Evoked Potentials and Blink Reflex Patterns in Patients with Migraine without Aura and Frequent Episodic Tension-Type Headache. An Overview.

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Abstract
Headache is defined as any pain related to the head or the face. Headache is a common and burdensome condition and is considered one of the major complaints in everyday life for many people. The majority of people will experience headaches at a certain time in their life. There are many different types of headaches, with tension headaches being the most prevalent. Although most headaches are not hazardous, a few types might be a sign of a serious underlying problem. Four types of headaches are classified as primary headache disorders: trigeminal autonomic cephalalgias, migraine, tension-type headaches, and other primary headache disorders. Primary headache disorders are headaches that have no connection with an underlying medical condition. Numerous researches have focused on the central electrophysiological patterns in individuals with primary headache disorders. Despite the discrepancies between different research efforts, the overall picture strongly suggests that primary headache disorders can be the source of multiple patterns found in visual evoked potentials, Brainstem Auditory Evoked potentials and blink reflex. These patterns could be helpful in the diagnosis of different primary headache disorders as well as understanding the pathophysiology of various headache disorders.

Key words: Migraine, Tension-Type, Visual Evoked Potentials, Brainstem Auditory Evoked Potentials, Blink Reflex

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Introduction
For many people, headache is a serious issue in everyday life. The majority of people will experience headaches at some point in their life. The primary sign of a headache is pain in the head or face. There are many different types of headaches, with tension headaches being the most common. While most headaches are not harmful, other kinds might be a sign of a more serious underlying disease.

As per the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, headache disorders came in third place among 369 conditions in terms of years lived with disability (YLDs) for both genders. Among individuals aged 15–49, they ranked first, accounting for 8% of all-cause YLDs. Migraine came in second place, accounting for 7.3% of these YLDs. (1)

In a hospital-based study in Sohag university hospital (a tertiary center in Sohag governorate),
89% of cases had a primary headache, 10.2% had a secondary headache, and 0.8% had painful cranial neuropathy. 50.6% of headaches were of the migraine type and 33.6% were of the tension type. Migraine was the most common presentation due to the under recognition of tension type headache due to its lower disability than migraine, according to patients and medical professionals. It was discovered that whereas women predominate in primary headaches, (especially migraine), the male to female ratio for tension-type headaches is one to five. Every year, 12–15% of Americans suffer from the two main types of headache disorders: migraine and tension-type headache. The fourth most frequent reason people visit the emergency room is headaches. And one of the top 10 reasons people live with disability in the globe. Three quarters of those who get migraines have migraines with aura, and around one-third of them have a premonitory stage before their headaches start. In a 2022 study, the researchers discovered that 52.0% of the populations investigated had an active headache problem of any form (males 44.4%, females 57.8%), 14.0% had migraine (males 8.6%, females 17.0%), and 26.0% had tension-type headache (males 23.4%, females 27.1%). In contrast, tension-type headache only accounted for 7.2 million YLDs worldwide in 2016 whereas migraines caused 45.1 million due to their significantly higher disability weight.

Corona virus disease (COVID 19) period and lifestyle are both impacted by primary headache diseases. Stress, poor nutrition, bad posture, and inactivity are all detrimental to one's lifestyle. One result of COVID-19 is increased screen time, which includes social media and virtual meetings. Other effects include psychological stress and social isolation, in which it is seen have a bad impact on motivation, concentration, attention, problem solving, reasoning, perception, and coordination.

**VEP patterns in patients with migraine without aura**

In neurological diseases, visual evoked potentials (VEPs) are a reliable electrophysiological technique. VEPs express the electrical activity of the visual pathways all the way up to the optic nerve and calcarine cortex. Regardless of the patient's level of consciousness or attention, these potentials provide a non-invasive method of examining how the human visual system functions by monitoring neural pool activity in response to stimuli. Early studies of VEP changes in migraine revealed that none of the migraine patients or the healthy individuals had VEP amplitude asymmetries. From the central electrode, individuals with migraines without aura did not show any discernible variation in VEP latencies or amplitudes. Studies that examined the flash or pattern evoked potentials' amplitude came up empty. First, the VEP amplitude (averaged over blocks and days) did not differ between the migraine group and the control group. For both medium and large checks, migraine with aura patients showed substantially greater P1N2 amplitude and higher N1P1 amplitude than Migraine without aura patients.

In the preattack phase (within 72 hours of the following attack), P1N2 amplitude was greater than in an interictal recording from the same patient. VEP and photophobia did not appear to be correlated. Patients with MA had larger VEP N1P1 and P1N2 amplitudes than those with Migraine without aura. About 80% of migraine with aura and 70% Migraine without aura have interhemispheric asymmetry that is significant.

As regard the habituation VEP which by definition is the reduction in behavioral response to recurrent stimuli that in turn have no association to neither sensory adaptation, motor fatigue nor fatigue. Between migraineurs and controls, there were no variations in VEP amplitude habituation. But in 2015, deficient VEP habituation to repeated stimuli was noticed by Veronika Rauschel. et al., and Di Clemente L. et al., Migraine without aura in volunteers in good health, who typically lack internal habituation, can get more used to recurrent visual stimuli after receiving anodal tDCS (Transcranial Direct Current Stimulation) across the visual cortex. Habitation of N70-P100 to controls and interictal migraineurs was noticed. There was no difference in first block amplitudes or N70, P100, and N145 latencies between the healthy controls and migraineurs habituation of the N1-P1 transient -VEP component was lesser in between attacks. During an attack,
the interictal transient -VEP (as well as Steady-state VEP) abnormalities were normalized. (21)
Concerning Steady-state VEP (SS-VEP), by employing the state (SS) response, which is a neurop-physiological response that is stationary and produced overly by repetitive exposure to the (above 4 Hz-visual stimulus) and that can be examined using a Fourier transform. In Migraine without aura as well as MA, the SS-VEP frequently has a larger amplitude. (22) Relative reduction in SS-VEP response was detected also by Nguyen BN, et al 2016. (23)

**VEP in patients with frequent episodic tension type headache**
In tension-type headache patients, P100 wave and P2 wave latencies were normal. P100, P2, N3, and P3 wave latencies were shown to be greater in migraine patients when compared to control group and patients with tension type headache in a study comparing tension type headache with migraine patients. (24) Also, when compared to healthy controls, it was revealed that children with tension type headache did not exhibit any appreciable VEPs abnormalities. (25,26)
Both migraine and tension type headachewere shown to have the same SSVEP abnormalities. These results prompted the authors to postulate that the two basic headache types have a common neurological malfunction that manifests as an excessive brain response to visual stimuli, presumably as a result of aberrant cortical inhibition. (27) Laila Elmously et al., in 2015 documented that there were no significant discrepancies in the amplitude of P100 or latency between the tension type headache patient group and the control group in a study carried out in Egypt. tension type headache's negative effects on cortical excitability, particularly in the occipital cortex, may be accountable for this. These findings suggest that, in terms of VEP, migraine can be differentiated from tension type headache. (28)

**Brainstem Auditory Evoked Potentials (BAEB) patterns in patients with migraine without aura:**
The electrical signals generated by the nervous system within the first 10 ms after a transient acoustic stimulus are known as brainstem auditory evoked potentials (BAEPs). They were used for hearing testing and audimetry, intraoperative monitoring, neurophysiological research, and neuro-diagnostic testing. The earliest description of brainstem auditory evoked potentials (BAEPs) by Jewett et al. (1970) identified them as a group of 5-7 vertex-positive waves that were activated by sound and originated in the brainstem. (29) These potentials have been used to reveal abnormalities of the auditory pathways in the auditory nerve and brainstem. They are also referred to as short-latency auditory evoked potentials (SLAEPs), brainstem auditory evoked responses (BAERs), and auditory brainstem responses (ABRs).

AEPs, or auditory equivalent of potentials, are classified as having a short, intermediate, or long delay based on the auditory circuits that act as their generators. Although middle- and long-latency AEPs emerge in the auditory cortex, short-latency AEPs start in the brainstem. (30)
Studies of brainstem auditory evoked responses (BAER), or short latency AEPs, show a variety of diverse outcomes in migraine. Neither asymmetries nor abnormalities could be detected when compared to controls and when recording (BAER) in migraine with aura patients in more than 8 days after attack according to Benna et al., 1985 and Sand T, Vingen JV., 2000. (31,32) On other hand, Increased and asymmetric wave I-V latencies could be detected when recording (BAER) in Migraine without aura patients in more than 1 week after attack. (33) But during the attacks, Prolonged interp- eak latencies in Migraine without aura (as well as in migraine with aura). patients was revealed with No interictal differences when compared to control group. Also, Interictal Asymmetry in latencies of I, II, III and V waves could be detected. (34) The latency and amplitude of the N1, P2, and N2 components of cortical long-latency auditory evoked potentials did not differ significantly between migraineurs and controls. (35)

The study of sensory "gating" is an approach to the study of auditory evoked potentials which is dynamic. Another feature of how information is
processed centrally is the gating of sensory input. A well-known example of this phenomenon is the suppression of the cortical response to a test stimulus after the same conditioning stimulus. The auditory evoked cortical potential's middle-latency P50 component is extremely sensitive to gating. Three days following the last attack and prior to the next, patients with migraine without aura showed a significant drop in both their auditory P50 response and gating in comparison to healthy volunteers. An additional technique useful for evaluating physiologic central nervous system responses using AEPs is the intensity dependency of AEPs (IDAP), which quantifies the amplitude increase of auditory evoked cortical responses with increasing stimulation intensities. Between occurrences of migraine, the intensity dependence of AEPs-amplitude was shown to abruptly rise with increasing stimulus intensity. By using these techniques, it was discovered that migraineurs had increased intensity dependence of N1-P2. Furthermore, there was an appreciable decrease in the interictal-increased intensity dependence of auditory evoked potential both before and during the attack; in other words, during a migraine episode, the increased intensity dependence of auditory evoked potential normalizes. Apart from the examination of sensory "gating", habituation is also another important tool in studying headache. N1-P2 amplitude is potentiated at high stimulus intensities only. Nothing different from controls was found by Sand and Vingen. Also, migraineurs are more potentiated by high-than-low-intensity-stimulations according to Ambrosini et al.

**BAEP patterns in patients with TTH**

Children and adolescents with tension type headache who had BAEP recordings did not differ from those who had healthy children in terms of the parameters. Only in individuals with migraine, particularly those with aura, were latencies in the III and IV waves of the BAEP observed to be extremely prolonged. They were significant when compared to latencies observed in children with tension-type headaches and the control group. Regarding the BAEP data, there are no appreciable changes between the TTH patients and control group in a study done in Egypt by Laila et al. This study shows that BAEP can differentiate between tension-type headaches and migraines.

**Blink Reflex patterns in patients with migraine without aura**

Blink Reflex: The electrical equivalent of the physiologic corneal reflex Various muscles innervated by the facial nerve are stimulated electrically, and responses are recorded across the supraorbital nerve. When conducting the test, two responses could be discriminated. R1 is the Blink Reflex's initial potential. It usually happens at around 10 ms (millisecond) and is only visible on the side ipsilateral to the side that was stimulated. R2 is the blink reflex's second evoked potential. Conventionally, R2 is the second evoked potential ipsilaterally and R2′ (R2 prime) is the second evoked potential contralaterally. Reflex arcs that are indirect, or polysynaptic, are thought to be the source of these potentials. The R2 responses' initial afferent and terminal efferent segments are identical to those of R1. Studies on the blink reflex in migraine have produced variants in results. A multitude of reasons contribute to this, including the frequency of crises, how far apart they are from one another, whether one side predominates over the other, the form of stimulation used, and the use of precautionary medication. The early study for blink reflex discovered that while The R1 latency measurements did not differ much generated by supraorbital stimulation, patients with migraine had considerably longer R2 latencies. No relationship between the side of pain and the position of the recording was discovered with consideration to the pain side. Extensive inhibition of the R2 interneurons at a bulbopontine level has been proposed as the cause of the lack of any connection on the painful side, despite aberrant responses being generated when stimulation was provided from both sides. When BR testing was performed using normal methods on migraine patients during the interictal phase and measurements of R1 and R2 latencies, R2 amplitudes, and area were compared with those of the control group, no discernible intergroup
difference was seen. Also, there was no difference between those with unilateral migraine and those with bilateral pain in terms of any of the blink reflex components, whether they had an aura or not. Yet, Patients with migraines with an aura did not differ from controls. Zeynep Unal et al. discovered once more in 2016 that the migraine group had substantially longer latency values than the control group on the right and left sides (RR1 and LR1) as well as on the ipsilateral and contralateral R2 on the left side (LR2i and LR2c).

Considering Nociception-specific blink reflex (nBR), it was revealed that R2 amplitude was noticed to increase and decreased latency on the same side of the pain in patients with migraine exclusively during attacks. Conversely, however, Coppola et al., 2007 discovered There is no distinction between patients and controls. As regard habituation, De Mariniset al., declared that Those who had an attack within 72 hours had a significantly diminished blink reflex habituation. Migraine without aura (as well as migraine with aura) patients have a frequency-dependent-deficiency in nBR R2 habituation, while MA patients' deficit is less obvious. Positive relationship between migraine frequency and habituation rate in Migraine without aura.

**Blink reflex patterns in patients with tension type headache**

First of all, many authors discovered that the ipsilateral R2 and contralateral R2 responses were within normal amplitudes and sizes in BR in the episodic type tension type headache when blink reflex was tested on patients having Migraine without aura and patients having episodic tension type headache. According to reports, BR values in tension type headache patients are normal, and the trigeminal, face, and BR arc interneurons are all intact. In another study on patients with tension-type headaches, the blink reflex was induced. The process of giving paired shocks at different interstimulus intervals produced the recovery cycle. The authors reported normal values of R1, R2, and R2' latency, amplitude, and size in individuals with episodic and chronic tension type headache and migraine without aura. However, they discovered that the chronic tension type headache and episodic tension type headache groups showed reduced recovery of the R2t response at the 300- and 500-ms interstimulus intervals, but the migraine without aura group exhibited behavior more in line with the controls. A substantial latency extension of ipsilateral R2 and contralateral R2 values in favor of tension type headache patients was seen when the group having tension type headache was compared to the healthy control. This bolsters the notion that key pathways in the etiology of tension type headache cannot be disregarded.

Comparing the blink reflex in healthy volunteers and patients having persistent tension-type headache. The latencies of the R1 and R2 component have no significant changes between the two types of groups. After electrically stimulating the trigeminal cutaneous region by a concentric electrode, which is believed to stimulate the A Delta nociceptive-afferent, the BR may be measured. Similar to the R2, this stimulation method causes a reflex reaction that is mostly nociceptive in nature (nBR). Only one research examined the nBR in tension type headache and discovered that the nBR characteristics of patients with chronic tension type headache and control group were the same. It also implies that continuous increases in ipsilateral ocular muscle activity were linked to the electrical stimulation which is painful.

Reduced R3 component threshold was seen in chronic headache sufferers at the mildest headache, and it was hypothesized that the trigeminal circuits may have become more sensitive centrally.

**Conclusion**

Many countries became aware that headache disorders represent an important threat to public health. In spite of the discrepancies among different studies, the overall picture resulting from evaluation of the patterns that we find in central electrophysiological maneuvers clearly confirms that primary headache disorders can cause these patterns which may help us not only in the diagnosis of different types of primary headache disorders, but
also in understanding the pathophysiology of different headache disorders either primary or secondary.

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