ANHEDONIC DEPRESSION: AN ENDOPHENOTYPIC APPROACH

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Introduction

Anhedonia, or the lack of reactivity to pleasurable stimuli, is a core feature and potential endophenotype of major depressive disorder (MDD) [1]. It has been suggested that a lowered hedonic capacity in MDD might become manifest in the form of reduced sensitivity to reward. Subjects with higher depressive symptoms show reduced reward responses [2] and several studies, using neuroimaging, have associated dysfunctions in the brain reward system with anhedonia [3,4]. The purpose of this study was to assess the correlation between anhedonia and a lowered reward sensitivity in patients with MDD and to validate anhedonia as a potential endophenotype in MDD. Reward sensitivity was measured objectively in patients with MDD in order to test the hypothesis that depressed patients with high anhedonic symptoms show reduced responsiveness to reward compared to patients with low or no anhedonic symptoms.

Materials and methods

Forty medicated patients meeting DSM-IV criteria for MDD performed a probabilistic reward task [2]. Within a signal-detection paradigm, subjects were presented with a mouthless cartoon face on a computer screen (Figure 1). A difficult-to-distinguish short or long mouth appeared on the face for 100 msec and participants were asked to identify which mouth was presented long.

Three blocks of 100 trials were presented. Subjects received monetary rewards after a subset of the correct answers. An asymmetric reward ratio was used such as correct responses for one stimulus were rewarded three times more frequently than correct responses of the other stimulus. Prior studies using this paradigm have shown that healthy controls develop a bias for the more frequently rewarded stimulus, whereas subjects with elevated depressive, particularly anhedonic, symptoms develop a smaller or no bias over the three blocks [5].

Anhedonia was measured by the Snaith-Hamilton pleasure scale (SHAPS), a validated self-report scale [6].

Results

Based on the dichotomous SHAPS scores the depressed group (MDD) was divided into a high anhedonic (highA; SHAPS≤7) and low anhedonic (lowA; SHAPS>7) subgroup. Sixteen healthy volunteers (HV) were recruited as controls (Table 1). No group differences emerged for age or gender.

<table>
<thead>
<tr>
<th>Group</th>
<th>LowA</th>
<th>HighA</th>
<th>HV</th>
<th>Statistics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>44.2</td>
<td>37.1</td>
<td>47.1</td>
<td></td>
<td></td>
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<tr>
<td>SHAPS</td>
<td>3.2</td>
<td>14.1</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*mean ± SD, **SHAPS=Snaith-Hamilton pleasure scale, dichotomous scores

Linear mixed models were used to model the longitudinal pattern of change in the task over the three blocks. This takes into account the auto-correction among repeated measurements from the same individual. Furthermore, the random effect in the mixed model accounts for the natural heterogeneity in the result of the task.

Results on general task performance, as assessed by reaction time, accuracy and the ability to discriminate between the two mouths, showed no significant differences across blocks and between groups (Table 2).

<table>
<thead>
<tr>
<th>Statistics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discriminability</td>
<td>0.49</td>
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<tr>
<td>Accuracy</td>
<td>0.15</td>
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<tr>
<td>Reaction Time</td>
<td>0.43</td>
</tr>
</tbody>
</table>

As expected, accuracy for the more rewarded (rich) stimulus was significantly higher than for the less rewarded or lean condition in HV (F = 6.45, p = 0.01), borderline significantly higher in lowA (F = 4.46, p = 0.05) and not significantly different in HighA (Figure 2).

Conclusions

These results support the hypothesis that impairment of reward responsiveness might underlie lowered hedonic capacity in Major Depressive Disorder. The computer task objectively assesses reward sensitivity in both depressed patients and healthy volunteers and the results correlate significantly with the SHAPS, a self-report scale on anhedonia. Furthermore, the task is able to successfully distinguish a subgroup of depressed patients with high anhedonic symptoms. These preliminary findings supports the claim that anhedonia is a promising endophenotype for major depressive disorder. Further research on this topic is currently underway, since this data is part of an ongoing study on identifying subtypes of major depressive disorder and assess their underlying neurochemical mechanisms.

Literature cited

For further information
Please contact e.vrieze@kuleuven.be for more information on this and related projects.

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