A case-control association study between Obsessive-Compulsive Disorder (OCD) and the MCP-1 -2518G/A polymorphism in a Chinese sample

Xinhua Zhang,1 Yingying Yin,1 Shiguo Liu,2 Xu Ma3

1Department of Psychology and Psychiatry, Medical College, Qingdao University, Qingdao, China
2Shandong Provincial Key Laboratory of Metabolic Disease, The Affiliated Hospital of Medical College, Qingdao University, Qingdao, China
3National Research Institute for Family Planning, Beijing, China

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Abstract

Objective: To investigate the association between Obsessive-Compulsive Disorder (OCD) and a functional polymorphism of MCP-1 in the Chinese Han population. Method: We genotyped and performed a case-control association analysis of the MCP-1 -2518G/A polymorphism in 200 OCD patients and 294 healthy control subjects. Results: There was no significant difference in MCP-1 -2518G/A genotypic and allelic frequencies between OCD cases and controls ($\chi^2 = 1.123$, df = 2, $P = 0.57$ by genotype; $\chi^2 = 0.802$, df = 1, $P = 0.37$ by allele). Conclusions: Our results indicated that MCP-1 -2518G/A may not play a major role in the genetic predisposition of the Chinese Han population to OCD. However, further studies using a larger number of subjects are required to obtain a clear conclusion.
Introduction

Obsessive-Compulsive Disorder (OCD) is a mental disorder characterized by repetitive, obsessive thinking and compulsive behavior. Its lifetime prevalence is 1.9–3.3%, which makes OCD the fourth most common mental disorder behind phobias, substance dependence, and major depression. In the last several years, a number of studies have found an association between OCD and proinflammatory cytokines such as TNF-α and interleukin-10, as well as natural-killer and T-cell function.

Mainly derived from perivascular astrocytes, monocyte chemoattractant protein 1 (MCP-1) increases blood brain barrier (BBB) permeability and attracts leukocytes across the BBB, which possibly draws autoantibodies in the serum of OCD patients to the basal ganglia. When associated with the BBB endothelium, MCP-1 plays a role in mediating: 1.) the differentiation of neural stem cells into neurons, astrocytes and oligodendrocytes and 2.) the regulation of adult subventricular zone-derived progenitor cell migration after striatal cell death. Together, these roles indicate an intimate association between neurodevelopmental and neuroregenerative processes regulated by inflammatory mediators. The MCP-1 -2518G/A polymorphism may affect the transcriptional activity of monocyte MCP-1 production and the severity of organ inflammation.

We hypothesized that MCP-1 might increase the risk of OCD. We performed an association study between OCD and the 2518G/A polymorphism of MCP-1 to examine the hypothesis that this functional variant may influence the etiology of OCD in a Chinese Han population.

Materials and Methods

Study Population

A total of 200 OCD patients [mean age = 28.92 years and SD = 10.85 years; 35.6% females; 64.4% males] were recruited from the Affiliated Hospital of Medical College, Qingdao University. All of the patients were diagnosed according to DSM-IV diagnostic criteria. Probands with a history of neurologic or metabolic diseases, bipolar or psychotic disorder, or current substance dependence were excluded. Control subjects were selected from among healthy volunteers from Qingdao University, and all had no history of any psychiatric disorder. The Ethics Committees of Qingdao University Medical College Hospital approved the study, and all of the subjects provided written informed consent.

Discussion

A number of studies have demonstrated a connection between OCD and infections, thus indicating the existence of possible immune dysfunction in OCD. Consequently, many interesting candidate genes encoding cytoactive material, such as inflammatory factors, warrant investigation, and a series of studies has already been performed. Unfortunately, the results of these studies were quite inconsistent. Konuk and colleagues found a significant increase in the plasma levels of TNF-α...
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Table 1 Genotype distribution and relative allele frequencies of the MCP-1 -2518G/A polymorphism in Chinese individuals with (n = 200) or without (n = 294) OCD

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Genotype frequency (%)</th>
<th>Allele frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>G/G</td>
<td>G/A</td>
</tr>
<tr>
<td>OCD</td>
<td>200</td>
<td>70 (0.350)</td>
<td>98 (0.490)</td>
</tr>
<tr>
<td>Controls</td>
<td>294</td>
<td>97 (0.330)</td>
<td>139 (0.473)</td>
</tr>
</tbody>
</table>

and IL-6 in OCD patients compared with healthy controls. As mentioned above, MCP-1 is a critical chemokine that is closely associated with neuroinflammatory conditions of various etiologies, while its deficiency protects against inflammation in the brain. We hypothesized that MCP-1 could increase the risk of OCD, but there has been no evidence supporting our hypothesis to date. This is the first report investigating a single nucleotide polymorphism in MCP-1 in relation to OCD. Our results showed no significant differences in -2518G/A genotypic and allelic frequencies between 200 OCD cases and 294 controls. It is unlikely that this result is due to quality control issues as the experiment was carefully designed, we used proper equipment that had a high accuracy, and the sequences of several PCR products were verified by direct sequencing. The patient and control samples were chosen carefully and randomly, and those individuals who had mental disabilities, drug and/or alcohol dependence, or metabolic, psychiatric, or neurological diseases were excluded. The genetic background of the sample was also strictly considered. However, the following reasons could explain our negative results. The most likely reason is low power due to limited sample size (only 14.8%). Additionally, MCP-1 could play only a minor role, thus contributing only a small increase in risk that could be undetectable due to the small sample size. Moreover, the onset age of OCD and the rate of patients with an earlier onset of OCD could not be excluded. Therefore, further research targeting other populations should be performed, which would provide a better understanding of MCP-1 expression functionality.

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Disclosures

Shigu Liu

Employment: Shandong Provincial Key Laboratory of Metabolic Disease, The Affiliated Hospital of Medical College, Qingdao University, Qingdao, 266003, China.

Yingying Yin

Employment: Department of Psychology and Psychiatry, , Medical College, Qingdao University, Qingdao, 266021, China.

Xinhua Zhang

Employment: Department of Psychology and Psychiatry, , Medical College, Qingdao University, Qingdao, 266021, China.

Xu Ma

Employment: National Research Institute for Family Planning, Beijing, 100081, China.

Xinhua Zhang and Yingying Yin contribute equally to this work.

* Modest
** Significant
*** Significant. Amounts given to the author’s institution or to a colleague for research in which the author has participation, not directly to the author.

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