History of premenstrual mood change and postpartum episodes are associated with perimenopausal episodes in women with bipolar disorder

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Bipolar Disorder
BDRN Research Network

Background

- Previous research has shown that key reproductive life events are potential triggers of mood episodes in women with bipolar disorder.

- The association with childbirth has been studied in depth. In contrast, there is a paucity of research into mood episodes in women with bipolar disorder in relation to the menopause.

- Although limited by small sample sizes, studies published to date suggest the menopause is a period of increased risk of relapse for women with bipolar disorder and indicate potential association between perinatal and perimenopausal mood episodes (Blehar *et al* 1998; Robertson-Blackmore *et al* 2008; Marsh *et al* 2009; Marsh *et al* 2015).

Aim

To establish whether history of premenstrual mood change and postpartum episodes are associated with perimenopausal episodes In a large sample of women with bipolar disorder.

Methods

Participants
- Postmenopausal women with a lifetime DSM-IV diagnosis of bipolar disorder (n=339).

- All women were recruited to an ongoing UK programme of research into the genetic and non-genetic determinants of bipolar disorder (Bipolar Disorder Research Network, BDRN).
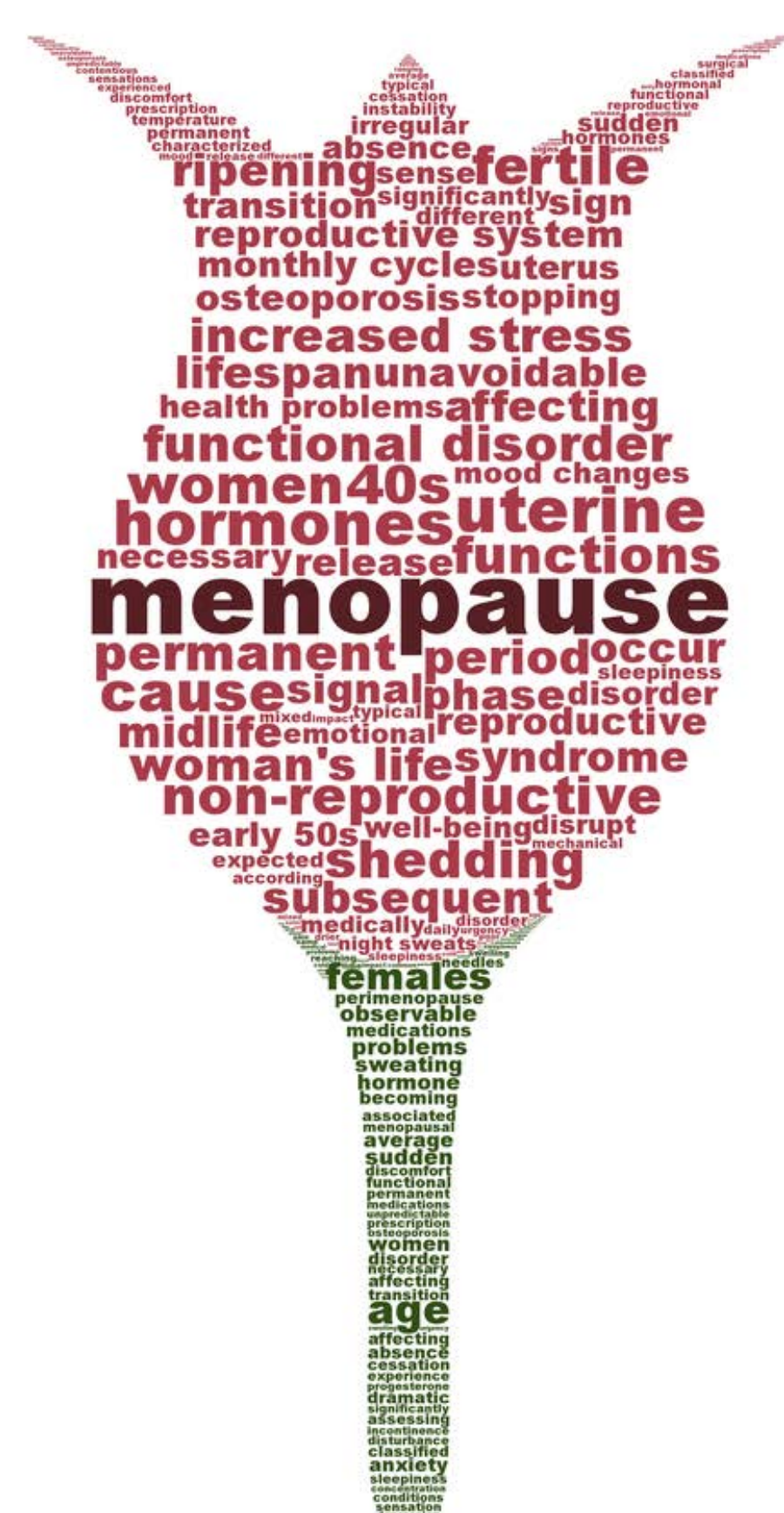
Clinical Assessment
- **Lifetime psychiatric history:** details of lifetime illness course were measured via semi-structured interview (Schedules for Clinical Assessment in Neuropsychiatry, SCAN, Wing *et al* 1990) and review of medical case notes. Diagnoses and lifetime-ever clinical ratings, including **history of postnatal mood episodes**, were made using all available clinical data.

- **Perimenopausal illness episodes:** postmenopausal women were asked via a postal questionnaire to report the presence or absence of any illness episode at the time of the menopause and provide details about the episode.

- **Premenstrual syndrome:** the self-report Premenstrual Symptoms Screening Tool (PSST, Steiner *at al* 2003) was used to measure lifetime diagnosis of **premenstrual dysphoric disorder** (present/absent) and a broader lifetime diagnosis of **moderate/severe premenstrual syndrome** (present/absent).

Statistical Analysis

- Demographic and lifetime clinical characteristics of **women who reported presence (n=200, 59%) and absence (n=139, 41%) of a perimenopausal mood episode** were compared. Chi squared tests were used to compare categorical data. Mann Whitney U tests were used to compare all continuous variables as none were normally distributed.

- Binary logistic regression was used to determine whether a history of postnatal mood episodes and premenstrual syndrome episodes could predict whether or not a woman experienced a mood episode in relation to the menopause after controlling for other significant differences between groups.

Case Example

- 65 year old woman with bipolar I disorder.
- Age 14 years. **Menarche**: coincided with first mood episode.
- Age 25 years. Birth of first son: **postpartum psychosis** onset within 2 weeks of delivery, lasted 3 months.
- Age 27 years. Birth of second son: **postpartum psychosis** onset within a week of delivery lasted 8 weeks, followed by major depressive episode.
- Between ages 27-37 years. No major mood episodes.
- Age 37 years. Onset of **menopause**: episode of mania followed by severe depressive episode. Symptoms refractory to medication, responded to ECT.
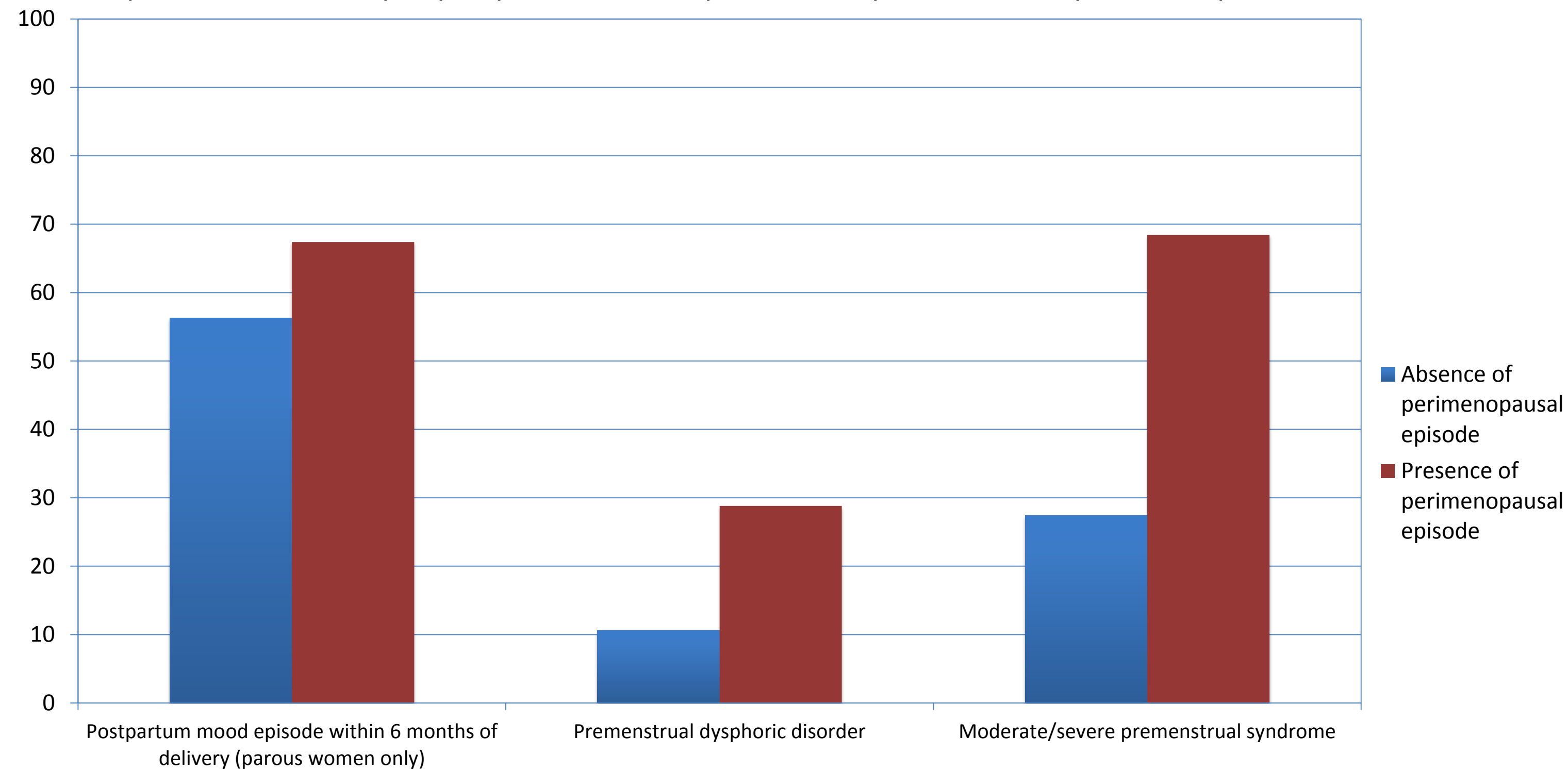
Results

- Presence of perimenopausal episode was significantly associated with being younger at interview and at illness onset, and being less likely to work or have worked in a professional occupation (**Table 1**).

Table 1. Lifetime demographic and clinical characteristics of postmenopausal women with bipolar disorder with and without perimenopausal mood episodes.

	Absence of perimenopausal episode (n=139)	Presence of perimenopausal episode (n=200)	p-value
Age at interview in years, median (IQR)	58 (11)	56 (9)	**p=0.040**
Never married or lived as married, % (n)	9.4% (13)	6.5% (13)	p=0.314
Professional occupation, % (n)	79.9% (111)	68.5% (137)	**p=0.003**
DSM-IV bipolar I disorder, % (n)	75.5% (105)	72.5% (145)	p=0.410
Age of illness onset in years, median (IQR)	25 (14.5)	21 (12)	**p=0.029**
Average number of episodes per year of illness, median (IQR)	0.51 (0.59)	0.63 (0.63)	p=0.236
History of suicide attempt, % (n)	10.8% (15)	15.0% (30)	p=0.189
History of rapid cycling, % (n)	25.2% (35)	21.0% (42)	p=0.906

- Presence of a perimenopausal episode was significantly associated with history of premenstrual dysphoric disorder (p<0.001) and the broader diagnosis of moderate/severe premenstrual syndrome (p<0.001) (**Figure 1**).
- There was a non-significant association between presence of a perimenopausal episode and history of postpartum mood episode (p=0.09) in the smaller sample of parous women only (**Figure 1**).

Figure 1. Proportions of postmenopausal women with bipolar disorder with and without perimenopausal mood episodes with history of postpartum mood episodes and premenstrual syndrome episodes.

Legend: Absence of perimenopausal episode (blue); Presence of perimenopausal episode (red). Categories: Postpartum mood episode within 6 months of delivery (parous women only); Premenstrual dysphoric disorder; Moderate/severe premenstrual syndrome.

- In multivariate regression models, controlling for differences between groups in age at interview, age at illness onset and occupation, the following **significantly predicted presence of perimenopausal episode**:
    - *History of postpartum mood episode*: odds ratio = **2.13** (95% CI 1.09 - 4.17; p=0.027).
    - *History of premenstrual dysphoric disorder*: odds ratio = **2.68** (95% CI 1.30 – 5.51; p=0.007).
    - *History of moderate/severe premenstrual syndrome*: odds ratio = **6.33** (95% CI 3.51 – 11.43; p<0.001).

Conclusions

- Some women who have bipolar disorder may be particularly sensitive to reproductive life events triggering mood episodes (menstruation, childbirth and menopause).
- Previous mood episodes in relation to the female reproductive life cycle may help clinicians predict individual risk of an episode for women with bipolar disorder approaching the menopause.

Limitations
- Relied on participant retrospective self-report of perimenopausal episodes and premenstrual symptoms.

Future research
- Prospective longitudinal studies of women with bipolar disorder providing frequent contemporaneous ratings of mood and reproductive life events are required.

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