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Cognitive performance in young and middle-aged adults with migraine: Investigating the correlation with white matter hyperintensities and psychological symptoms

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ABSTRACT

Introduction: This study aimed to evaluate the cognitive performance of migraine patients with (MwA) and without aura (MwoA) and investigate the correlation of white matter hyperintensities (WMHs) and psychological symptoms with their cognitive test scores.
Material and methods: Hundred migraine patients aged 20–55 years and 80 healthy volunteers with similar age, sex, and education level were enrolled. The total Montreal Cognitive Assessment (MoCA) scores were compared by age, sex, presence of aura, migraine duration, attack frequency, pain localization, presence and number of WMHs, and the scores of the Beck Depression Inventory and the Beck Anxiety Inventory (BAI).
Results: Forty-seven (47%) patients had MwA and 53 (53%) had MwoA. The performance of the MwA patients was significantly poorer than that of the MwoA patients and the healthy subjects on the MoCA scales. In particular, the results revealed lower scores in the subscales regarding visuospatial/executive functions, naming, memory, attention, and abstraction in MwA patients than in the MwoA patients. Compared to healthy controls, more number of migraine patients had WMHs. The presence and number of WMHs had no significant correlation with the MoCA scores of the migraine patients. There was a significant correlation of the BAI and BDI scores with the total MoCA scores considering all migraine patients.
Conclusions: This study suggested that MwA may be associated with low cognitive performance which was correlated with depression and anxiety but not with WMHs. Further, longitudinal studies for assessing the relationship between WMHs, cognitive functions, and migraine, and for establishing the causality are warranted.

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1. Introduction

Migraine is one of the most common pain disorders, and the prevalence in the general population ranges from 5% to 20% [1]. It is characterized by recurrent throbbing headaches, nausea and/or vomiting, and arousal sensitivity to stimulants such as light, sound, and movement. A significant proportion of the population (up to 21% of women and 6% of men) experiences migraine attacks [1,2]. As the headache progresses, various autonomic, affective, cognitive, and sensory symptoms may occur [3]. The extent of these different symptoms suggests that migraine is more than a headache. It is a complex neurological disorder affecting multiple cortical, subcortical, and brainstem regions; therefore, it is clear that the migraine brain differs from the non-migraine brain [4].

Increased evidence suggests that in many individuals, migraine is a chronic disease associated with significant comorbidities, including white matter hyperintensities (WMHs), which are associated with volume changes in the white and gray matter regions of the brain [5]. The pathophysiology of WMHs is unknown. Cortical spreading depression (CSD) is defined as a propagating wave of glial and neuronal depolarization that occurs during migraine aura [6]. CSD results in partial activation of matrix metalloproteinases, hypoperfusion of small penetrating arteries, and altered vascular permeability. This may cause hypoxic brain injury, manifesting as WMHs on magnetic resonance imaging (MRI) [6]. Atherosclerosis and increased age may be the main risk factors for the development of WMHs but in migraine patients, attack frequency, the duration of disease, presence of aura and possible comorbid disease are also important in the development of WMHs [7,8]. Stroke and WMHs are associated with an increased risk of dementia [9]; therefore, it can be hypothesized that migraine patients may have impaired cognitive function. Some previous studies have shown a deleterious effect of migraine on many cognitive skills, including verbal ability, attention, psychomotor ability, and memory [10,11]. Especially presence of migraine-related aura has been shown to be associated with cognitive impairment [12,13]. However, other studies have not shown any effect of migraine on cognitive skills [14,15]. Discrepancies between these studies may possibly be attributed to insufficient neuropsychological assessments. Moreover, to our knowledge, only a few studies have considered the possible relationship between cognitive performance and the psychological symptoms or behavioral disturbances frequently seen in migraine patients [4,16].

This study aimed to evaluate the cognitive status of migraine patients with and without aura and investigate the association of WMHs and psychological symptoms with their cognitive function.

2. Material and methods

This prospective case–control study was performed at the Neurology Clinic between May 2016 and May 2017. Hundred migraine patients aged 20–55 years and 80 healthy volunteers with similar age, sex, and education level were enrolled.

The study was approved by local ethics committee. A detailed, written informed consent form was obtained from each subject before initiating the study. The inclusion criterion for migraine patients was the diagnosis of migraine according to the International Classification of Headache Disorders III (beta version) (ICHD-III) [17]. Exclusion criteria were as follows: other ICHD-III diagnosis (e.g., tension type headache, cluster headache, etc.); history of cerebrovascular disease, cardiovascular disease, diabetes mellitus, arterial hypertension, or hyperlipidemia; somatic or psychiatric disorders (e.g., major depression or psychosis according to DSM-5 criteria); smoking cigarettes or alcohol/substance abuse; current pregnancy, lactation, or hormonal contraceptive use; use of drugs such as antiplatelet agents, anticoagulants, statins, or hormonal drugs; renal, metabolic, inflammatory, infectious, or immune disease; or possible ''symptomatic migraine'' in which the MRI showed disorders such as ischemic infarcts, arteriovenous malformations, or brain tumors.

For at least 3 days before and after the neuropsychological tests, all the patients were migraine free and were not taking rescue medications to avoid any possible impact related to the attacks or to the pharmacological treatments. To ensure this, all patients were interviewed 3 days after the cognitive assessments.

The control group patients were selected from among the relatives of the migraine patients, hospital employees, or the general population. Written consent was obtained from them for voluntary participation in the study. The inclusion criteria for the control group were as follows: absence of migraine, the maximum frequency of any headache less than 1 episode per month (e.g., tension type headache, or any other type of chronic headache) and the absence of a diagnosed psychiatric disorder (e.g., major depression or psychosis). Exclusion criteria for the healthy controls were the same as those for the migraine patients.

Demographic and clinical characteristics such as disease duration, frequency of migraine attacks (number of migraine attacks per month), pain localization, and the presence of aura were recorded.

2.1. *Cognitive assessment*

The Montreal Cognitive Assessment (MoCA) [18] was used for evaluating the cognitive function of the migraine patients and healthy controls. The MoCA is a 30-point test that assesses several cognitive domains; it takes 10–15 min to complete. Mild CI is indicated by a total score <15.5 on the following subscales: visuospatial/executive functions, naming, memory, attention, language, abstraction, and orientation [19].

2.2. *Assessment of depression and anxiety*

Depression and anxiety symptoms were evaluated using the BDI and the BAI scores, respectively. The Beck depression and anxiety inventories comprise 21 questions and are scored between 0 and 63 points. The depression and anxiety cut-off values were taken as BDI score ≥10 points and BAI score ≥17 points, respectively [20,21].

2.3. *White matter hyperintensities*

All participants underwent whole-brain MRI using the same 1.5 T MRI scanner (Siemens Verio). The scans included ≥3

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