Gender differences in the association between mood characteristics and polymorphisms of glial cell line-derived neurotrophic factor (GDNF) in patients with depression

Eszter Kotyuk Ph.D.,1,2, Nora Nemeth MD,2, Zsuzsa Halmai3, Gabor Faludi MD, DSc, Maria Sasvari-Szekely Ph.D, DSc and Anna Szekely Ph.D.2

Introduction:

Glial cell-line derived neurotrophic factor (GDNF) regulate the neuron’s survival, growth and morphological differentiation, thus they have a key role in synaptic plasticity and efficiency. GDNF is a potent neurotrophic factor for dopaminergic neurons with a potential therapeutic applicability in Parkinson’s disease.

Studies identified connections between GDNF plasma level and mood disorders (e.g. bipolar disorder, major depression; Wang et al., 2011; Barbosa et al., 2011; Otsuki et al., 2008; Michel et al., 2008).

Aim: We observed a significant gender-SNP interaction among the healthy individual sample: the effect of the rs3812047 A allele as a risk factor of anxiety was more pronounced in males, then in females. Here, we tested if this gender-SNP interaction is present among patients with major (MDD) or bipolar depressive disorder (BPD).

Methods:

Hungarian version of the Hospital Anxiety and Depression Scale (HADS, Muszbek, K., et al., 2006):

• Self-report questionnaire; 14 items divided into two subscales:
  • 7 measuring anxiety and 7 depression related states.
  • straightforward and reversed items as well
  • scored from 0-3 based on the related response category
  • the final score of the scales are summed up from the appropriate items’ scores.
  • They range from 0 to 21.

Reliability statistics:

Anxiety subscale’s Chronbach Alpha: 0.786 (scale mean: 13.72 ± 4.231)
Depression subscale’s Chronbach Alpha: 0.853 (scale mean: 12.76 ± 4.813)

Results:

Male and female HADS mean anxiety scores across the GDNF SNPs:

<table>
<thead>
<tr>
<th>HADS Anxiety</th>
<th>Full sample</th>
<th>BPD</th>
<th>MDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>n=3096140 C</td>
<td>13.91(±4.2)</td>
<td>14.10(±3.6)</td>
<td>11.57(±4.9)</td>
</tr>
<tr>
<td>Allele main effect p</td>
<td>0.047</td>
<td>0.712</td>
<td>0.006</td>
</tr>
<tr>
<td>Gender main effect p</td>
<td>0.299</td>
<td>0.042</td>
<td>0.076</td>
</tr>
<tr>
<td>Interaction p</td>
<td>0.047</td>
<td>0.607</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Mean HADS anxiety scores for GDNF rs3096140 alleles by gender on the MDD sample:

<table>
<thead>
<tr>
<th>HADS Anxiety</th>
<th>C allele</th>
<th>T allele</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>11.72(±5.6)</td>
<td>12.63(±5.9)</td>
</tr>
<tr>
<td>Female</td>
<td>10.57(±7.7)</td>
<td>12.46(±5.6)</td>
</tr>
</tbody>
</table>

Conclusion:

According to our previous results GDNF polymorphisms are in association with mood characteristics on healthy and clinical samples as well.

Here, we analyzed if there are some similar gender effects as we observed on the healthy sample.

A significant allele-gender interaction effect was demonstrated on the HADS anxiety scale in case of the MDD sample.

These results suggest that the effects of GDNF polymorphisms on anxiety are more pronounced in males not only on a sample of healthy young adults, but in case of MDD patients as well. Interestingly the same allele-gender interaction was not observable in case of the BPD patients.

Further studies are needed to clarify whether these polymorphisms, located near to the alternative splicing site of the GDNF gene, have any functional role or they are rather markers of linked functional variants.

Acknowledgement:

Members of the psychogenetic laboratory; members of the PCR laboratory; the participants of the study. Funding: NIH-FIRCA (RO3 TW07856-01A1); OTKA (CK 80289, K81466).

References:
