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Research paper

Mania triggered by sleep loss and risk of postpartum psychosis in women with bipolar disorder

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ABSTRACT

Background: Women with bipolar disorder are at high risk of affective psychoses following childbirth (i.e. "postpartum psychosis", PP) and there is a need to identify which factors underlie this increased risk. Vulnerability to mood dysregulation following sleep loss may influence risk of PP, as childbirth is typified by sleep disruption. We investigated whether a history of mood episodes triggered by sleep loss was associated with PP in women with bipolar disorder (BD).

Methods: Participants were 870 parous women with BD recruited to the Bipolar Disorder Research Network. Lifetime diagnoses of BD and perinatal episodes were identified via interview and case notes. Information on whether mood episodes had been triggered by sleep loss was derived at interview. Rates of PP were compared between women who did and did not report mood episodes following sleep loss.

Results: Women who reported sleep loss triggering episodes of mania were twice as likely to have experienced an episode of PP (OR = 2.09, 95% CI = 1.47–2.97, $p < 0.001$) compared to women who did not report this. There was no significant association between depression triggered by sleep loss and PP ($p = 0.526$).

Limitations: Data were cross-sectional therefore may be subject to recall bias. We also did not have objective data on sleep disruption that had occurred during the postpartum period or prior to mood episodes.

Conclusions: In clinical practice, a history of mania following sleep loss could be a marker of increased vulnerability to PP, and should be discussed with BD women who are pregnant or planning to conceive.

1. Introduction

Women with bipolar disorder are at increased risk of affective psychoses (i.e. including mania, mixed episodes and psychotic depression) in the postpartum period (Jones et al., 2014). These episodes have traditionally been labelled as 'postpartum psychosis' (PP), with the majority of episodes having a sudden onset, typically within the first two postpartum weeks (Brockington et al., 1981; Heron et al., 2007). In the general population, PP affects approximately 1 in 1000 parous women (Kendell et al., 1987). In contrast, 20–30% of parous women with a history of bipolar disorder have experienced an episode of PP (Di Florio et al., 2013; Jones and Craddock, 2001; Wesseloo et al., 2016). This, combined with other evidence (reviewed in Jones et al., 2010), suggests that PP may be best conceptualised as a bipolar diathesis combined with a vulnerability to a puerperal (i.e. childbirth-related) trigger.

Research to date has primarily focused on how childbirth might trigger episodes of bipolar illness. Proposed triggers include changes in medication, the psychosocial adaption to parenthood, and obstetric complications, in addition to biological factors such as the dramatic hormonal changes that occur following delivery. To date, the most promising factors implicated in the aetiology of PP include primiparity, dysregulation of immune system function, and genetic factors (see Jones et al., 2014, for a recent review).

However, a plausible but understudied candidate for triggering PP is sleep disruption, which has been associated with the onset of mania (Wehr, 1991) and, of course, is characteristic of the perinatal period (Beebe and Lee, 2007). Sleep loss is a commonly reported antecedent of manic episodes (Jackson et al., 2003), a finding corroborated in clinical case-studies, longitudinal studies of sleep and mood within individuals with BD, and experimentally-induced sleep deprivation studies (Bauer et al., 2006; Leibenluft et al., 1996; Wehr, 1991, 1989; Wehr et al., 1987, 1982). This, in combination with findings that sleep deprivation can be a dramatic but short-term treatment for depression (Benedetti,

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2012; Benedetti et al., 2001), has led to the hypothesis that acute sleep loss has mania-inducing effects (Wehr, 1991; Wehr et al., 1987; Wu and Bunney, 1990). Examination of the biological mechanisms that may underlie this effect is ongoing, although recent theories propose that sleep loss exerts an antidepressant effect by resetting processes that are a result of abnormal clock genes (Bunney and Bunney, 2013).

To date, few studies have examined the association between perinatal sleep loss and PP (Lewis et al., 2016). A retrospective study of parous women found that those who developed PP had significantly longer labours and were more likely to give birth during the night (Sharma et al., 2004), suggesting that women with PP experienced greater sleep disruption in the perinatal period. Furthermore, a case study of 3 women with a history of PP found that they became manic or hypomanic following experimentally-induced sleep deprivation (Strouse et al., 1992). Conversely, one of the few prospective studies on PP and perinatal sleep comparing the sleep of pregnant women with a history of BD or PP (i.e. a group at high risk of PP) to pregnant healthy controls found no significant differences in sleep/wake patterns during pregnancy between these groups (Bilszta et al., 2010). However, due to insufficient sample size, the authors were unable to compare the sleep of women who relapsed following childbirth to those who remained well. Thus it remains unclear whether women who develop PP experience greater sleep disturbance prior to episode onset. However, an alternative explanation is that women who develop PP are more sensitive than average to the sleep disturbances that typify the perinatal period. This hypothesis is plausible for two reasons. First, research examining responses to sleep deprivation finds that there is considerable variation within healthy populations, with some individuals showing more pronounced neurobehavioural sequelae than others (Rupp et al., 2012) and emerging evidence suggests that this might be moderated by genetic factors (Groeger et al., 2008; Kuna et al., 2012). Second, although it is thought that individuals with psychiatric disorders are more vulnerable to the negative effects of sleep disturbance than healthy populations, there is evidence of variation in response to sleep deprivation within the BD population. For example, Benedetti and colleagues have found that an antidepressant response to sleep deprivation in individuals with BD is associated with genetic factors (Benedetti et al., 2012; Benedetti and Smeraldi, 2009). This variation within the BD population in how individuals respond to sleep loss may extend to women in the perinatal period, with some women with BD being more sensitive to perinatal sleep disturbance and therefore potentially more susceptible to PP.

In light of the above literature, and given that episodes of PP typically have a manic presentation (Brockington et al., 1981), we hypothesised that women with BD who report episodes of mania being triggered by sleep loss would be more likely to experience PP than those who do not report sleep loss as a trigger for manic episodes. This paper explores this hypothesis in parous women (i.e. women who have given birth) who were recruited to the Bipolar Disorder Research Network (BDRN, bdrn.org).

2. Methods

2.1. Recruitment

Data were analysed from an ongoing large clinical and molecular genetic research programme of mood disorders, the Bipolar Disorder Research Network (BDRN). Participants are recruited systematically and non-systematically from a variety of settings including UK community mental health teams, media and patient support organizations (such as Bipolar UK). Recruitment methods and further information about BDRN has been reported elsewhere (Di Florio et al., 2013). The research programme has UK National Health Service (NHS) Research Ethics Committee approval and local Research and Development approval in all participating NHS Trusts/Health Boards. All participants included in the study reported here met DSM-IV criteria for bipolar disorder, were ≥ 18 years of age and provided written informed consent. Exclusion criteria were affective illness experienced only in relation to alcohol, substance dependence, physical illness or medication. The participants included in the current analysis were recruited between November 2007 and July 2013, as this was the period in which questions on triggers of mood episodes (described below) were added to the main interview.

2.2. Assessments

Research psychologists or psychiatrists administered all assessments and diagnostic procedures. Evidence suggests that risk of PP is greatest for women with bipolar I disorder (BD-I) (Di Florio et al., 2013), thus we limited the current analyses to women with a lifetime DSM-IV diagnosis of BD-I. Best estimate lifetime diagnoses according to DSM-IV were based on psychiatric history ascertained via a semi-structured interview, the Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990) and available psychiatric case-notes. Interview and case note data were also combined to determine key clinical variables such as occurrence of psychiatric episodes in the perinatal period. In cases where there was doubt, diagnostic and clinical ratings were made by at least two members of the research team blind to each other's rating and consensus was reached via discussion where necessary. The inter-rater reliability for DSM-IV diagnoses, for both lifetime and perinatal episodes, was high ($\kappa = 0.85$ and 0.92 respectively).

Data collected on all the pregnancies of each parous woman were used to make lifetime ratings of postpartum episodes. PP was defined as a lifetime DSM-IV manic, mixed, psychotic depression or other psychotic episode occurring within 6 weeks of delivery. Postpartum depression (PD) was defined as a lifetime DSM-IV episode of non-psychotic depression with onset within 6 weeks of delivery, with no lifetime episodes of PP. The temporal association of episodes to childbirth was chosen as 6 weeks based on previous research indicating that the majority of postpartum episodes occur within this time-frame and to include both DSM-IV and ICD-10 definitions of the postpartum period (Di Florio et al., 2013). Women were assigned to PP or PD categories in a hierarchical manner so that in instances where women had experienced both PP and PD, they were assigned to the PP group.

Information on triggers of past manic and depressive episodes was derived at interview, where participants were asked about triggers of their episodes of mania and depression, which included specific questions about sleep loss, physical illness, non-prescription drug use, medication and alcohol. Interviewers made it clear to participants that (1) questions referred to triggers rather than early warning signs, and (2) for an event to qualify as a trigger it had to have occurred during a euthymic period. If participants could not distinguish whether sleep loss (or any other trigger) had acted as early warning sign or trigger, their responses were rated as ‘unsure’.

For our analyses, we focused on whether women had reported that sleep loss had triggered manic or depressive episodes. Responses were used to group women into (i) those who reported that their episodes of mania were triggered by sleep loss versus those who did not (i.e. “sleep loss triggering mania”) and (ii) those who reported that their episodes of depression were triggered by sleep loss versus those who did not (i.e. “sleep loss triggering depression”). As data were retrospective, it is possible that women who reported sleep loss as a trigger of mood episodes were referring solely to episodes that had occurred in the postpartum period. To reduce the likelihood of this, we excluded women who had only experienced mood episodes in relation to childbirth.

2.3. Statistical analysis

All analyses were conducted using SPSS version 20. In primary analyses, we used chi-square tests to examine associations between sleep loss triggering mania and lifetime PP. Specifically, we compared