Characterizing the Neural Substrates of Irritability in Women: A 7T fMRI Study

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BACKGROUND
• Irritability, a prominent feature of perinatal depression, detrimentally impacts maternal mental health and child development; yet it remains poorly understood and understudied.
• Hormone manipulation in euthymic non-pregnant women produces transient affective symptoms—including irritability—like that experienced in the perinatal period.

METHODS
• Participants (n=22) completed an 8-week hormone manipulation protocol using Lupron that included a pre- and post-manipulation 7T fMRI scan.

<table>
<thead>
<tr>
<th>Participant Demographics</th>
<th>Pre</th>
<th>Post</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>31.8</td>
<td>31.8</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>3.1</td>
<td>2.9</td>
</tr>
<tr>
<td>IDAS Ill-Temper Change (Post-Pre)</td>
<td>0.5</td>
<td>2.4</td>
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<tr>
<td>BOLD Activation Change (Post-Pre)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Accumbens</td>
<td>-0.06</td>
<td>0.02</td>
</tr>
<tr>
<td>Right Accumbens</td>
<td>-0.06</td>
<td>0.23</td>
</tr>
<tr>
<td>Right Amygdala</td>
<td>-0.02</td>
<td>0.23</td>
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</tbody>
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• Each fMRI visit included the Affective Posner Task, designed to induce frustration through rigged feedback (60% of correct responses rigged to provide “Too Slow” feedback with no reward).
• Because previous research implicated the nucleus accumbens, amygdala, caudate, and putamen in irritability, we extracted BOLD % signal change from these structurally derived ROIs during induced frustration in the Affective Posner Task.
• Univariate regressions compared the relationship between change in ROI BOLD activation during induced frustration (post-pre) and change in a self-reported measure of irritability (post-pre).

RESULTS
• Three key striatal/limbic region activation changes from pre- to post-hormone manipulation positively correlated with IDAS Ill-Temper change:
  • Left accumbens (t=3.04, p<0.01, adjR²=0.28)
  • Right accumbens (t=2.10, p<0.05, adjR²=0.14)
  • Right amygdala (t=3.29, p<0.01, adjR²=0.32)

DISCUSSION
• The nucleus accumbens and right amygdala are significantly implicated in hormonally-induced irritability and correlate with a well-established clinical outcome.
• This is the first study using 7T fMRI to elucidate the neurobiology of irritability with a homogenous onset; establishing a potential biological target for treatment of irritability and perinatal depression.

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