

## Recent Developments in Neuroimaging for the Evaluation of Migraines

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### ABSTRACT

Although migraines are a common disease, the pathophysiology of migraines is not completely understood. A clinical diagnosis of a migraine is currently made based only on the symptoms, because a clinically useful biomarker or laboratory test for the diagnosis of migraines has not been established. The recent advances in neuroimaging have improved the understanding of the pathophysiology of migraines. These neuroimaging studies may provide useful biomarkers for the diagnosis and monitoring of migraines. Anatomical magnetic resonance imaging (MRI) of the brain is mainly used to rule out secondary headaches. However, a statistical analysis of the MRI findings revealed volume loss of some brain regions. Diffusion tensor imaging (DTI) revealed faint functional changes of white matter fibers. Recently tract-based statistical analysis (TBSS) has provided an objective statistical analysis of the DTI findings for each patient. TBSS revealed reduced fractional anisotropy in some brain regions, like the corpus callosum. These brain regions are associated with pain processing, so these anatomical and functional alterations may cause chronification of migraines. These imaging findings may be diagnostic for migraines and effective to predict the prognosis and select therapeutic interventions and medications that will provide the best outcome.

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**Key words:** Migraine; Cortical thickness; MRI; Diffusion tensor imaging; Neuroimaging, Volumetry

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### EDITORIAL

Although migraines are a common disease, the pathophysiology of migraines is not completely understood. A clinical diagnosis of a migraine is currently made based only on the symptoms, because a clinically useful biomarker or laboratory test for the diagnosis of migraines has not been established. The recent advances in neuroimaging have improved the understanding of the pathophysiology of migraines. These neuroimaging studies may provide useful biomarkers for the diagnosis and monitoring of migraines.

Although cerebral infarctions were frequently accompanied with migraine, the pathological relationship between the two conditions is not clearly understood. Anatomical magnetic resonance imaging (MRI) of the brain is mainly used to rule out secondary headaches. However, a statistical analysis of the MRI findings revealed volume change of some brain regions. Functional and metabolic reductions have also been observed in these regions.

Chong *et al* reported the presence of cortical thinning at the bilateral postcentral gyrus in cases presenting with episodic migraine and compared these patients with healthy controls<sup>[1]</sup>. These 27 migraine patients were mostly female, and the mean age was 33.6 years. They did not analyze cortical thickness in relation to either the disease duration or headache frequency. Kim *et al.* reported cortical thickening to be present in the bilateral postcentral gyrus in migraine patients without aura and compared their findings with control subjects<sup>[2]</sup>.

This thickening was related to both the disease duration and headache frequency. They excluded male patients because of a sex difference in regard to cortical thickness. The final study population comprised 56 female migraine patients, with a mean age of 35.7 years. These 2 studies had almost the same patient background and both used the 3T MR device, the same software and the same analysis methods. However, the results were completely contradictory. DaSilva *et al.* reported that migraineurs had a thicker somatosensory cortex than age and sex matched controls<sup>[3]</sup>. They discussed that individuals suffering from acquired pain disorder may thus develop thinning of the cortex, while the long-term overstimulation of the sensory cortex may cause thickening of the sensory cortex. Maleki *et al.* analyzed sensory cortical thickness for migraineurs<sup>[4]</sup>. In high attack frequent migraineurs, the degree of sensory cortical thickness was higher than in healthy control, however, in low attack frequency migraineurs, the cortical thickness was lower than that in healthy control. They concluded that cortical thinning is the result of initial damage and as the frequency of migraine increases, and increased demand of sensory processing may thus be compensated by adaptive cortical thickening. The mean age of migraine patients was more than 40, and mostly female. They did not analyze the disease duration. Large amounts of medication were administered to high attack frequency migraineurs. Messina *et al.* analyzed both cortical thickness and the cortical surface area in patients with migraine<sup>[5]</sup>. They demonstrated a reduced cortical thickness and surface area in the regions subserving pain processing and an increased cortical thickness and surface area in the regions involved in the executive functions and visual motion processing. These cortical thickness and surface area abnormalities were not related with the migraine disease duration and attack frequency. The cortical surface area increases during fetal development, while cortical thickness changes during the life span. In migraine patients, cortical surface area abnormalities were more frequently observed than cortical thickness changes, thus suggesting that congenital abnormalities therefore exist more frequently than acquired changes in migraine. Cortical thickness is according to age and sex. As a result, the cortical thickness should be analyzed among same age and sex groups in relation with the disease duration and attack frequency. In addition, therapeutic intervention may affect cortical thickness. Therefore, before discussing whether or not changes in cortical thickness may be the cause or result of migraine, we should first investigate the natural course of cortical change in patients with migraine.

Diffusion tensor imaging (DTI) revealed faint functional changes of white matter fibers. Recently tract-based statistical analysis (TBSS) has provided an objective statistical analysis of the DTI findings for each patient. TBSS revealed reduced fractional anisotropy (FA) in some brain regions, like the corpus callosum. These brain regions are associated with pain processing, so these anatomical and functional alterations may cause chronification of migraines.

Schmitz *et al.* showed a significantly reduced FA in the superior, medial frontal lobe in patients with migraine, and a longer disease duration in patients demonstrating a reduced frontal FA. They included only female migraine patients and the age-FA correlation was not analyzed<sup>[6]</sup>. Szabo *et al.* analyzed DTI using TBSS and found a reduced FA in right frontal white matter clusters in migraine<sup>[7]</sup>. The attack frequency or migraine duration was not associated with FA change. They discussed that structural changes could be the consequence of maladaptive plastic changes or some degenerative process caused by the migraine pathology. Yuan *et al.* demonstrated

a reduced FA in genu and splenium of corpus callosum in migraine patients and these changes correlated with the disease duration<sup>[8]</sup>. FA is known to be related with age, so FA should be evaluated using age-matched controls.

If these changes are the result of repeated migraine attacks, they likely correlate with the duration and frequency of the migraine. However, if these changes are observed in young patients with recently started migraines, these changes may indicate a predisposition for or cause of migraines. The effects of therapeutic intervention on the functional changes of MRI findings should be investigated. These imaging findings may be diagnostic for migraines and effective to predict the prognosis and select therapeutic interventions and medications that will provide the best outcome.

The cortical thickness and FA are related with the duration and frequency of migraine in some studies, but not in other studies. These unstable results indicated the change of cortical thickness and FA are not simple results of the pathology of migraine. Therefore, further regression analyses using homogenous patients groups and longitudinal studies should be carried out to elucidate the pathophysiology of migraine.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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