Neural Correlates of Postpartum Depression: Elevated Monoamine Oxidase A (MAO-A) Binding in Prefrontal and Anterior Cingulate Cortex

Julia Sacher1,2, Alan A. Wilson2, Sylvain Houle2, Leslie Romano1,2, Jinoos Hamidi1, Pablo Rusjan2, P. Vivien Rekkas2, Donna Stewart4, & Jeffrey H. Meyer1,2

1Vivian M. Rakoff PET Imaging Centre at Centre for Addiction and Mental Health, University of Toronto, Canada,
2Mood and Anxiety Disorders Division, Centre for Addiction and Mental Health and Department of Psychiatry, and University Health Network, Department of Psychiatry, University of Toronto, Canada,
3Clinic of Cognitive Neurology, University of Leipzig and Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany,
4Women’s Health Program and the Toronto General Research Institute, University Health Network, University of Toronto, Canada.

References


Abstract

Purpose of the study: Determining the neurochemical underpinnings of postpartum depression (PPD) in humans is challenging because post-mortem studies are almost impossible as an investigation tool and the demands of motherhood in combination with PPD make recruitment for neuroimaging studies difficult. The purpose of this Positron Emission Tomography (PET) study was to determine binding of the Monoamine-Oxidase A (MAO-A) enzyme metabolizing monoamines, in brain regions associated with sad mood and pessimism in women suffering from PPD.

Methods: We have scanned fifteen first onset, antidepressant naïve, postpartum depressed subjects who were within 1.5 years since delivery and twenty-one healthy, age-matched women using [11C]Harmine Positron Emission Tomography (PET) to measure MAO-A total distribution volume (MAO-A VT) in the prefrontal cortex (PFC), anterior cingulate cortex (ACC), thalamus, putamen, ventral striatum, hippocampus, and midbrain.

Results: In postpartum depression, MAO-A VT was significantly greater in the PFC and ACC (MANOVA, F(15,25) = 7.45, p = 0.002; mean difference 22% and 20% respectively). Similar results were found in the other brain regions.

Conclusions: We identified substantial MAO-A binding elevations as a key mechanism for the neurobiology of major depressive episodes (MDE) with postpartum onset. Elevated MAO-A Vc in the PFC and ACC argues that enhanced monoamine loving substrates in these regions are important pathophysiological components of PPD and that MAO-A inhibitors should be investigated for treating PPD.

Background

With a prevalence rate of 13 % PPD represents the most common complication of childbearing and increases the lifetime risk for major depressive disorder (MDD) [1, 2]. Monoamine Oxidase A (MAO-A) is elevated during early onset major depressive episodes (MDE) [3] and recurrence of MDE [4]. An index of MAO-A levels is measurable with [11C]Harmine PET [5, 6]. We have previously identified a neurobiological model for postpartum depression that MAO-A inhibitor moclobemide for treatment of postpartum depression (PPD) is considered as a promising strategy in the treatment of severe postpartum depression. We infer that treatment with MAO-A inhibitors should be continued in postpartum depression whereas women who develop PPD will continue to show increased MAO-A binding in frontal brain areas. In this study we aim to investigate MAO-A binding in prefrontal cortex and anterior cingulate cortex of PPD and postpartum euthymic women within the first year following delivery. Our primary ROIs were those which serotonin depletion has been best demonstrated to influence MAO-A substrate availability (7 e.g. prefrontal cortex, anterior cingulate cortex).

Methods

15 women who were suffering from PPD and 21 healthy women completed the protocol (table 1). The absence of any past or present DSM-IV Axis I disorders was determined using the Structured Clinical Interview for DSM-IV nonpatient edition and the Hamilton Scale for Depression. PET Imaging Each woman underwent a single session of [11C]Harmine PET scanning. Women refrained from breastfeeding for more than 13 half-lives of the radiotracer (260 minutes) after injection. Radioactivity in breast milk was measured at approximately 250 minutes after injection and was indistinguishable from background activity at that time. [11C]Harmine was administered as a bolus intravenously and PET scanning was taken continuously for the first 10 min (ABBS system) and manual samples were taken at 5, 10, 15, 20, 30, 45, 60 and 90 min. Continuous arterial blood radioactivity levels were counted using an ABBS system. Parent and metabolite concentration were measured using HPLC. [11C]Harmine was of high radiochemical purity (> 96 %) and high specific activity. PET scans were acquired using a single point source, 137Cs (T = 30.2 years, Eγ = 662 keV) and used for attenuation correction. Analysis Regions of interest (ROI) for the prefrontal cortex and the anterior cingulate cortex were drawn on magnetic resonance imaging (GE Signa 1.5 T scanner, T1 & PD-sequences) scans that were co-registered to each summed [11C]Harmine PET image using a mutual information algorithm. We identified substantial MAO-A binding elevations in frontal areas. We propose a chain of events in postpartum depression: Elevated monoamine oxidase A (MAO-A) enzyme metabolizing monoamines, in brain regions associated with sad mood and pessimism in women suffering from PPD.

Results

As shown on the demographics table 1, there were no significant differences in age (t(33) = 0.68, p = 0.50) nor phase of menstrual cycle (t(33) = 0.42, p = 0.67) at the time of scanning between groups. MAO-A VT was significantly greater in PPD in prefrontal and anterior cingulate cortex: multivariate analysis of variance, MANOVA, F(20,15) = 3.0, p = 0.002. In postpartum depression, MAO-A VT was also significantly greater in all brain regions: MANOVA, effect of group (PPD versus controls), F(20,15) = 3.10, p = 0.015 (see also figure 1). The mean Edinburgh Depression Scale in the PPD was 15.93 ± 2.84.

Conclusions

We propose a sustained MAO-A binding elevation as a central neurobiological correlate for postpartum depression (figure 2). We infer that treatment with MAO-A inhibitors should be considered as a promising strategy in the treatment of severe postpartum depression. Clinical trials investigating the reversible MAO-A inhibitor moclobemide for treatment of postpartum depression would be the next step in this direction. Our findings suggest categorizing PPD as being more similar to early onset major depressive disorder and dissimilar to late onset major depressive disorder (associated with neurodegenerative disease). These findings also have implications for developing novel prevention strategies for PPD that specifically target preventing the persistence of elevated MAO-A levels between early postpartum and subsequent PPD.

References


Tabelle 1

<table>
<thead>
<tr>
<th>Healthy Subjects</th>
<th>Postpartum Depressed Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>34.15 ± 5.55</td>
</tr>
<tr>
<td>Menstrual cycle</td>
<td>0.68 (17)</td>
</tr>
<tr>
<td>Subjects with 1 child</td>
<td>9</td>
</tr>
<tr>
<td>Subjects with 2 or more children</td>
<td>7</td>
</tr>
<tr>
<td>Subjects with 3 children</td>
<td>4</td>
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</table>
| Women’s Health Program and the Toronto General Research Institute, University Health Network, University of Toronto, Canada.

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