

BRAIN ABNORMALITIES IN RELATIVES OF PATIENTS WITH MCD

Quantitative MRI Detects Abnormalities in Relatives of Patients with Epilepsy and Malformations of Cortical Development

Merschhemke M, Mitchell TN, Free SL, Hammers A, Kinton L, Siddiqui A, Stevens J, Kendall B, Meencke HJ, Duncan JS

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Malformations of cortical development (MCD) are a common etiology for epilepsy. Lamina heterotopia, bilateral subependymal heterotopia, and lissencephaly have a genetic basis. No gene mutations have yet been identified in patients with focal cortical dysplasias. The aim of this study was to use quantitative morphometric tools to determine if there were gray-matter abnormalities in relatives of patients with MCD. We studied 19 relatives of 13 probands with MCD and 58 healthy controls with high-resolution magnetic resonance imaging (MRI). The relatives and controls had no neocortical abnormalities on visual inspection. MRI data were analyzed with voxel-based morphometry and autoblock analysis. Voxel-based morphometry showed significant increases of gray matter in nine of 10 probands, five of 19 relatives, and five of 58 controls. The autoblock analysis showed significant abnormalities in seven of eight probands, eight of 19 relatives, and two of 57 controls. This finding suggests structural abnormality in the brains of a greater number of relatives of MCD patients than would be expected, and in the context, a reasonable inference is that this reflects subtle genetically determined cerebral abnormalities, although acquired pathologies are possible and are not excluded.

COMMENTARY

Prior research demonstrated that rates of malformations of cortical development (MCD) are increased in first-degree relatives of patients with MCD and epilepsy. What remains to be determined is whether first-degree relatives with magnetic resonance images (MRIs) that appear normal may harbor abnormalities that could be detected if quantitative processing procedures were used. Merschhemke et al. applied two sophisticated quantitative MRI postprocessing procedures to the MRIs of 19 relatives of 13 probands with MCD and 58 healthy controls. The techniques included voxel-based morphometry (VBM) of gray matter and autoblock analysis, both capable of quantifying regional gray- and white-matter distribution.

The authors report quantitative abnormalities of gray-matter distribution in the MRIs of relatives whose scans appeared normal on visual inspection. VBM revealed significant regions of increased gray matter in 26.3% of the relatives compared with 8.6% of the controls. Autoblock analyses revealed abnormalities in 42.1% of the relatives compared with 3.5% of the controls. Overall, the authors detected significantly more subtle abnormalities in relatives compared with controls, which may represent previously unrecognized genetically determined MCD. Alternately, relatives may share with patients common genes that result in their having similarities of cerebral development, without actually acquiring MCD.

The use of sophisticated morphometric processing techniques is an interesting feature of the research by Merschhemke et al. The findings across techniques (i.e., VBM and autoblock analysis) are not mirror images, and future comparison of morphometric techniques within the same population may help to clarify the differential sensitivity and relative strengths of various postprocessing procedures. Finally, this study suggests that quantitative MRI procedures may prove helpful in the search for genes involved in cerebral development.

by Bruce Hermann, Ph.D.