Conclusion: Anhedonia is a prominent symptom associated with TRD. Higher levels of anhedonia in TRD patients compared to non-TRD patients were associated with greater D2/D3 binding in the right anterior cingulate cortex, indicating lower levels of dopamine in this region contribute to greater anhedonia.

Methods: Patients with TRD (n=15) and without TRD (n=37) and healthy controls (n=50) completed the Dimensional Anhedonia Rating Scale (DARS), and measures of depressive symptoms and physical activity. The TRD patients only also underwent positron emission tomography to measure extrastriatal dopamine D2/D3 binding using 11C-FLB 457.

Results: There was a statistically significant difference between depression scores between TRD and non-TRD depressed patients, which was mediated by higher levels of low mood, worthlessness and anhedonia in the refractory group. Depressed patients had lower scores on the DARS (indicating greater anhedonia) compared to healthy controls. TRD patients also had increased anhedonia compared to non-TRD patients. In the TRD group, the DARS total score was associated with greater D2/D3 binding in the right anterior cingulate cortex, indicating lower levels of dopamine in this region contribute to greater anhedonia.

Conclusion: Anhedonia is a prominent symptom associated with TRD. Higher levels of anhedonia in TRD patients compared to non-TRD patients were associated with greater D2/D3 binding in the right anterior cingulate cortex, indicating lower levels of dopamine in this region contribute to greater anhedonia.

Non-TRD vs. TRD

DARS score

- Greater D2/D3 binding correlated with lower DARS total score in the TRD group, indicating lower levels of dopamine contribute to greater anhedonia.

Anhedonia is a prominent symptom in treatment resistant depression and is linked to low dopaminergic functioning.

Findings of increased D2/D3 binding potential in the anterior cingulate cortex is consistent with EEG reports demonstrating increased ACC activity with greater anhedonia ratings (Wacker et al, 2009).

Nonresponders to venlafaxine prefrontal cortex transcranial magnetic stimulation were more anhedonic and had greater connectivity from the left VMPFC to the right DLPFC among other frontal regions (Dowen et al, 2014). Along with present data showing greater D2/D3 binding in the DLPFC in high anhedonia patients, this suggests the DLPFC may be particularly involved in the subjective experience of anhedonia.

It is necessary for the present neuroimaging findings to be replicated with a larger sample size.

Table 1: Demographic and Clinical Profile

<table>
<thead>
<tr>
<th>Variable</th>
<th>TRD (n=15)</th>
<th>Non-TRD (n=37)</th>
<th>Healthy Controls (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.4 (18.8)</td>
<td>41.7 (15.5)</td>
<td>37.8 (13.1)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>66.7%</td>
<td>51.4%</td>
<td>42.0%</td>
</tr>
<tr>
<td>Education (yrs)</td>
<td>16.3 (3.2)</td>
<td>14.0 (3.9)</td>
<td>13.8 (3.9)</td>
</tr>
<tr>
<td>Age of onset</td>
<td>22.0 (7.5)</td>
<td>23.3 (13.9)</td>
<td>23.0 (13.9)</td>
</tr>
<tr>
<td>Duration of MDE</td>
<td>108 (32)</td>
<td>25.0 (38.4)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Key inclusion criteria: Treatment Resistant Depression patients
- Age between 21 to 71
- Hamilton Rating Scale for Depression-17 item (HRS-D-17) > 20
- No other primary Axis I disorder
- Failed to respond > 4 treatments for current MDE

Non-TRD Patients
- Age between 18-60
- Meet DSM-IV criteria for current MDE
- No other primary Axis I disorder
- Have not failed ≥ 1 treatment for current MDE

Healthy Controls
- Age between 18-60
- No psychiatric history
- No history of antidepressant use
- No significant medical illness

PET acquisition and analysis:
- [11C]-FLB 457 (10mCi) was injected to the vein and emission data was acquired over 90 minutes in 15 1-min. frames and 15 5-min. frames

Binding potential calculated using simplified reference tissue (cerebellum) method.

Conclusions

- Anhedonia is a prominent symptom in treatment-resistant depression and is linked to low dopaminergic functioning.
- Findings of increased D2/D3 binding potential in the anterior cingulate cortex is consistent with EEG reports demonstrating increased ACC activity with greater anhedonia ratings (Wacker et al, 2009).
- Nonresponders to venlafaxine prefrontal cortex transcranial magnetic stimulation were more anhedonic and had greater connectivity from the left VMPFC to the right DLPFC among other frontal regions (Dowen et al, 2014).
- Along with present data showing greater D2/D3 binding in the DLPFC in high anhedonia patients, this suggests the DLPFC may be particularly involved in the subjective experience of anhedonia.
- It is necessary for the present neuroimaging findings to be replicated with a larger sample size.

Table 2: Distribution of DARS scores in MDD and healthy controls

<table>
<thead>
<tr>
<th>DARS Score</th>
<th>OD</th>
<th>MO</th>
<th>HC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Cumulative</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
</tbody>
</table>

DARS Total Score vs. healthy controls

TRD patients had higher DARS total scores compared to non-TRD patients and healthy controls.

Figure 1: CESD item scores in TRD vs. non-TRD

Figure 2: Anhedonia scores in TRD patients vs. healthy controls

Figure 3: D2/D3 binding correlation with DARS total score

Figure 4: D2/D3 binding correlation based on low vs. high DARS total score (>16)

References


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