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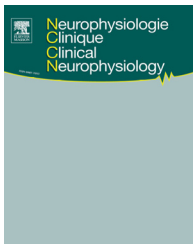

ORIGINAL ARTICLE/ARTICLE ORIGINAL

Deficient prepulse inhibition of blink reflex in migraine and its relation to allodynia☆

L'inhibition du réflexe de clignement par un stimulus préalable est déficiente dans la migraine : relation avec l'allodynie

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Summary
Objective. — Prepulse inhibition (PPI) of the blink reflex (BR) is a reduction in BR excitability due to a conditioning stimulus, reflecting sensory gating by brainstem structures. We aimed to analyze PPI changes during a painful episode in chronic or episodic migraine and its relation to allodynia, since abnormal brainstem filtering has been hypothesized in migraine pathophysiology.
Methods. — We included 20 patients with migraine during headache episode, and age- and gender-matched 22 healthy subjects. We recorded BR after unconditioned and conditioned supraorbital stimuli. For conditioned stimuli, we applied preceding subthreshold stimulus to the median nerve at wrist. The presence of PPI was compared between the two groups, as well as the specific BR parameters (latency, amplitude or area of R1 and R2 components) in unconditioned (test) and conditioned (PPI) paradigms.
Results. — In the patient group, seven (35%) patients did not have R2-PPI whereas all healthy subjects had R2-PPI ($P = 0.003$). Healthy subjects displayed significantly increased R1 amplitude and reduced R2 amplitude and area after conditioned stimuli. In migraine patients, we observed significant reduction only in R2 amplitude. Logistic regression demonstrated that allodynia was independently related with the presence of PPI (beta: −0.535, $P = 0.021$).

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Conclusions. — Our study provides evidence for sensory gating impairment at brainstem level in migraine headache, related to the presence of allodynia.

MOTS CLÉS
Allodynie ;
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Réflexe de clignement

Résumé
Objectif. — L'excitabilité du réflexe de clignement (RC) peut être modifiée par l'application préalable d'un stimulus de conditionnement (*prepulse inhibition* [PPI]), témoignant d'un filtrage sensoriel exercé par le tronc cérébral. Nous avons cherché à analyser les modifications de la PPI au cours d'un épisode douloureux de migraine chronique ou épisodique et sa relation avec l'allodynie, puisque des anomalies de filtrage du tronc cérébral anormal ont été évoquées dans la physiopathologie de la migraine.
Méthodes. — Nous avons inclus 20 patients au cours d'un épisode de migraine et 22 sujets sains, appariés en âge et sexe. Nous avons enregistré le RC à la stimulation supra-orbitaire non conditionnée et conditionnée. Comme stimuli conditionnés, nous avons appliqué une stimulation sensitive infraliminaire du nerf médian au poignet. La présence de PPI a été comparée entre les deux groupes, ainsi que les paramètres spécifiques du RC (latence, amplitude ou aire des composantes R1 et R2) dans les paradigmes non conditionné (test) et conditionné (PPI).
Résultats. — Dans le groupe migraine, 7 patients (35 %) n'avaient pas de R2-PPI, alors que tous les sujets sains l'avaient ($p = 0{,}003$). Les sujets sains présentaient significativement une augmentation de l'amplitude du R1 et une diminution de l'amplitude et de l'aire du R2 après stimulation conditionnée. Les migraineux ne présentaient qu'une réduction de l'amplitude du R2. Une analyse par régression logistique a montré que l'allodynie était indépendamment liée à la présence de la PPI (bêta : −0,535 ; $p = 0{,}021$).
Conclusions. — Notre étude fournit des arguments en faveur de l'existence d'une perte de filtrage sensoriel par le tronc cérébral dans la migraine, de façon corrélée à la présence d'allodynie.

Introduction

The clinical features of migraine are commonly related to structures largely innervated by the trigeminal nerve. Possible pathophysiological mechanisms of migraine are also attributed to sensitization of the trigeminovascular system and its central connections, as a result of a cascade of events known as spreading depression [9]. Using functional neuroimaging studies during attacks, increased activation has been shown in the ipsilateral locus ceruleus, dorsal raphe nucleus and periaqueductal gray matter in the ipsilateral dorsolateral pons [41].

This close association of clinical features and pathophysiology of migraine with the trigeminal system and brainstem nuclei has led to the use of electrophysiological methods, most frequently blink reflex (BR), to explore the functional role of these structures. The blink reflex is usually performed using supraorbital electrical stimulation. Briefly, it has two components and reflects the structural and functional state of related circuits involving the brainstem [17]. Although there are studies reporting prolonged BR latencies in migraine [2], BR was found to be normal in a large cohort of patients with chronic migraine, and this relatively simple reflex would not be affected unless there is significant brainstem damage [6]. The nociceptive BR, which is obtained using specific stimulation patterns or electrodes, was found to be facilitated during migraine attacks [23], but normal during the interictal period in migraine without aura [10]. Conversely, there is near consensus that habituation of BR is reduced and its excitability recovery is increased in migraine [14,15], including in chronic migraine during interictal periods [13] or in patients exhibiting allodynia [40]. Thus, it is generally agreed that the interictal lack of habituation of the nociceptive BR is a well-known hallmark of migraine [12,24,32], even in asymptomatic individuals with a family history of migraine and a possible genetic predisposition to migraine. In addition, one study investigating the effect of trigeminal nociceptive stimulation on BR and pain showed that painful conditioning stimulation, particularly to the right temple, produced strong suppression of the R2 component of the BR to low-intensity stimuli, and suppression of R2 to high-intensity stimuli [16].

Prepulse inhibition (PPI) is a neurophysiological method in which inhibition of a reflex response is generated by applying a subthreshold stimulus before the test stimulus [19,20,44]. It differs from habituation, which is the decrement of a response after repeating the same stimulus [11]. During conditioned analysis of BR, R2 magnitude is reduced after certain interstimulus intervals (ISIs), whereas short ISI leads to facilitation of R1 [4,21,37]. It is theorized that the neural correlate of PPI is a network involving basal ganglia and the pontine reticular formation [25,38]. Using PPI, abnormal sensory modulation has been shown in some painful disorders such as fibromyalgia [26].

Since PPI represents sensory gating at the brainstem level, which was hypothesized to be altered in migraine,