

## BLINK REFLEX IN MIGRAINE

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### Abstract

Background: The trigemino vascular system is involved in the pathophysiology of migraine. Blink reflex is an easy method to study trigeminal system. This study aimed to evaluate the blink reflex (BR) (R1 R2i R2c latencies) in patients with migraine with or without aura and to compare their BR with healthy individuals. Materials and Methods: This is an analytical cross-sectional study of 30 migraine patients and 30 age-matched controls assessed by a blink reflex study collected in the department of neurology from 2023 to 2024 at Saveetha Medical College and Hospital. The blink reflex latency mean values and p values in migraine patients were compared with those of the control group. The right- and left-sided R1, as well as R2-i and R2-c latency values, were analyzed with a students t test. Results: Both right and left R1 latency are significantly longer in the migraine group compared to the control (p 0.0001), indicating delayed early reflex responses in migraine. Specifically, females tend to have longer R1 ipsilateral and contralateral late reflex components in migraine, and this is statistically significant with P-value <0.05. Conclusion: The results obtained in the BR in the present study demonstrate the presence of dysfunction in the trigemino-vascular system or in its connections with the brain stem in migraine headaches. Further studies are required to assess if the severity, frequency, and subtype (episodic or chronic, without aura) of migraine have any bearing on their blink reflex and if blink reflex abnormalities can be used as a prognostic tool.

**Keywords:** Blink Reflex; Trigemino Vascular System; Migraine.

### INTRODUCTION

Cerebral vessels, the trigeminal nerve and its brain stem nuclei, as well as some cortical centers are all involved in the pathogenesis of migraine attack. Pain-sensitive cranial structures (large vessels, pia mater vessels, dura mater and venous sinuses) are innervated mostly by the first branch of the trigeminal nerve. In case of trigemino-vascular system activation, impulses are transmitted centrally to the spinal trigeminal nucleus and then they reach the cerebral cortex via the thalamus. Apart from that central transmission of pain, neurotransmitters are also released from the trigeminal nerve endings located around the vessels. Sensory fiber endings of the trigeminal nerve release calcitonin gene-related peptide (CGRP), P substance (SP), neurokinin A, and nitric oxide (NO). All those compounds are involved in the neurogenic inflammation that may activate nociceptive fibers, leading to the central transmission of the pain impulses. According to the predominant recent views, excessive discharges within the spinal nucleus of the trigeminal nerve are considered the primary cause of headache in migraine. As the result of that stimulation, neurogenic inflammation ensues, as well as secondary vascular changes related to the release of inflammatory mediators [1, 2, 3, 4, 5].

Electrophysiological studies, including blink reflex studies, remain the most valuable method of assessment of trigeminal nerve function. The blink reflex constitutes bilateral electromyographic reaction of the orbicularis oculi muscle in response to unilateral electrical stimulation of the supraorbital nerve, which is a branch of the trigeminal nerve. The blink reflex consists of two responses: an early response (R1) which is exclusively ipsilateral to the side of stimulation, and a late bilateral response, which is ipsilateral (R2i) or contralateral (R2c) to the side of stimulation. The reflex arc of R1 passes through the pons: stimulation from sensory fibers is transmitted to the sensory nucleus of the trigeminal nerve in the pons.

In the case of R2 and R2', the reflex arc passes through the medulla oblongata: stimulation from sensory fibers is transmitted to the nucleus tractus spinalis of the trigeminal nerve, and then travels through the polysynaptic uncrossed (R2i) or crossed (R2c) neuronal pathway of the reticular formation to the motor nucleus of the facial nerve – the ipsilateral (R2i) and contralateral (R2c) [6, 7]. In a study by Bank et al, 43 migraine patients and 31 healthy individuals were studied using blink reflex, and R1 latency elicited by a supraorbital stimulation did not differ significantly from those of the control group, while significantly longer R2 latencies were found.(8) This study aimed to evaluate blink reflex(BR)(R1 R2i R2c latencies )in patients with migraine with or without aura and to compare their BR with healthy individuals .

#### **Aim and Objectives:**

- The aim of this study is to investigate the presence or absence of latency prolongation in patients with migraine using blink reflex test
- To assess if blink reflex can serve as a marker of migraine in patients who have unclassified headache

#### **MATERIALS & METHODS**

- It is an analytical cross sectional study of 30 migraine patients and 30 age matched controls assessed by blink reflex (BR) study collected in the department of Neurology from 2023-2024 of Saveetha Medical College and Hospital as per the inclusion and exclusion criteria mentioned below.
  - Ethics committee approval and informed consents from patients were obtained.
- **Inclusion Criteria:**
    1. Patients diagnosed with migraine with/without aura according to HIS (International headache society 2) classification.
    2. Patients who are co-operative and are willing to give informed consent.
    3. Patient from 18-50 years of age of either gender
  - **Exclusion Criteria:**
    1. Present or past systemic or neurological disease
    2. Patients who had received prophylactic treatment within the previous 1 month.
    3. Patient less than 18 years and more than 50 years.
    4. Patients who are non co-operative and are not willing to give informed consent.

**Procedure:** it is non-invasive method .NATUS ULTRAPRO S 100 9033G070 four channel machine in the clinical Neurophysiology lab was used.

- The test procedure is clearly explained to the patient. • All the subjects who will be selected are asked to fill the data sheet with informed written consent. Stimulation of the trigeminal nerve activates a reflex pathway along the brainstem, resulting in a contraction of the orbicularis oculi. The Blink Reflex reflects the integrity of the afferent and efferent pathways including the proximal segment of the facial nerve.
- Recording Sites: 2 Channel Study
- Active: Placed over the inferior portion of the orbicularis oculi near the inner canthus
- Reference: Placed 2 cm laterally
- Ground: Placed on the forehead
- Stimulation: Ipsilateral supraorbital notch of same side
- Cathode: Supraorbital notch
- Anode: 2-2.5cm directly above cathode on forehead (rotation of anode around cathode helps establish the best position of stimulating electrode and reduce shock artifact)
- Measurements: Onset latency of R1 response-ipsilateral to the side of stimulation only Onset latency of R2 response ipsilateral and contralateral to the side of stimulation

### Precautions Taken

1. Procedure was explained and informed consent was taken.
2. The stimulation and recording site were properly cleaned. Before stimulation the subjects were relaxed.
3. Ambient room temperature(27-33 degree) was maintained in clinical physiological laboratory.
4. Electrode placements were checked prior to stimulation.

### Statistical Analysis :

All parameters assessed. R1 R2i R2c latencies compared with 30 age matched controls. SPSS software was used to evaluate data. students t test (t-statistic) was used for the comparison. p values were obtained

### OBSERVATIONS & RESULTS

Recording from 30 patients and 30 controls who fulfill the inclusion criteria yielded analyzable blink reflex study data. Mean, Standard deviation, p values for R1, R2i, and R2c are expressed below out of 30 patients 24 are females and 6 are males .3 male and 8 female patients who belongs to Age group 20-30, 2 male and 10 female patients who belongs to Age group 31-40, 1 male and 6 female patients who belongs to Age group 41-50 .The percentage of females and males 80%&20%. The percentage of male and female of Age group 20-30 is 50% & 33%. The percentage

of male and female of Age group 31-40 is 33% & 42%. The percentage of male and female of Age group 41-50 is 17% & 25%. The blink reflex latency mean values and p values in migraine patients compared with control group. Distribution of demographic variables of migraine and control group depicted in (table 1). The right- and left-sided R1, as well as R2i and R2c latency values were compared with those of the control group, and longer latencies were detected in the patient group with a p value < 0.0001 which is statistically significant (table 2). Longer latencies for R1 and R2i on the left side, and for R2c on right side, compared to males (table 3)

**Table 1: Distribution of Demographic Variables of Migraine and Control Group**

Variable	Migraine group	Healthy controls
Age (in years) (Mean ± SD)	38.2 ± 9.2	36.8 ± 10.5
Gender		
Males	6	12
Females	24	18

**Table 2: Comparison of Latency Values Obtained in Migraine and Control Groups on Eye Blink Reflex Test**

Latency	Migraine group (Mean ± SD)	Control group (Mean ± SD)	t-statistic(P-value)
R1 Latency (ms)			
Right	11.79 ± 0.54	9.9 ± 1.2	7.86 (0.0001)*
Left	12.009 ± 0.31	10.1 ± 0.91	10.87 (0.0001)*
R2 Latency (ms)			
Right R2i	35.596 ± 0.24	32.5 ± 1.34	12.45 (0.0001)*
Right R2c	38.27 ± 0.66	34.2 ± 0.93	19.54 (0.0001)*
Left R2i	34.21 ± 0.83	31.7 ± 0.32	15.45 (0.0001)*
Left R2c	36.96 ± 0.58	33.8 ± 0.87	16.55 (0.0001)*
R1-Early component ;R2i-Ipsilateral late component;R2c-Contralateral late component SD-Standard deviation T test-Student's t-test			

1. R1 Latency (ms) - Both right and left R1 latencies are significantly longer in the migraine group compared to the control group (p < 0.0001 for both comparisons), indicating delayed early reflex responses in migraine patients.
2. R2 Latency (ms):-For all components (right R2i, right R2c, left R2i, and left R2c), latencies are significantly prolonged in the migraine group compared to the control group (p < 0.0001 for all comparisons). This suggests delayed ipsilateral and contralateral late reflex components in migraine patients.

**Table 3: Gender based Comparison of Latency Values in Eye Blink Reflex Test among Patients**

Latency	Males	Females	t-statistic (P-value)
RIGHT			
R1	11.96 ± 0.58	11.74 ± 1.33	0.83 (0.4)
R2i	35.2 ± 3.02	35.69 ± 3.43	0.58 (0.55)
R2c	36.93 ± 3.37	38.6 ± 2.1	2.3 (0.02)*
LEFT			
R1	11.4 ± 1.34	12.16 ± 1.04	2.45 (0.01)*
R2i	33.16 ± 2.24	34.47 ± 2.31	2.22 (0.02)*
R2c	36.43 ± 3.18	37.09 ± 2.58	0.88 (0.38)

From the above table, it was observed that

- Specifically, females tend to have longer latencies for R1 and R2i on the left side, and for R2c on right side, compared to males and its is statistically significant with P-value <0.05. However, there are no significant differences observed in certain parameters (R1 and R2i on the right side, and R2c on the left side).

## DISCUSSION

The purpose of the present study is to extend the knowledge of electrophysiological investigation of blink reflex. Involvement of trigeminal nerve in the pathophysiology of migraine has been detected in experimental studies on animals and humans. This was secondary to the understanding that the trigeminal system innervated the extra and the intracranial arteries and the nociceptive pathway.

This study was conducted to investigate the trigeminal nerve involvement non-invasively. Studies conducted with regards to blink reflex in migraine have priory shown differences in inference. Aktekin et al. conducted BR tests on migraine patients during interictal phase using standard methods and compared measurements of R1 and R2 latencies, R2 amplitudes, and area with those of control group without finding any significant intergroup difference(9)

Sand et al. compared patients who experience migraine-type headaches with control group during interictal phase, and stated that R2 amplitude values were not different.(10) In a study by Bank et al. 43 migraine patients and 31 healthy individuals were studied using blink reflex, and R1 latency elicited by a supra orbital stimulation did not differ significantly from those of the control group, while significantly longer R2 latencies were found in 22 (51.2%).(8)

In the present study blink reflex latency mean values and p values in migraine patients compared with control group. The right- and left-sided R1, as well as R2i and R2c latency values were compared with those of the control group, and longer latencies were detected in the patient group with a p value < 0.0001, which is statistically significant. Longer latencies were found in female individuals may be due to selection bias because of more number of females in the present study. In the present study amplitudes are not taken as priority

## CONCLUSION

The results obtained in blink reflex in the present study demonstrates presence of dysfunction in trigemino-vascular system or in its connections with the brain stem in patients with migraine headache and support trigemino-vascular hypothesis in migraine. This dysfunction is also present in the interictal period.

Further studies are required to asses if severity, frequency, subtype (episodic or chronic, with or without aura) of migraine has any bearing on the blink reflex and if blink reflex abnormalities can be used as a prognostic tool.

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