BRAIN IMAGING IN MIGRAINE: AN UPDATE

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Overview

Research involving functional and structural imaging of the brain has contributed to describing pathophysiologic mechanisms of migraine. These imaging studies have yielded insights into migraine brain function or structure during migraine attacks, between attacks, in patients who have episodic migraine, those with chronic migraine, those with migraine aura, during task performance, in response to sensory stimulation, and when the brain is at rest. A few studies have investigated the central effects of migraine abortive treatment. More recent studies have begun to investigate the use of imaging data for classifying migraine and predicting clinical outcomes at the level of the individual patient.

Migraine Pathophysiology: Imaging During a Migraine Attack

Imaging studies during migraine attacks have studied different stages including aura, premonitory, headache, and post-treatment phases. Many studies have investigated migraine attacks triggered by substances such as nitroglycerin or calcitonin gene-related peptide, while others have captured spontaneous attacks. These studies have demonstrated the hypothalamus to be involved in the premonitory phase of migraine, the early involvement of the brainstem in initiating a migraine attack, and the expected activation of pain-processing regions during the headache phase. Following abortive treatment, most of the regions that show within-attack activations return to their baseline state, perhaps with the exception of regions in the brainstem.

Migraine Pathophysiology: Imaging Between Migraine Attacks

Imaging during the inter-ictal period has demonstrated atypical structure in numerous regions throughout the brain, including regions that are part of the “pain-matrix”. These studies have measured cortical thickness, regional volumes, white matter tract integrity, and brain shape. In many studies, the extent of structural abnormalities correlates with measures of disease burden such as number of years with migraine and headache frequency or with presence of symptoms during migraine attacks like cutaneous allodynia.

Inter-ictal functional imaging studies have mostly investigated stimulus-induced brain activation patterns and resting functional connectivity. Event-related studies demonstrate that people with migraine have enhanced activations in response to pain within brain regions that facilitate pain processing. Meanwhile, pain-inhibiting brainstem regions are hypoactivated in response to pain, especially amongst those individuals who develop cutaneous allodynia during migraine attacks. This greater pain-facilitation in combination with less pain-inhibition likely contributes to the enhanced pain experience found in people with migraine and might contribute to the development of allodynia during migraine attacks. Individuals with migraine, especially those who have aura, also have enhanced activation of visual processing regions when exposed to visual stimuli. This enhanced response likely relates to the photosensitivity associated with migraine. Finally, resting state functional connectivity studies have demonstrated that people with migraine have atypical functional communication between numerous brain regions and amongst many core resting state networks. Several studies have found positive correlations between more severe migraine manifestations and the extent of aberrant functional connectivity.

Can Imaging Data be Useful for Developing Migraine Biomarkers

Brain imaging data have been utilized to develop migraine classifiers and to predict long-term migraine outcomes. A study using measures of brain structure developed models that accurately classified single brain MRIs as being from an individual with chronic migraine vs. a healthy control with 86% accuracy and being from an individual with chronic migraine vs. episodic migraine with 84% accuracy. A resting state functional connectivity study differentiated individuals with migraine from healthy controls with 81% accuracy, with even higher classification accuracies amongst those who had greater number of years with migraine. An analysis that combined structural data with functional connectivity data identified individuals who had migraine without aura with 84% accuracy. Finally, a study that measured amygdala and hippocampal volumes at baseline and then collected migraine outcome data 2 years later found that baseline right hippocampal volume was positively associated with at least a 50% reduction in headache frequency at 2 years.

Conclusions and Future Directions

Structural and functional brain imaging has contributed to the description of migraine pathophysiology during the premonitory, aura, headache, post-treatment, and inter-ictal phases. Recent studies have begun to explore the utility of brain imaging data for classifying migraine and for predicting outcomes. Future imaging studies should aim to validate published findings, investigate similarities and differences between migraine and other headache types, combine data obtained via multiple imaging sequence types, and build data models that prospectively predict migraine outcomes and treatment responses.

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