17	5 years	5~10	2~6	b, t	Tightness
18	F	17	3 years	5~10	6~12	b, t	Tightness, pressure
19	M	17	2 years	5	2~6	b, f, t	Tightness
20	F	38	18 months	12~15	2~24	b, f, o	Pressure
21	M	17	1 year	5~10	2~4	b, f, t	Tightness

M: male; F: female; b: bilateral; f: frontal; t: temporal; o: occipital

standard method as follows: the activity of both head side temporal muscles was registered with surface electrodes, as the active electrode was placed over the muscle belly, and the referent on the cheekbone arch. Nervus mentalis (n. mentalis) was stimulated with electrical stimuli with duration of 0.1 ms in the projection of foramen mentale in maximum voluntary contraction of masticatory muscles. To avoid reflex habituation, the frequency of stimulation used was about 1 min^{-1}. The stimulus intensity was 3 to 5 times the sensory threshold (ranged from 12 to 24 mA), which corresponds to the subject's sensation of light pain radiating to the teeth. First the right n. mentalis and second the left n. mentalis were stimulated consecutively, as the activity was registered in two channels from both temporal muscles. Ten traces with duration of 250 ms and predelay of 50 ms were superimposed. The curves obtained were subjected to full-wave rectification in some of the patients.

The curves were evaluated visually after recording on a paper, and the following conditional classification was accepted: Type 1—normal S2 (Fig.1a); Type 2—S2 suppression with reduction of its duration and presence of action potentials in the suppression period with summation amplitudes ranging from 20% to 80% of the initial total sum amplitude (Fig.1b); Type 3—complete absence of S2 (Fig.1c).

Results were compared with normative values of the laboratory obtained from 30 healthy persons with age and sex matched to the study cohort. The Statgraphics Plus Version 2.1 statistical system was used. For data analysis, the χ^2 test and confidence interval (*CI*) were applied. A level of $P<0.05$ was considered statistically significant.

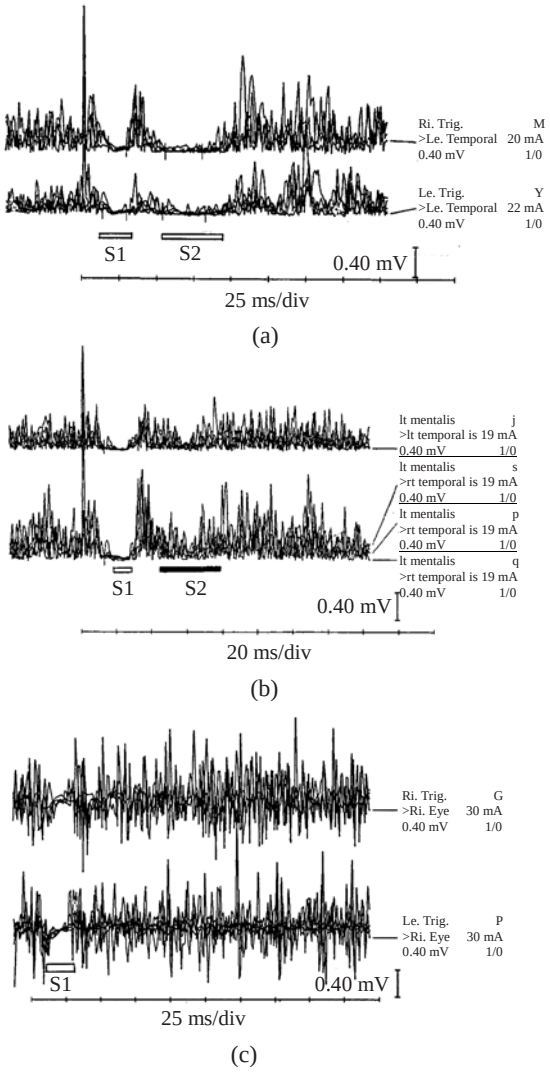

Fig.1 MIR with (a) normal S2 (Type 1 recording), (b) changed but available S2 (Type 2 recording), and (c) complete absence of S2 (Type 3 recording)

RESULTS

The second period of suppression (S2) was reduced in intensity and duration in 10% of controls and 66.7% (*CI*=45.3%~85%; $P<0.05$) of patients with episodic TTH ($\chi^2=74.9$; $P<0.001$). Type 1, normal S2, was recorded in 7 (33.3%) patients (Fig.1a). Type 2, changed but available S2, was found in 11 patients (52.4%) (Fig.1b). Three patients (14.3%) demonstrated Type 3 recording, corresponding to the most marked change (Fig.1c).

The distribution of the three types of recordings in accordance with the age, duration of disease, and frequency and duration of attacks is shown in Table 2. Certain teenage patients with episodic TTH exhibited marked pathological changes of S2 in contrast to older individuals. No significant correlation between the duration of disease and headache frequency was found.

DISCUSSION

We reported the significant changes of S2 in the patients with episodic TTH. Patients with personal or

Table 2 Distribution of age, duration of disease, and duration and frequency of attacks according to MIR changes

Type of S2 suppression	Patient number														
	Age (year)				Duration of disease (month)				Duration of attacks (h)				Frequency of attacks (day per month)		
	≤20	21~30	31~40	41~50	≤6	7~12	13~24	>24	2~4	5~6	7~12	>12	≤5	6~10	11~15
1	4	1	1	1	−	4	1	2	2	2	2	1	4	1	2
2	7	−	3	1	5	−	3	3	3	5	2	1	1	5	5
3	3	−	−	−	1	1	3	−	1	−	1	1	1	−	2

family history of migraine were not included to avoid the reduction of habituation of the nociception-specific blink reflex (Di Clemente *et al*., 2007). The comparatively limited number of patients included in the present study does not allow a strong conclusion to be drawn but several tendencies emerged.

Firstly, the abnormalities in S2 were demonstrated in 66.7% of the patients with episodic TTH, whereas they were presented in 16.3% of the total number of patients. These results are in concert with the findings of Wang and Schoenen (1994), suggesting that the genesis of the chronic and episodic TTH is similar. Exteroceptive suppression of temporalis muscle activity has been reported to be reduced mainly in chronic TTH (Miles *et al*., 1987; Cruccu *et al*., 1989; Wallasch, 1991; Schoenen and Agrégé, 1993; Wang *et al*., 1995; Lipchik *et al*., 2000; Aktekin *et al*., 2001). The correlation is specific, because in patients with migraine, post-lumbar puncture headache, headache in inflammatory diseases, and mass lesions, similar changes were not found (Miles *et al*., 1987; Paulus *et al*., 1992; Raudino, 1994; Zwart and Sand, 1995). The explanation of this fact could be searched in a wider cholinergic dysfunction that might lie in the background of the reduced pain thresholds and the reduction of S2 as epiphenomenona. The changes observed in TTH are also due to hyperexcitability of the reticular nuclei, which inhibit the medullary inhibitory interneurons mediating S2 (Göbel *et al*., 1993; Wallasch and Göbel, 1993; Neufeld *et al*., 2000).

To some extent, our results are in contrast to the findings of Wallasch *et al*.(1991). They reported shortened duration of S2 in patients suffering from chronic TTH compared to migraineurs and controls. However, patients with episodic TTH exhibited late suppression periods of temporal muscle activity of differing durations. The discrepancy might be explained by the age of our patients, and future investigations could be useful to verify such a correlation.

It is impressive that more marked changes in S2 were observed in the youngest group of patients. Furthermore, the duration of disease and episode frequency do not form any significant correlation towards the types of S2. Younger patients with more marked changes in S2 represent a group of predisposed individuals, which would most likely develop chronic TTH in the future, while in older patients the genesis is not that closely linked with dysfunction of the cholinergic inhibitory systems. However, more studies need to be done with more patients with episodic TTH, as well as their prospective studies.

In conclusion, the second period of suppression (S2) in MIR was reduced in intensity and duration, or was absent in 66.7% of the patients with episodic TTH. A tendency for differentiation of the group of patients with TTH at young age and with marked changes in S2, has been formed. They might most likely differ in prognosis from other episodic TTH patients.

References

Aktekin, B., Yaltkaya, K., Ozkaynak, S., Oguz, Y., 2001. Recovery cycle of the blink reflex and exteroceptive suppression of temporalis muscle activity in migraine and tension-type headache. *Headache*, **41**(2):142-149. [doi:10.1046/j.1526-4610.2001.111006142.x]

Cruccu, G., Cruccu, G., Agostino, R., Inghilleri, M., Manfredi, M., Ongerboer de Visser, B.W., 1989. The masseter inhibitory reflex is evoked by innocuous stumuli and mediated by A beta afferent fibers. *Exp. Brain Res.*, **77**(2):447-450. [doi:10.1007/BF00275005]

Di Clemente, L., Coppola, G., Magis, D., Fumal, A., De Pasqua, V., Di Piero, V., Schoenen, J., 2007. Interictal habituation deficit of the nociceptive blink reflex: an endophenotypic marker for presymptomatic migraine? *Brain*, **130**(3):765-770. [doi:10.1093/brain/awl351]

Göbel, H., Dworschak, M., 1996. Exteroceptive suppression of activity of the temporal muscle. Principles and applications. *Der Nervenarzt*, **67**(10):846-859. [doi:10.1007/s001150050062]

Göbel, H., Dworschak, M., Wallasch, T.M., 1993. Exteroceptive suppression of temporalis muscle activity:

perspectives in headache and pain research. *Cephalalgia*, **13**(1):15-19. [doi:10.1046/j.1468-2982.1993.1301015.x]

Headache Classification Subcommittee of the International Headache Society, 2004. The international classification of headache disorders, 2nd Ed. *Cephalalgia*, **24**(Suppl. 1): 9-160.

Lipchik, G., Holroyd, K.A., O′Donnel, F.J., Cordinqley, G.E., Waller, S., Labus, J., Davis, M.K., French, D.J., 2000. Exteroceptive suppression periods and pericranial muscle tenderness in chronic tension headache: effects of psychopathology, chronicity and disability. *Cephalalgia*, **20**(7):638-646. [doi:10.1046/j.1468-2982.2000.00105.x]

Miles, T.S., Türker, K.S., Nordstrom, M.A., 1987. Reflex responses of motor units in human masseter muscle to electrical stimulation of the lip. *Exp. Brain Rres.*, **65**(2):331-336. [doi:10.1007/BF00236305]

Neufeld, J.D., Holroyd, K.A., Lipchik, G.L., 2000. Dynamic assessment of abnormalities in central pain transmission and modulation in tension-type headache sufferers. *Headache*, **40**(2):142-151. [doi:10.1046/j.1526-4610.2000.00020.x]

Ongerboer de Visser, B.W., Cruccu, G., Manfredi, M., Koelman, J.H., 1990. Effects of brainstem lesions on the masseter inhibitory reflex: functional mechanisms of reflex pathways. *Brain*, **113**(3):781-792. [doi:10.1093/brain/113.3.781]

Paulus, W., Raubüchl, O., Straube, A., Schoenen, J., 1992. Exteroceptive suppression of temporalis muscle activity in various types of headache. *Headache*, **32**(1):41-44. [doi:10.1111/j.1526-4610.1992.hed3201041.x]

Raudino, F., 1994. Is temporomandibular dysfunction a cranial dystonia? An electrophysiological study. *Headache*, **34**(8):471-475. [doi:10.1111/j.1526-4610.1994.hed3408471.x]

Schoenen, J., 1993. Exteroceptive suppression of temporalis muscle activity: methodological and physiological aspects. *Cephalalgia*, **13**(1):3-10. [doi:10.1046/j.1468-2982.1993.1301003.x]

Schoenen, J., Agrégé, M.D., 1993. Exteroceptive suppression of temporalis muscle activity in patients with chronic headache and in normal volunteers: methodology, clinical and pathophysiological relevance. *Headache*, **33**(1):3-17. [doi:10.1111/j.1526-4610.1993.hed3301003.x]

Schoenen, J., Bottin, D., Sulon, J., Gaspard, U., Lambotte, R., 1991. Exteroceptive silent period of temporalis muscle in menstrual headache. *Cephalalgia*, **11**(2):87-91. [doi:10.1046/j.1468-2982.1991.1102087.x]

Wallasch, T.M., 1991. A study on the exteroceptive suppression of the masseter, temporalis and trapezius muscles produced by mental nerve stimulation in patients with chronic headaches. *Cephalalgia*, **11**(3):162-163. [doi:10.1046/j.1468-2982.1991.1103160.x]

Wallasch, T.M., Göbel, H., 1993. Exteroceptive suppression of temporalis muscle activity: findings in headache. *Cephalalgia*, **13**(1):11-14. [doi:10.1046/j.1468-2982.1993.1301011.x]

Wallasch, T.M., Reinecke, M., Langohr, H.D., 1991. EMG analysis of the late exteroceptive suppression period of temporal muscle activity in episodic and chronic tension-type headaches. *Cephalalgia*, **11**(2):109-112. [doi:10.1046/j.1468-2982.1991.1102109.x]

Wallasch, T.M., Niemann, U., Kropp, P., Weinschütz, T., 1993. Exteroceptive silent periods of temporalis muscle activity: correlation with neuropsychological findings. *Headache*, **33**(3):121-124. [doi:10.1111/j.1526-4610.1993.hed3303121.x]

Wang, W., Schoenen, J., 1994. Reduction of temporalis exteroceptive suppression by peripheral electrical stimulation in migraine and tension-type headaches. *Pain*, **59**(3):327-334. [doi:10.1016/0304-3959(94)90018-3]

Wang, W., de Pasqua, V., Gerard, P., Schoenen, J., 1995. Specificity and sensitivity of temporalis ES2 measurements in the diagnosis of chronic primary headaches. *Headache*, **35**(2):85-88. [doi:10.1111/j.1526-4610.1995.hed3502085.x]

Woolf, N.J., 1991. Cholinergic systems in mammalian brain and spinal cord. *Prog. Neurobiol.*, **37**(6):475-524. [doi:10.1016/0301-0082(91)90006-M]

Yemm, R., 1972. Reflex jau opening following electrical stimulation of oral mucose membrane in man. *Arch. Oral Biol.*, **17**(3):513-523. [doi:10.1016/0003-9969(72)90067-2]

Yu, S.K., Schmitt, A., Sessle, B.J., 1973. Inhibitory effects on jaw muscle activity of innocuous and nocuous stimulation of facial and intraoral sites in man. *Arch. Oral Biol.*, **18**(7):861-870. [doi:10.1016/0003-9969(73)90056-3]

Zwart, J.A., Sand, T., 1995. Exteroceptive suppression of temporalis muscle activity: a blind study of tension-type headache, migraine, and cervicogenic headache. *Headache*, **35**(6):338-343. [doi:10.1111/j.1526-4610.1995.hed3506338.x]