

SC106. Analysing cortical expression patterns of migraine-associated genes: a new perspective on migraine genetics

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Introduction

Migraine is a complex multifactorial neurological disorder with a major genetic component. During the past few decades significant progress has been made in our understanding of both the rare monogenic forms of this condition and the more common polygenic migraine types. Most genetic-pathophysiological studies have focused on gene function, leaving anatomical information at an organ level at best. Nonetheless, it is well established that gene expression in the brain is not homogeneous, resulting in different concentrations of DNA products throughout the different regions. Therefore, in this study, we evaluated cortical expression patterns of migraine-associated genes to determine whether this approach could provide additional information in the investigation of migraine genetics.

Objectives

To explore cortical expression patterns of migraine-associated genes using digital maps.

Materials and methods

Three-dimensional digital maps of familial hemiplegic migraine and common migraine-associated genes were mined from an open-source database. These models were constructed using information from the Allen Brain Atlas (500 samples per hemisphere extracted from the brain of six different donors with no known history of neurologic or neuropsychiatric disorders) and subsequently validated in positron emission tomography experiments. Gene expression models of the 38 genes where susceptibility loci for migraine have been mapped in seminal genome-wide association studies were grouped based on their similarity using neural networks clustering implemented in MATLAB®.

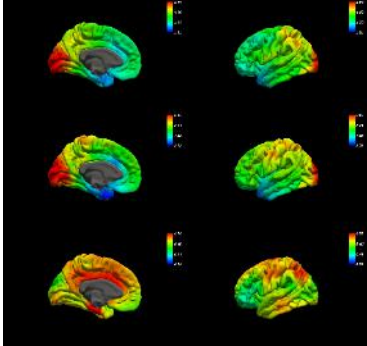
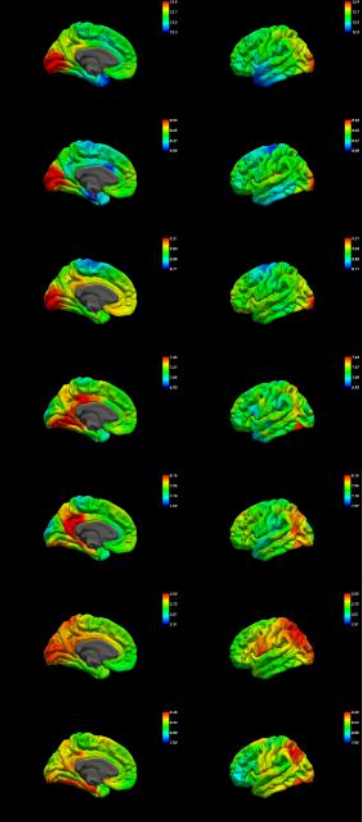
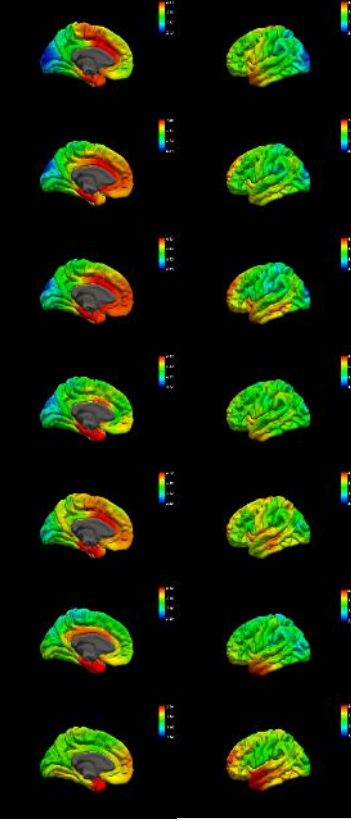
Results

Gene expression showed marked contrasts in key regions previously implicated in migraine pathophysiology in most cases. Numerous genes exhibited similar expression patterns.

Conclusion

Gain or loss of function of migraine-associated genes could produce focal functional alterations in specific regions associated with migraine pathophysiology. A new

paradigm including both gene function and topographical expression might be superior to currently disseminated approaches. Translational studies are warranted.

<p>FHM CACNA1A SCN1A ATP1A2</p>	<p>Cluster1 ITPK1 NEGR1 ZCCHC14 MPPED2 DOCK4 GPR1 PHACTR1</p>	<p>Cluster 2 TSPAN2 YAP1 GJA1 HEY2 C7orf10 SLC24A3 TRPM8</p>
		
<p>Cluster 2 (cont) REST MRVI TGFB2 FGF6</p>	<p>Cluster 3 ASTN2 MEF2D ADAMTSL4 IGSF9 KCNK5</p>	

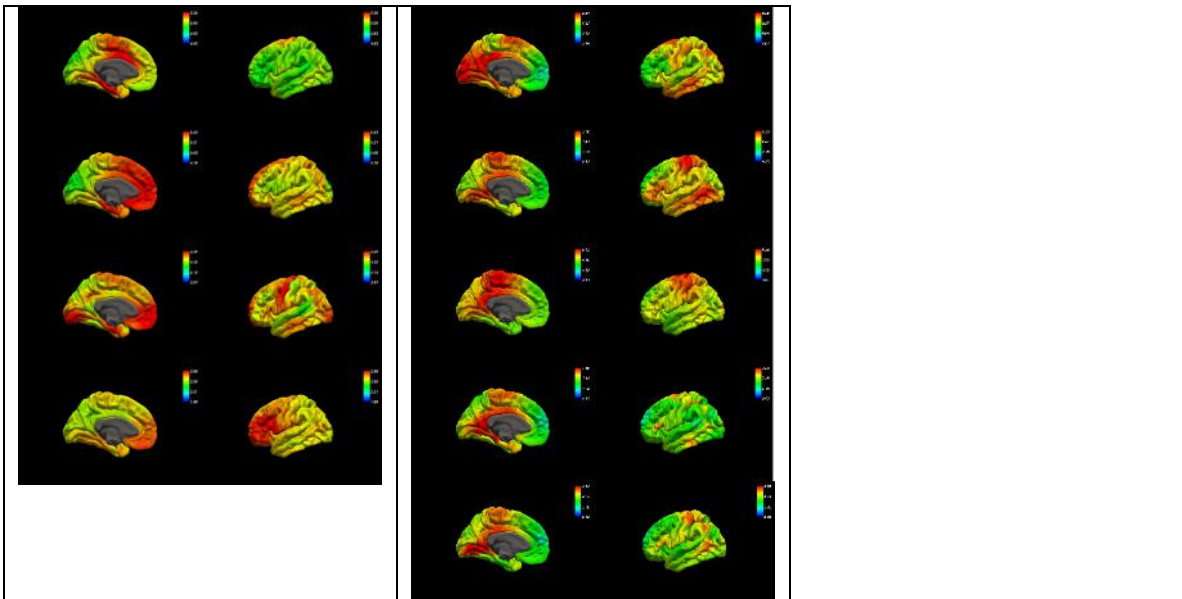


Fig 1. Familial hemiplegic migraine genes and larger clusters of common migraine-associated genes.