Alteration of NMDA glutamate receptor gene expression in major depressive disorder

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Introduction and Objective

Major depressive disorder (MDD) is a common mental illness that affects millions of people worldwide. Previous studies have shown altered glutamatergic neurotransmission in several brain regions of patients with MDD [1, 2, 3]. Moreover, an elevated glutamate levels of serum, plasma and cerebrospinal fluid were observed in MDD patients [4, 5, 6], which may lead to alteration in N-methyl-D-aspartate (NMDA) glutamate receptors. A previous study found an elevated platelet glutamate receptor supersensitivity in MDD suggesting a response to glutamate stimulation [7]. Therefore, the aim of this study was to examine the mRNA expression of NMDA receptor subunits NR1 and NR2B in peripheral white blood cells of MDD patients. 

Materials and Methods

1. Subjects
The patients diagnosed as MDD were recruited from the Clinical Psychiatry, Naresuan University Hospital, Phitsanulok, Thailand. The diagnosis of MDD was based on criteria in the Diagnostic and Statistical Manual of Mental Disorders-fourth edition (or DSM-IV). The normal controls without any lifetime psychiatric diagnosis and treatment were invited to the study and recruited from the healthy volunteers with age matching. Samples were obtained from peripheral blood between 8.00 a.m. and 10.00 a.m. All subjects were given written informed consent. The experimental protocols were approved by the Human Ethics Committee of Naresuan University.

2. Reverse transcription polymerase chain reaction (RT-PCR)

Blood samples were collected for mRNA extraction. cDNA synthesized from mRNA was used for RT-PCR technique. NR1, NR2B and a house keeping gene beta-actin were amplified in PCR master mix. PCR products were then separated with agarose gel and stained with ethidium bromide. Subsequently, the bands of PCR products were photographed under UV illumination and the intensities of bands were measured using Scion Image 4.0.2 software.

Table 1 Demographic data of subjects with MDD and healthy controls (mean ± SD)

<table>
<thead>
<tr>
<th>MDD</th>
<th>Healthy control</th>
</tr>
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<tbody>
<tr>
<td>NR1</td>
<td>NR2B</td>
</tr>
<tr>
<td>n</td>
<td>14</td>
</tr>
<tr>
<td>Age (year)</td>
<td>39±17.5</td>
</tr>
<tr>
<td>Age of onset (year)</td>
<td>37±19.1</td>
</tr>
<tr>
<td>Duration of illness (month)</td>
<td>17±24.7</td>
</tr>
</tbody>
</table>

Table 2 Pearson’s correlation coefficient between mRNA expression and age, age of onset and duration of illness.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age</th>
<th>Age of onset</th>
<th>Duration of illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR1</td>
<td>0.172</td>
<td>0.215</td>
<td>0.038</td>
</tr>
<tr>
<td>NR2B</td>
<td>0.264</td>
<td>0.266</td>
<td>0.389</td>
</tr>
<tr>
<td>Control</td>
<td>0.680</td>
<td>0.127</td>
<td>0.607</td>
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Results

The band intensities of NMDA receptor subunits were normalized with the intensities of beta-actin bands. Figure 1 shows the mRNA expression of NR1 and NR2B were significantly increased in patients with MDD (P<0.003 and P=0.013 respectively) when compared with healthy controls. However, there were no correlations between NR1 and NR2B mRNA expression and age, age of onset and duration of illness in MDD patients. In addition, no correlation between NR1 and NR2B mRNA expression and age was found in healthy controls (Table 2).

Discussion and Conclusion

Several studies have determined the altered NMDA expression levels in several brain regions of MDD patients [8, 9]. The present study is the first to examine mRNA expression levels of NMDA subunits NR1 and NR2B in peripheral white blood cells of MDD patients. We found that mRNA levels of NR1 and NR2B were increased in MDD patients compared with healthy controls. There have been several studies reporting elevated serum and plasma glutamate levels of patients with MDD [4, 5, 6]. Supersensitivity of platelet glutamate receptor was observed in MDD patients suggesting a response to glutamate stimulation [7]. Therefore, the elevation of NR1 and NR2B mRNA expression found in this study may be up-regulation in response to glutamate stimulation in MDD patients.

However, there were no correlations between NR1 and NR2B mRNA expression and age of both groups. Furthermore, there were no correlation between NR1 and NR2B mRNA expression and age of onset and duration of illness in MDD patients, which suggested that the up-regulation of NR1 and NR2B mRNA expression are not affected by age, age of onset and duration of illness, but there are related to the disease.

The results of this study suggest that the alteration of NR1 and NR2B mRNA may be used as a peripheral marker of glutamate function in MDD. Moreover, our observation also support glutamatergic neurotransmission abnormality in MDD and provide further evidence for medication of depression.

Acknowledgements

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References

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