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Editorial

Is sleep disruption a trigger for postpartum psychosis?

Katie J. S. Lewis, Russell G. Foster and Ian R. Jones

Summary
An episode of postpartum psychosis can be devastating for a woman and her family, and it is vital we understand the factors involved in the aetiology of this condition. Sleep and circadian rhythm disruption is a plausible candidate but further research is needed that builds on the latest advances in chronobiology and neuroscience.

Declaration of interest
None.

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Postpartum psychosis and sleep/circadian rhythm disruption

Postpartum psychosis, a severe episode of mania or psychosis following childbirth, occurs following around 1 in every 1000 births and requires prompt identification and treatment. Despite investigation of hormonal, immunological and genetic factors,[1] the precise aetiology of postpartum psychosis and the nature of the childbirth-related trigger remain unclear. However, episodes of postpartum psychosis are frequently characterised by symptoms of mania, and women with a history of bipolar disorder have a particularly high risk of postpartum psychosis (around 20%[2]), suggesting that many episodes of postpartum psychosis are a manifestation of bipolar disorder triggered by childbirth. One possibility is that postpartum psychosis is triggered by similar factors to non-puerperal mania, one of the most common being sleep and circadian rhythm disruption (SCRD).[3] The greatest sleep disruption occurs in the immediate perinatal period,[4] which closely coincides with the onset of postpartum psychosis symptoms.[5] Therefore it is possible that SCRD incurred in the perinatal period increases the risk of postpartum psychosis in vulnerable women.

A relationship between sleep disruption and postpartum psychosis is often assumed but the evidence base is surprisingly lacking. A frequently cited study by Sharma and colleagues reported that women with postpartum psychosis were more likely to give birth at night and have a longer duration of labour, suggesting that increased sleep disruption played a role in the onset of their illness.[6] In contrast, a prospective study of 'high-risk' pregnant women (i.e. those with a history of bipolar disorder or postpartum psychosis) found no significant differences between their sleep during pregnancy compared with healthy pregnant women.[7] However, as only three of the women in this study relapsed on giving birth, this study was not able to compare the sleep of women who developed postpartum psychosis with that of those who remained well. Both studies also relied solely on subjective or indirect measures of sleep. Therefore, despite being a plausible hypothesis, more work is clearly needed on the association between SCRD and postpartum psychosis before we are able to draw firm conclusions.

Previously, researchers have highlighted the need to conduct prospective studies of SCRD that include both objective and subjective measures of sleep throughout the perinatal period.[8] In addition, we suggest that future studies are informed by recent findings in neuroscience and chronobiology. In the past decade there has been a heightened awareness of the physiological and psychological consequences of SCRD within both healthy and psychiatric populations. It is prudent, therefore, that our current understanding of the mechanisms underlying sleep and circadian rhythm regulation inform future research on the aetiology of postpartum psychosis.

The neuroscience of sleep and circadian rhythms

We can only provide a brief overview of the mechanisms governing sleep and circadian rhythms here, but for more detail see Jagannath *et al*.[9] At the heart of the circadian timing system is a small structure located within the ventral hypothalamus called the suprachiasmatic nuclei (SCN). Individual SCN neurons generate an approximately 24 h oscillation in cellular activity, and the coupling of these individual oscillators allows the SCN to act as the 'master' clock within the body. Such circadian rhythms are driven by a transcriptional–translational feedback loop that modulates the expression of clock genes and clock-controlled genes. Originally it was assumed that the SCN alone drives 24 h rhythms in physiology and behaviour, but we now appreciate that most cells in the body also have the capacity to generate approximately 24 h rhythms, and the role of the SCN is to sustain and coordinate the activity of the circadian network across the tissues and organ systems of the body. The daily adjustment of our physiology by the circadian system has no adaptive value unless the 'internal day' and external day are appropriately aligned. Jet lag represents the classic miss-match between internal and external time. The circadian system is synchronised to the dawn/dusk cycle by specialised photoreceptors within the eye that project to the SCN.[10,11] The SCN then, in turn, entrains the peripheral oscillators throughout the body.

But sleep–wake timing involves more than just the circadian system. Homeostatic processes within the brain drive sleep propensity such that the longer we are awake the greater the need for sleep. A key element of the sleep drive is adenosine, which builds up in the brain as a result of the breakdown of adenosine

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triphosphate. Caffeine antagonises adenosine receptors, which is why we feel less tired after a cup of strong coffee! The circadian system allows the expression of this sleep drive at night and sustains wakefulness during the day. Multiple brain structures and neurotransmitter systems give rise to the different states of sleep and consciousness, indeed, our increasing understanding of how the brain generates sleep is one of the recent success stories of neuroscience research. It is also the complexity of sleep generation and regulation that makes sleep vulnerable to disruption. An abnormality in any one of the key neurotransmitter systems of the brain (such as serotonin or dopamine) will ultimately have an impact on sleep.[9]

SCRD and bipolar disorder

Recent evidence suggests that the neural mechanisms underlying sleep and circadian systems overlap with those implicated in bipolar disorder (see Murray & Harvey[12] for a review). First, the neurotransmitters implicated in mood regulation and bipolar disorder such as serotonin and dopamine have also been found to influence sleep and circadian rhythms. Second, some genetic studies have found associations between polymorphisms in clock genes and bipolar disorder (although results are not consistent). Third, there is evidence that lithium exerts its therapeutic action via glycogen synthase kinase-3 beta (GSK-3β), a regulator of the circadian clock. In addition, therapies that aim to stabilise sleep and biological rhythms have been associated with reduced rates of relapse.[13]

Individual variation in response to SCRD

As discussed above, studies of clock genes in bipolar disorder have produced inconsistent results, leading some researchers to propose that there may be variation between individuals with bipolar disorder in the extent that SCRD is a trigger for episodes of illness. Findings in healthy populations suggest that sleep deprivation may affect neurobehavioural functions to a greater degree in some individuals.[14] In addition, there is evidence that vulnerability to SCRD is under genetic influence, with one twin study reporting a heritability estimate of 83.4%[15] and studies in healthy populations finding associations between vulnerability to sleep loss and variation in sleep and circadian rhythm genes such as *PER3*.[16] Sleep characteristics such as circadian instability could therefore be very promising candidate endophenotypes to explore in bipolar disorder.[12]

Implications for research on postpartum psychosis and clinical practice

It has been over a decade since the initial call for research on sleep disruption as a risk factor for postpartum psychosis,[8] yet there continues to be a dearth of research in this area. More work is clearly needed, particularly research that is informed by recent findings within the field of sleep and circadian neuroscience. Based on the literature outlined above, we propose three avenues. First, given that the majority of episodes of postpartum psychosis are bipolar in nature, research on postpartum psychosis should be informed by knowledge of how SCRD influences the course of bipolar disorder including the neurotransmitters and genetic factors that may be involved. Second, research should account for individual variation in response to SCRD, which may increase risk of relapse following sleep-depriving events such as protracted labour. Finally, future research should incorporate more objective measures of sleep, such as actigraphy. Refining research questions in light of such information will bring us closer to identifying women who are most vulnerable to the effects of perinatal SCRD and postpartum psychosis.

The ultimate aim of research in this area is to procure findings translatable to clinical practice. Identifying those who are most vulnerable to the effects of SCRD can help to focus specific interventions on women for whom they are most beneficial. Combined with other measures of high risk, such as a history of bipolar disorder, individual differences in response to SCRD could be used to give more accurate and individualised assessment of risk of severe postpartum episodes. This could potentially help women and their clinicians make the very difficult decisions about use of medications in the perinatal period. For those women in whom SCRD is likely to be a triggering factor, provisions may then be taken to (a) prevent the woman from experiencing extensive sleep loss, (b) monitor sleep in the perinatal period and (c) plan interventions to administer if a critical level of sleep loss is detected.

However, as the majority of clinicians will not have access to sophisticated measures of SCRD, it is imperative that research utilises behavioural correlates of sleep disturbance. Possible measures of SCRD in a clinical setting include brief questionnaires and sleep diaries completed by patients and/or clinicians, as well as actigraphy. Thus, future protocols should incorporate a variety of subjective and objective measures of sleep in order to determine which indices are reliable at detecting incipient postpartum mood episodes.

To conclude, awareness of current research on SCRD should guide future research on postpartum psychosis. Measures of SCRD may be used to identify (and monitor) individuals who are at high risk of postpartum psychosis in addition to being useful in treatment and prevention strategies. It should be noted that risk for postpartum psychosis is most likely influenced by a myriad of factors, thus the physiological effects of perinatal SCRD may interact with other risk factors (for example immunological, genetic, hormonal) to increase risk. However, the first step is to understand and quantify the increase in risk (if any) that is conferred by perinatal SCRD. Hopefully, such efforts will bring us closer to understanding the aetiology of this severe postpartum disorder and therefore improve our ability to help women at high risk.

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poems by doctors

Mrs Noone

Rowena Warwick

she is all talk,
layers of cigarette smoke, her filthy coat,
her thick Irish accent, muffle her words.
I tune in. *It hurts*, she says, *I hurt*.
I . . . her stream of noise goes on and on like an echo.
She says *I might as well be dead*.

I'm on my own now, everyone else is dead,
the carer comes, skips the evenings, won't talk,
it's always the same, every day an echo
of the last. I say, *first, let's get you out of that coat*.
I think of the patients waiting, I don't want her to feel hurt,
I must listen, not hurry, I must let her have her words.

All we have in this room are words
to get her on to the couch so we can help her, deaden
the pain, her knees, her hips, the places that hurt,
but Mrs. Noone beats us back with her talk
of Ireland, the old days. She hangs on to her stinking coat
holds it to herself like armour, giving us only its echo.

I know, in my own life, there is no space for any echo,
colleagues, husband, home, I am surrounded by words.
So I coax her, attempt to liberate her coat,
my fingers sink into the moth-eaten fur, its deadness
lingers. Her frown deepens but her talk
continues. *That last doctor . . . like razors . . . hurt*.

She looks at me. *Is that needle going to hurt?*
Her eyes with their sagging lower lids have an echo
behind them, which says more than all her talk.
I'll do my best I say, but my words
seem inadequate to comfort this woman with her long-dead
husband, her handbag of treasures and her pernicious coat.

If only we could get her to lie down, lose the coat.
The clock creeps on but we are halted, each wasted minute hurts,
the assistant and I share a glance, swallow up the dead
time. She won't move, this garrulous, pungent, echo
of a woman, though she must know that our words
and our time are metered, despite all our talk.

Then the coat gives way, her mouth slackens, all echoes
end as her body is revealed, in all its hurt. Her words
stop. The air between us is dead, without talk.

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