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Reduced gray matter in the anterior cingulate gyrus in familial schizophrenia: A preliminary report

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ABSTRACT

Few brain imaging studies of schizophrenia involve samples with enhanced genetic homogeneity. We compared MRI volumetric data between individuals with 1q21–q23 linked familial schizophrenia associated with *NOS1AP* and their first and second degree unaffected relatives. We found significant gray matter reductions in the anterior cingulate gyrus in both affected individuals and their unaffected first degree relatives when compared with their unaffected second degree relatives. These results suggest that the changes are primarily due to genetic risk and not illness effects, and may represent an intermediate phenotype.

1. Introduction

Structural magnetic resonance imaging (MRI) studies have repeatedly identified regions of gray matter (GM) deficits in schizophrenia compared with unaffected volunteers (Honea et al., 2005). Unaffected relatives of individuals with schizophrenia also have differences in brain structure when compared with unrelated healthy controls, suggesting that some of the volumetric differences seen in schizophrenia may be related to the familial genetic risk of developing the disease (Goghari et al., 2007). However, individuals in the samples studied to date are likely to have various genetic risk factors for schizophrenia, and this etiologic heterogeneity may limit the ability to attribute specific MRI findings to genetic liability. We studied a relatively homogeneous subtype of familial schizophrenia, highly significantly linked to 1q21–q23 (Brzustowicz et al., 2000), comparing affected individuals to their unaffected relatives at two different degrees of relatedness. This allowed us to comment on whether changes may be due to genetic risk as opposed to the illness or its treatment.

2. Methods

2.1. Study sample

We studied 35 subjects (12 males; 23 females) from seven Canadian families of European descent: 11 meeting DSM-IV criteria for narrowly defined schizophrenia (SZ; mean age at onset = 23.0 y, SD = 5.9 y), and their unaffected first degree (UA1; $n = 17$) and second degree (UA2; $n = 7$) relatives (none of whom met criteria for any schizophrenia spectrum disorder (Wratten et al., 2009)). No participants had a history of serious brain injury or mental retardation. Informed consent was

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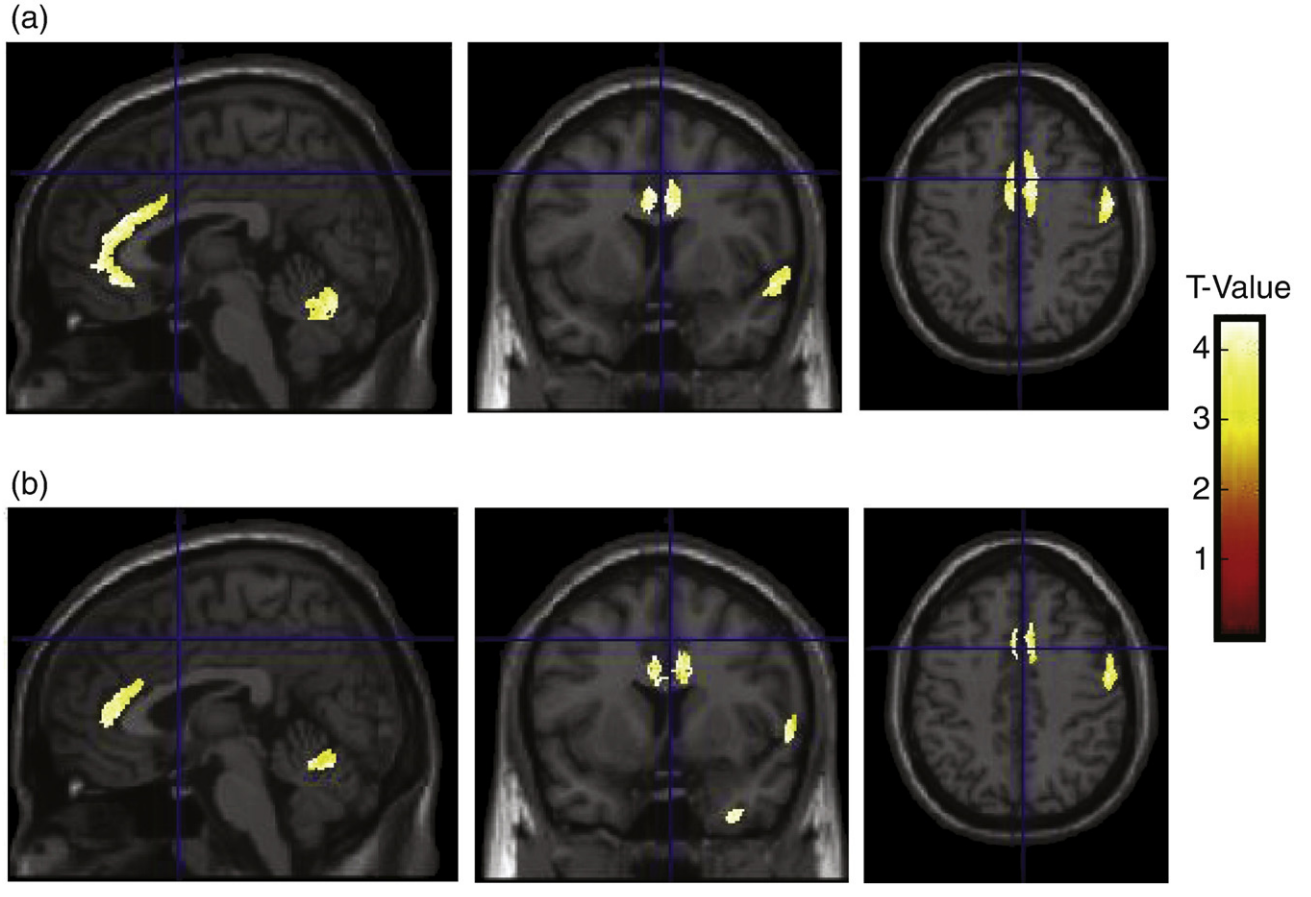

Fig. 1. VBM group differences in regional GM in1q21–q23 linked familial schizophrenia. Separate T contrasts were used to test for differences. Group data are plotted on sections of a normalized template brain scan. (a) SZ and UA2 groups show significant GM differences of smaller cluster size in the right AC gyrus (see text), right superior temporal gyrus (Talairach coordinates {44, −27, 5}; $p = 0.006$), and right posterior cerebellum (Talairach coordinates {56, −55, −22}; $p = 0.018$). (b) UA1 and UA2 groups show comparable significant GM differences of smaller cluster size in the right AC gyrus (see text), right superior temporal gyrus (Talairach coordinates {41, −29, 5}; $p = 0.031$), and right posterior cerebellum (Talairach coordinates {55, −73, −29}; $p = 0.022$).