Introduction
Primary dysmenorrhea (PDM) is a common gynecological disorder in women of the reproductive age. These patients suffer from cyclic cramping pain, which may lead to anxiety, stress, and negative mood.

Our previous study reported that PDM subjects of BDNF Met carrier demonstrated regional gray matter volume reduction as compared to PDM with Val homoygote, including pain and emotional-related regions.

Animal studies have reported the association between the variants of the brain-derived neurotropic factor (BDNF) Val66Met polymorphism and BDNF. Val66Met polymorphism has been suggested to be associated with anxiety-related behavior and impaired emotion recognition ability in animal and human studies, respectively.[1][2]

Our recent study reported that PDM is associated with higher anxiety and PDM subjects with BDNF Met carrier demonstrated regional gray matter volume reduction as compared to PDM with Val homoygote.

In the present study, we used magnetoencephalography (MEG)-imaging genetics to investigate the effect of BDNF Val66Met polymorphism on cortical responses to emotional prosody.

Materials and Methods

- 55 PDM patients and 54 normal control (NC) subjects were recruited during the peri-ovulatory phase (OV phase, days 12–16 of the menstrual cycle).
- Genotype analysis: BDNF Val66Met (rs6265)
- Psychological assessment:
  - Spielberger State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Pain Catastrophizing Scale (PCS), McGill Pain Questionnaire (MPQ)
- Stimuli
  - Single-sound in four different emotions (neutral, happy, sad and angry)
  - Each block consisted of 375 stimuli (3 blocks; neutral: 180 trials, happy, sad, angry: 60 trials/each emotion)
- Data acquisition
  - MEG scanner (Vectorview, Elekta Neuromag, Helsinki, Finland)
- Data analysis
  - Dividing subjects into three groups based on their genotypes, including Val/Val, Val/Met, and Met/Met.
  - Auditory evoked field (AEF): Comparison of the latency and amplitude at the peak of time components: M50 (45 to 90 ms after stimuli onset), M100 (100 to 150 ms after stimuli onset) as well as peak-to-peak features (M50-M100)
- Statistics analysis
  - Between-group comparison of psychological scales using two-sample t-test
  - Separate one-way ANOVA in each PDM and NC group for between-genotype comparison

Results

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>P-value (F value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>State Anxiety</td>
<td>37.5 (7.5)</td>
<td>34.9 (13.9)</td>
<td>34.9 (6.5)</td>
<td>35.1 (7.1)</td>
<td>0.014* 0.012 0.015</td>
</tr>
<tr>
<td>Trait Anxiety</td>
<td>43.2 (10.6)</td>
<td>42.7 (6.5)</td>
<td>39.2 (8.2)</td>
<td>36.5 (10.6)</td>
<td>0.017*</td>
</tr>
<tr>
<td>BDI</td>
<td>10.4 (13.6)</td>
<td>5.5 (8.7)</td>
<td>4.8 (2.8)</td>
<td>3.3 (1.1)</td>
<td>0.017*</td>
</tr>
<tr>
<td>BAI</td>
<td>6.6 (1.6)</td>
<td>6.1 (3.3)</td>
<td>6.4 (5.8)</td>
<td>6.1 (2.9)</td>
<td>0.022*</td>
</tr>
<tr>
<td>PCS</td>
<td>17.5 (10.4)</td>
<td>16.0 (7.4)</td>
<td>16.9 (8.0)</td>
<td>14.6 (6.1)</td>
<td>0.005*</td>
</tr>
</tbody>
</table>

Table 1. Between-group comparison of psychological scales by stratified analysis.

Discussion

- Using emotional prosody as a probe, our data pinpoint that BDNF–gene Val66Met polymorphism may be an emotional modulator in auditory processing of emotional voices.
- The attenuation of AEF response in Met-carrier PDM subjects is in accordance with the hypothesis that BDNF is involved in the activity-dependent synaptic activity. BDNF Met carriers may result in deficit in BDNF secretion.
- The deficit BDNF secretion may be effectuated via gene-environment (pain and emotional distress) interaction.

Key References