Postpartum Psychosis and Bipolar Disorder

Professor Ian Jones
April 2016
Bipolar Disorder

**DEPRESSION**
- Low mood
- Loss of enjoyment
- Fatigue
- Psychomotor retardation
- Insomnia
- Loss of appetite / weight
- Poor concentration
- Hopelessness
- Suicidality

**MANIA**
- Elevated mood
- Irritability
- Goal directed activity
- Psychomotor agitation
- Reduced need for sleep
- Racing thoughts / speech
- Distractible
- Inflated self esteem
- Increased libido
A Spectrum of Affective Disorders

Normal fluctuation
Unipolar Depression
Bipolar II
Bipolar I

Mania
Depression
Sex differences in Bipolar disorder

- Women with BP disorder have:
  - More rapid cycling
  - More seasonal pattern
  - More (longer) depressive episodes
  - More mixed and dysphoric mania
  - More BP II
  - More comorbidity with medical disorders - particularly thyroid disease, migraine, obesity, and anxiety disorders
  - Less substance abuse
  - Less completed suicide
  - Later onset

- Reproductive life events
  - Menarche
  - Menstrual cycle
  - Menopause

(reviewed in DiFloria and Jones, 2011)
Pregnancy and Childbirth

“I thought I liked babies, but, as it turned out, I mainly like baby clothes.”
Psychiatric disorder and childbirth - concept with a long history

“A young woman in child-bed not well purged after birth and delivery, fell into a great delirium suddenly without any disease afore going. She was angry most with her best friends, husband and mother, but she spoke many things religiously ……” – Felix Plater 1602

“The beautiful wife of Carcinator, who always enjoyed the best of health, was many times attacked by melancholia after childbirth and remained insane for a month, but recovered with treatment” – Jao Rodrigues de Castelo Branco 1551
Important today
What mood episodes occur following childbirth?

- **Blues**
  - 50% or more
  - Onset: days 2 - 5
  - Duration: a few days
  - Symptoms: mood lability
  - Treatment: self limiting

- **Postnatal depression**
  - 10 - 15%
  - Onset: few days – 6 months
  - Duration: weeks – months – years
  - Symptoms: typical symptoms of depression
  - Treatment: antidepressants – psychotherapy (CBT)
What mood episodes occur following childbirth?

- **Postpartum / puerperal psychosis**
  - 1 in 1000 – around 50% first episodes
  - Onset: first two weeks typical
  - Duration: weeks – months
  - Symptoms: severe affective psychosis, mood symptoms, mixed, perplexity.
  - Rapidly progressing and changing picture, “kaleidoscopic”
  - Treatment: psychiatric emergency, medication, admission
The importance of the concept of Postpartum Episodes

- Cause great personal suffering for women
- Wide ranging influences including on relationships with partner and children
- Possible long term consequences for the social and cognitive development of the child
- Reduce stigma
- Important in the political fight for services for women at this time
- May help us understand the *aetiology* of mood disorders
What have we learnt about postpartum triggering?
The BDRN Study

N = 6007

- Cardiff University
- Prifysgol Caerdydd
- University of Birmingham
- University of Worcester
- Wellcome Trust
- The Stanley Medical Research Institute

- Bipolar UK
- Other
- NHS services
1. The postpartum is a period of high risk

Kendell et al 1987
Admissions per week


Kendell et al 1987
Severe postpartum episodes have a rapid onset following delivery

Heron, et al. 2007
Is this due to stopping medication?

Pregnancy (Weeks 1–40)

Postpartum (Weeks 41–64)

% Remaining Stable

Weeks at Risk Off Lithium

2. Specific relationship with bipolar .....very high risk in women with previous PP

Robertson, Jones and Craddock, 2005
Is the risk across all psychiatric illness?

Munk-Olsen et al. 2006

![Bar chart showing relative risk of admission in first postpartum period for different psychiatric illnesses.]

Munk-Olsen et al. 2006
High risk for women with bipolar disorder

Munk-Olsen et al 2009
Perinatal Episodes Across the Mood Disorder Spectrum

Arianna Di Florio, MD; Liz Forty, PhD; Katherine Gordon-Smith, PhD; Jess Heron, PhD; Lisa Jones, PhD; Nicholas Craddock, FRCPsych, PhD; Ian Jones, MRCPsych, PhD

<table>
<thead>
<tr>
<th>Category</th>
<th>BPI (%)</th>
<th>BPII (%)</th>
<th>MDD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>980</td>
<td>232</td>
<td>573</td>
</tr>
<tr>
<td>Narrow Mania / Mixed / affective psychosis (6 weeks)</td>
<td>33.3%</td>
<td>9.1%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Intermediate Plus Depression (6 weeks)</td>
<td>55.5%</td>
<td>40.1%</td>
<td>47.1%</td>
</tr>
<tr>
<td>Broad Any perinatal episode (pregnancy or within 6 months)</td>
<td>69.4%</td>
<td>69.0%</td>
<td>67.4%</td>
</tr>
</tbody>
</table>
For each pregnancy...

Bipolar I disorder, N=1691
Bipolar II disorder, N=592
Recurrent major depression, N=803

perinatal depression
perinatal mania/psychotic depression

proportion of pregnancies affected
Risk not increased across the bipolar spectrum

Number of episodes/year of illness

Number of postpartum episodes/deliveries

BD-I (N=275)*
BD-II (N=62)
RMD (N=275)*
p<0.001
Women with a previous PP are at very high risk

Robertson, Jones and Craddock, BJPych 2005

Episodes of PP per 1000 deliveries
3. Different causal factors important for PP and PND

*OR: 0.36, 95% CI 0.246-0.517, p<0.01

Di Florio et al, Bipolar Disorders 2015
Childbirth most potent trigger

Di Florio et al, Bipolar Disorders 2015
What are the triggers?

• Bio-psycho-social
  – Stress – significant life event
  – Specific issues in transition to parenthood - CSA
  – Sleep disruption
  – Hormonal changes
    • sex steroids
    • Thyroid
    • HPA axis
  – Immunological factors
Parity strongly associated with risk of PP

Bipolar I disorder (929 women, 1780 pregnancies).

Di Florio et al, JAD 2015
……but not for Postpartum Depression

Bipolar I disorder (929 women, 1780 pregnancies)

Di Florio et al, JAD 2015
Pre-eclampsia

- Inadequate placentation
- Abnormal release of aniogenic and antiangiogenic factors
- Systemic illness with CNS effects
- Disruption of the blood brain barrier
- Psychosis – not merely postictal
- Association with mood symptoms
ON THE CAUSES, SYMPTOMS, AND TREATMENT OF PUERPERAL INSANITY.

BY JAMES REID, M.D.

PHYSICIAN TO THE GENERAL LYING-IN HOSPITAL, ETC.

The term, puerperal insanity, is not only understood to imply aberration of the mind, or derangement of the cerebral functions in the puerperal state itself, but to include those attacks which occur sometimes during the period of gestation, as well as those which we more frequently meet with some months after parturition, whilst the patient is suckling her infant.

The same cause will occasionally produce both puerperal convulsions and puerperal mania. A case of this description was received into the female lunatic ward of St. Giles' Infirmary about the

Another point of connexion between the two complaints is, “that each of them is more liable to attack the female in her first accouchement than in after ones.

James Reid. Journal of Psychological Medicine: 1848
Is sleep loss an important trigger?

“Let’s try getting up every night at 2:00 AM to feed the cat. If we enjoy doing that, then we can talk about having a baby.”
Sleep loss associated with PP but not PND

High Mood Usually Triggered by Sleep Loss
(n = 527)

χ² = 7.312, P = .004, OR = 2.02, 95% CI = 1.21-3.40

Lewis et al, submitted
But... childhood sexual abuse associated with PND

<table>
<thead>
<tr>
<th></th>
<th>NO ABUSE</th>
<th>ABUSE</th>
<th>NO SEXUAL ABUSE</th>
<th>SEXUAL ABUSE</th>
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<tbody>
<tr>
<td></td>
<td>(N=480)</td>
<td>(N=134)</td>
<td>(N=525)</td>
<td>(N=89)</td>
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<tr>
<td></td>
<td>(78%)</td>
<td>(22%)</td>
<td>(85%)</td>
<td>(15%)</td>
</tr>
<tr>
<td>PP</td>
<td>157 (81%)</td>
<td>38 (19%)</td>
<td>168 (86%)</td>
<td>27 (14%)</td>
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<tr>
<td>PND</td>
<td>106 (72%)</td>
<td>42 (28%)</td>
<td>118 (80%)</td>
<td>30 (20%)</td>
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* p-value <0.05

Perry, DiFlorio et al, submitted
4. Postpartum triggering an important clue to aetiology

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Postpartum Psychosis - Are genetic factors involved?

“My family has a grand tradition, after a woman gives birth, she goes mad.”

Adrienne Martini
Vulnerability to postpartum episodes is familial

Chi-square = 15.77
p = 0.00007

Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls

The Wellcome Trust Case Control Consortium*

There is increasing evidence that genome-wide association (GWA) studies represent a powerful approach to the identification of genes involved in common human diseases. We describe a joint GWA study (using the Affymetrix GeneChip 500K Mapping Array Set) undertaken in the British population, which has examined ~2,000 individuals for each of 7 major diseases and a shared set of ~3,000 controls. Case-control comparisons identified 24 independent association signals at $P < 5 \times 10^{-7}$ in bipolar disorder, 1 in coronary artery disease, 9 in Crohn's disease, 3 in rheumatoid arthritis, 7 in type 1 diabetes and 3 in type 2 diabetes. On the basis of prior findings and replication studies thus far completed, almost all of these signals reflect genuine susceptibility effects. We observed association at many previously identified loci, and found compelling evidence that some loci confer risk for more than one of the diseases studied. Across all diseases, we identified a large number of further signals (including 58 loci with single-point $P$ values between $10^{-5}$ and $5 \times 10^{-7}$) likely to yield additional susceptibility loci. The importance of appropriately large samples was confirmed by the modest effect sizes
## Genetic Analysis of PP women

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<td>Aarhus University</td>
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* Data submitted included study participants across multiple cohorts
5. Pregnancy raises difficult issues in management
Summary and conclusions

- Childbirth an important trigger for mood episodes
- Specific relationship with bipolar disorder
- Important clinically – but also an important clue for research
- Different factors associated with PP and PND