Abstract

Schizophrenia is a debilitating mental disorder that affects approximately 1% of the world population and is associated with delusions, disorganized speech and behavior, hallucinations, and abnormal brain structure and function. The risk of developing schizophrenia is associated with both environmental and genetic risk factors. Schizophrenia is genetically heritable; it has been found that offspring have a 10% chance of inheriting the disease from an affected parent. Because of this genetic heritability, searches for schizophrenia genes have been long underway using genome-wide association studies (GWAS). One GWAS discovered gene is SMARCA2, a member of the SWI/SNF chromatin-remodeling complex. Single-nucleotide polymorphisms (SNPs) in SMARCA2 have also been associated with changes in gene expression. Koga, et al. associated SNPs in rs3763627 and rs3793490 with low SMARCA2 expression levels in the postmortem prefrontal cortex. Allelic determination of these two SNPs was performed for a selection of individuals with Schizophrenia and healthy controls using TaqMan genotyping assays. The data set was combined with magnetic resonance imaging (MRI) scans and calculated brain lobe volumes for each individual sample. It was found that the genotype GG in rs3793490 in affected individuals showed decreased frontal lobe gray matter volumes when compared to affected individuals who are T-carriers in the same SNP. However, this result cannot be concluded as statistically significant due to the small sample size of the GG group.

TaqMan Assay Procedure

Denaturation (95°C)

Annealing (60°C)

Reporter dye

Quencher dye

Unbound reporter dye fluoresces in light when unbound from quencher dye.

Tag Polymerase

Many cycles amplify the fluorescence. The fluorescence is interpreted for allelic discrimination using SDS 2.0 software.

Genotype Frequencies

<table>
<thead>
<tr>
<th>RS3793490 TaqMan Assay</th>
<th>RS3763627 TaqMan Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Probands</strong></td>
<td><strong>Controls</strong></td>
</tr>
<tr>
<td>AA : 244</td>
<td>AT : 54</td>
</tr>
<tr>
<td><strong>Experimental</strong></td>
<td></td>
</tr>
<tr>
<td>AA : 0.761</td>
<td>AT : 0.228</td>
</tr>
<tr>
<td><strong>Allele Frequency X² = 1.91</strong></td>
<td><strong>Allele Frequency X² = 0.349</strong></td>
</tr>
<tr>
<td>DF = 1</td>
<td>DF = 1</td>
</tr>
<tr>
<td>p-value = 0.167</td>
<td>p-value = 0.555</td>
</tr>
</tbody>
</table>

Lobe Volume Determination

- Lobe volumes were determined using BRAINS software developed at the University of Iowa.
- Brain structures are programmed into the software by location
- MRI cross sections are compiled by the program and are used to estimate the total volume of the brain structure

Frontal Lobe Gray Matter Volume in rs3793490 Patients and Controls

- Probands show a significantly lower frontal lobe gray matter volume than controls for the genotype GG
- GG probands show lower frontal lobe gray matter volume than probands or controls in the TG and TT genotypes
- Statistical relevance cannot be confirmed due to small sample size (GG frequency = 0.017)

Frontal Lobe Gray Matter Volume in rs3763627 Patients and Controls

- TT probands show smaller frontal lobe gray matter volumes than controls of the same genotype
- Statistical relevance cannot be confirmed due to small sample size (TT frequency = 0)

Conclusion

- The GG genotype in rs3793490 may be associated with decreased frontal lobe gray matter volumes in individuals with schizophrenia

References