<u>ORIGINAL RESEARCH</u>

Diagnostic Value of Blink Reflex Combined with Trigeminal Somatosensory Evoked Potential in Trigeminal Neuralgia

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ABSTRACT

Objective • To explore the diagnostic value of blink reflex combined with trigeminal somatosensory evoked potential (TSEP) in trigeminal neuralgia.

Methods • A total of 147 patients with trigeminal neuralgia were enrolled as the research objects between February 2022 and February 2023. After admission, all underwent blink reflex on affected/healthy sides and TSEP examinations. The diagnostic value of the blink reflex combined with TSEP was analyzed.

Results • The latency of R1, R2, and R2' waves (refers to the different nerve signal waveforms that are recorded when a facial nerve conduction speed test is performed) on the affected side was significantly longer than that on the healthy side (t = 26.324, 18.391, 20.801, Ps < .001), and latency of W1, W2 and W3 waves was also significantly longer than that on

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INTRODUCTION

Trigeminal neuralgia is a condition characterized by sudden, intense pain in the trigeminal nerve of the face. Patients may experience sensations such as electrocautery, tearing, and pinprick-like feelings during the attack, which can be very painful and last for several minutes.¹ Trigeminal neuralgia triggers include activities like talking, yawning, chewing, and most patients have unilateral pain.² Long-term severe pain can also have negative effects on a patient's physical and mental health.³ Uptodate, the pathogenesis of trigeminal neuralgia is not fully understood, it is believed to be the main physiopathological mechanism of perivascular the healthy side (t = 16.045, 10.814, 10.349, P < .001). The results of Pearson correlation analysis showed that the latency of R1, W1, W2, and W3 waves was positively correlated with the VAS score (r = 0.539, 0.611, 0.577, 0.586, P < .001). The results of receiver operating characteristic (ROC) curves analysis showed that area under the curve (AUC) values of R1, R2, R2, W1, W2, and W3 waves latency on the affected side in the diagnosis of trigeminal neuralgia were 0.753, 0.634, 0.651, 0.748, 0.756 and 0.736, respectively. The AUC of combined detection was 0.926, significantly greater than that of the single index (P < .001).

Conclusion • Blink reflex combined with TSEP monitoring can improve the diagnostic value of trigeminal neuralgia, and the latency is related to pain. (*Altern Ther Health Med.* 2023;29(8):352-355).

compression of the trigeminal nerve in the pontine cerebellar corner region.⁴ Electrophysiological tests like instantaneous reflexes and somatosensory evoked potentials of the trigeminal nerve can be used to evaluate the trigeminal nerve structure and brainstem central conduction pathway, but the methods used for stimulation and recording can vary.^{5,6} This study analyzed the diagnostic value of transient reflex combined with trigeminal somatosensory evoked potential for trigeminal neuralgia in 147 patients with trigeminal neuralgia from February 2022 to February 2023. Epidemiological research on trigeminal neuralgia has shed light on the prevalence and burden of this condition in the population. Studies have indicated that trigeminal neuralgia is relatively rare, with an estimated annual incidence of approximately 4 to 13 cases per 100 000 individuals worldwide⁷. The condition is more commonly reported in individuals over the age of 50, with a higher prevalence observed in females compared to males. As our understanding of trigeminal neuralgia continues to evolve, epidemiological research serves as a crucial tool in identifying at-risk populations, informing healthcare policies, and developing targeted interventions to alleviate the burden of this distressing condition.

PATIENTS AND METHODS Objectives

A total of 147 patients who are diagnosed with trigeminal neuralgia from February 2022 to February 2023 were selected as the study subjects, including 60 males and 87 females; the age range was 45-76 years, with a mean age of (58.61 ± 9.84) years; Age distribution as follows: 45-49 years: 23 patients, 50-54 years: 19 patients, 55-59 years: 25 patients, 60-64 years: 35 patients, 65-69 years: 24 patients, 70-76 years: 21 patients. The lesion side was left in 64 cases and right in 83 cases; there were 48 cases with a history of hypertension, 26 cases with a history of diabetes, and 17 cases with a history of coronary heart disease.

Inclusion and Exclusion Criteria

Inclusion criteria: 1. Participants must be diagnosed with trigeminal neuralgia with clinical symptoms and auxiliary examination results that meet the diagnostic criteria outlined in the "Chinese Expert Consensus on Diagnosis and Treatment of Trigeminal Neuralgia." 2. Participants must have a unilateral lesion. 3. Both blink reflex and trigeminal somatosensory evoked potential tests should be performed.

Exclusion Criteria: 1. Participants with secondary trigeminal neuralgia. 2. Individuals with a history of trigeminal neuralgia recurrence. 3. Participants with severe internal medicine diseases that cannot be controlled. 4. The use of analgesics before hospitalization. 5. Participants with a history of related treatments such as radiofrequency thermocoagulation and gamma knife irradiation. 6. Individuals with mental disorders.

Methods

Blink reflex examination: The patient was positioned in a supine/back-lying and advised to relax. The stimulating electrodes were placed at the supraorbital notch, with one electrode deep and the other shallow (2 cm apart). The recording, reference, and ground electrodes were placed at the midpoint of the lower eyelid muscle, the outer canthus, and the wrist, respectively. The instrument used was a keypoint multi-channel electromyography-evoked potential instrument (Viasys Healthcare, Denmark, 20162072196), with the following parameters: frequency of 0.5 Hz, current of 10-20 mA, and analysis of R1, R2, and R2' wave (refers to the different nerve signal waveforms that are recorded when a facial nerve conduction speed test is performed) latencies for 100 ms. Conducting trigeminal somatosensory evoked potential examination where The patient was positioned in a supine/back-lying and instructed to relax. The stimulating electrodes were placed inside the ipsilateral inferior orbital fissure, with one electrode deep and the other shallow (1 mm apart). The recording, reference, and ground electrodes were placed on the top of the head, the seventh cervical vertebra, and the forehead, respectively. The instrument used was a Keypoint multi-channel electromyography-evoked potential instrument, with the following parameters: pulse width of 0.05 ms, frequency of 3 Hz, stimulation intensity of 4-6 times

the sensory threshold, and superposition of 200 times. The analysis was conducted for 10 ms, and the latencies of W1, W2, and W3 waves were recorded. The visual analog scale (VAS) was used to evaluate the facial pain of the patients.

The scintillation reflex test and trigeminal somatosensory evoked potential test are used for the following reasons: Scintillation reflex test is an electrophysiological method to evaluate the structure of the trigeminal nerve and the central brain stem pathway by stimulating the trigeminal and facial nerves of the face. By recording the stimuli that trigger the reflex, abnormalities in trigeminal nerve conduction and potential dysfunction can be detected. This test can provide information about trigeminal nerve terminal conduction and help diagnose and understand the pathophysiological mechanism of trigeminal neuralgia. The trigeminal somatosensory evoked potential test can objectively reflect the conduction of electrical impulses. If there is damage or lesion in the conduction pathway, the disturbance of induced excitation conduction can change the waveform or parameters of the induced potential. By detecting W1, W2, and W3 waves (different waveforms of trigger potentials, which are recorded when neurophysiological tests are performed) from the trigeminal nerve, the conduction status of the trigeminal nerve in the brain stem can be assessed. This test helps to understand the pathophysiological changes of trigeminal neuralgia, such as edema, thickening, and distortion and provides an important reference for diagnosis and treatment.

Through the combination of these two tests, we can fully understand the characteristics and mechanisms of trigeminal neuralgia and provide support for its accurate diagnosis and effective treatment.

Statistical analysis

The data were processed using Statistical Product and Service Solutions (SPSS) version 22.0 software (IBM, Armonk, NY, USA). Normally distributed continuous data were expressed as mean \pm standard deviation ($\overline{x \pm s}$) and compared using a *t* test. Count data were expressed as frequency (n) or rate (%) and compared using the chi-square test. Pearson correlation coefficient was used for correlation analysis. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic value of the blink reflex combined with trigeminal somatosensory evoked potential, and the area under the curve (AUC) was used to evaluate the diagnostic performance. *P*<.05 was considered statistically significant.

RESULTS

Results of incubation period detection of each wave in the patient's blink reflex

The incubation period of R1, R2, and R2' waves on the affected side was significantly longer than that on the healthy side, and the differences were statistically significant (t = 26.324, 18.391, 20.801, P < .001). The result indicates that the wave latency of the affected side is significantly prolonged in the blink reflex test, which may be related to the abnormal function of the trigeminal nerve. See Table 1.

Results of incubation period detection of each wave in the patient's trigeminal somatosensory evoked potential

The incubation period of W1, W2, and W3 waves on the affected side was significantly longer than that on the healthy side, and the differences were statistically significant (t = 16.045, 10.814, 10.349, P < .001), t = 16.045, 10.814, and 10.349, respectively. This indicates that the wave latency of the affected side is significantly prolonged in the trigeminal sensory evoked potential test, which may reflect the abnormality of the trigeminal nerve conduction pathway. See Table 2.

Correlation between blink reflex, trigeminal somatosensory evoked potential, and VAS score

Patients had a VAS score of (4.59 ± 1.15) . The results of Pearson correlation analysis showed that the latency of R1, W1, W2, and W3 waves on the affected side was positively correlated with the VAS score (r = 0.593, 0.611, 0.577, 0.568, P < .001), but there was no significant correlation between R2 and R2' wave latency and VAS score (P = .084, 0.119). This means that the blinking reflex and the prolonged latency of trigeminal sensory evoked potentials may be closely related to the severity of trigeminal neuralgia. See Table 3.

Diagnostic value of blink reflex combined with trigeminal somatosensory evoked potential for trigeminal neuralgia

The results of the ROC curve analysis showed that the AUCs for the diagnosis of trigeminal neuralgia in the latent period of R1, R2, R2', W1, W2, and W3 on the affected side were 0.753, 0.634, 0.651, 0.748, 0.756, and 0.736, respectively, and the AUC for diagnosis of the above indexes was 0.926, which was significantly higher than that of each index (95%*CI* [0.897~0.955], *P*<.05). See Figure 1, Table 4.

DISCUSSION

Our findings regarding the delay in the latency period of R1, R2, and R2' waves on the affected side in trigeminal neuralgia patients are consistent with previous studies, supporting the idea of trigeminal afferent nerve function impairment in this condition. Regarding trigeminal somatosensory evoked potentials, our results showing significantly prolonged latency of W1, W2, and W3 waves on the affected side are in line with previous research findings, indicating possible pathological changes within the trigeminal nerve.

Trigeminal neuralgia is a complex condition with multiple proposed mechanisms. The vascular compression theory, supported by previous research, suggests that neurovascular conflict leads to nerve compression and irritation.³ Our study's findings align with this theory, as we observed nerve function impairment in trigeminal neuralgia patients.

The blink reflex arc of blink reflex detection is composed of the trigeminal nerve, facial nerve, and brainstem structures. This reflex is triggered by stimuli like tapping the face, sound, and light, and serves as a defense mechanism to protect the eyes. In this test, stimulating the supraorbital nerve will produce three reflexes on the stimulated side (R1 and R2 components) and the contralateral side (R2' component), where R1 is an early reflex,
 Table 1. Detection results of each wave latency in the patient's blink reflex (±s, ms)

Side differentiation	n	R1	R2	R2'
affected side	147	12.88 ± 0.71	37.14 ± 2.69	38.52 ± 2.41
healthy side	147	10.79 ± 0.65	31.84 ± 2.23	32.84 ± 2.27
t		26.324ª	18.391ª	20.801ª
P value		<.001	<.001	<.001

a difference between the affected side and the healthy side is statistically significant, $P\,{<}.001$

Table 2. Results of latency detection of each wave in the trigeminal nerve sensory evoked potential of patients $(\pm s, ms)$

Side differentiation	n	W1	W2	W3
affected side	147	1.05 ± 0.11	1.95 ± 0.10	2.78 ± 0.13
healthy side	147	0.87 ± 0.08	1.83 ± 0.09	2.64 ± 0.10
t		16.045ª	10.814ª	10.349ª
P value		<.001	<.001	<.001

a difference between the affected side and the healthy side is statistically significant, $P < .001\,$

Table 3. The correlation between blink reflex, trigeminalsomatosensory evoked potential, and VAS score

Indicators	r	P value	
R1	0.539ª	<.001	
R2	0.236	.084	
R2'	0.201	.119	
W1	0.611ª	<.001	
W2	0.577 ^a	<.001	
W3	0.586ª	<.001	

^aassociation is statistically significant, P < .001

 Table 4. Diagnostic value of blink reflex combined with

 trigeminal somatosensory evoked potential for trigeminal

 neuralgia

Indicators	AUC	95%CI	P value	Sensitivity (%)	Specificity (%)
R1	0.753	0.697~0.810ª	<.001	68.03	74.15
R2	0.634	0.571~0.697ª	<.001	36.05	85.71
R2'	0.651	0.588~0.714 ^a	<.001	53.06	73.47
W1	0.748	0.692~0.804ª	<.001	80.95	59.18
W2	0.756	0.700~0.812ª	<.001	84.35	58.50
W3	0.736	0.680~0.792ª	<.001	59.86	77.55
Combined	0.926	0.897~0.955ª	<.001	85.71	87.07

^aassociation is statistically significant, P < .001

Figure 1. ROC curve for the diagnosis of trigeminal neuralgia using blink reflex combined with trigeminal somatosensory evoked potential.



and R2 and R2' are late reflexes.8 The R1 reflex pathway is trigeminal nerve-trigeminal sensory nucleus-same side facial nerve nucleus-facial nerve, belonging to the skin exteroceptive nature; R2 and R2' are multi-axonal conduction reflex arcs, possible pathways are (1) skin receptor-trigeminal spinal nucleus-medulla oblongata-same side facial nerve nucleus-facial nerve, (2) trigeminal spinal nucleus-reticular structurecontralateral facial nerve nucleus-facial nerve. When one side of the patient's trigeminal nerve is completely damaged, all three reflex arcs disappear when the affected side is stimulated and are normal when the healthy side is stimulated; when the trigeminal nerve is not completely damaged, stimulating the affected side shows that the three reflex arcs have an extended latency period.⁹ The results of this study show that patients have varying degrees of delay in the latency period of the affected side R1, R2, and R2' waves, and no waveform disappearance is detected, which is consistent with previous reports,¹⁰ suggesting that the affected side has trigeminal afferent nerve function impairment.

Trigeminal somatosensory evoked potentials can objectively reflect the conduction of electrical impulses. If there is damage or lesion in the conduction pathway, the induced excitation conduction disorder will change the waveform or parameters of the induced potential.¹¹ The W1, W2, and W3 waves of trigeminal somatosensory evoked potentials are derived from the Gasserian ganglion, trigeminal nerve REZ area, and trigeminal sensory nucleus in the brainstem, respectively. Among them, the W1 wave latency is stable and has a high reference value. In this study, the latency of the affected side W1, W2, and W3 waves was significantly longer than that of the healthy side, which is consistent with the research results. The delay in the conduction of each component may be related to pathological changes in the trigeminal nerve, such as edema, thickening, and twisting. Based on current evidence, it appears that the nerve damage associated with trigeminal neuralgia occurs between the Gasserian ganglion and the main nucleus in the brainstem. This suggests that the damage is already present before the nerve conduction reaches the brainstem, which aligns with the theory of vascular compression mechanism. Trigeminal neuralgia patients will experience recurrent pain, and the stronger the pain signal, the more severe the nerve damage. The results of the correlation analysis in this study show that the latency of the affected side R1 wave, W1, W2, and W3 waves are positively correlated with the VAS score, suggesting that the blink reflex combined with trigeminal somatosensory evoked potential monitoring can also be used for the assessment of trigeminal neuralgia, providing information on the recovery of trigeminal nerve conduction after treatment. Both blink reflex and trigeminal somatosensory evoked potential detection can help understand trigeminal nerve function, but due to methodological differences and waveform instability, there are certain limitations in clinical applications. To improve the diagnostic efficiency of trigeminal neuralgia, this study used ROC curve analysis to analyze the diagnostic value of blink reflex combined with trigeminal somatosensory evoked potential. It was found that the above monitoring has a certain

diagnostic value for trigeminal neuralgia, and the combined diagnostic efficiency is significantly improved, with an AUC of 0.926 and a 95% CI. The clinical combined application of blink reflex and trigeminal somatosensory evoked potential for the diagnosis of trigeminal neuralgia can complement and enhance the stability and reliability of the diagnosis.

In this study, we monitored the blink reflex and trigeminal somatosensory evoked potential of patients and discussed its clinical significance in the diagnosis of trigeminal neuralgia. The results show that these monitoring indicators have some guiding value for evaluating the condition of patients with trigeminal neuralgia. Although this study has limitations that need to be considered. One limitation is the small sample size which may affect the stability and generalization of the research results. Conducting future multicenter, large-sample studies could help validate our findings more fully. Additionally, methodological differences may have influenced the results due to variations in the detection methods of the blinking reflex and trigeminal somatosensory evoked potential in the clinic. Therefore, future research should aim to optimize monitoring methods to improve the accuracy and consistency of detection.

In summary, the monitoring of the blink reflex combined with trigeminal somatosensory evoked potential can improve the diagnostic value of trigeminal neuralgia. The latency of its components is related to the patient's pain and has a certain guiding value for the assessment of the patient's condition. However, the sample size included in this study is small, and further confirmation is needed through multicenter, large-sample data analysis.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

HaoS and TQ designed the study and performed the experiments, WG and HaiS collected the data, YL, YD, and YW analyzed the data, HaoS and TQ prepared the manuscript. All authors read and approved the final manuscript.

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