



Maternal Sleep in Pregnancy and Postpartum Part II: Biomechanisms and Intervention Strategies

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Abstract

Purpose of Review As described in Part I of this two-part review, maternal sleep has wide-ranging implications for maternal health and overall family functioning. In addition, poor sleep quality and insufficient sleep are highly prevalent and characterized by considerable racial disparities.

Recent Findings Part II of this review discusses physiological mechanisms, including inflammation and appetite hormones, by which sleep impacts multiple facets of women's health during pregnancy and postpartum. These mechanisms are increasingly being delineated, but require further study and better integration with studies of behavioral and physical health outcomes. Further, there are multiple potential strategies for improving maternal sleep, providing the opportunity to tailor treatment approaches to individual needs.

Summary Ultimately, as a critical health behavior that is amenable to intervention, sleep provides a promising future direction for measurably impacting clinically relevant health parameters in women of childbearing age.

Keywords Sleep · Perinatal · Inflammation · Cellular aging · Intervention · Cognitive-behavioral therapy · Nutrition · Exercise · Infant · Maternal

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Introduction

As explicated in Part I of this two-part review, recognition of the importance of sleep in perinatal women is growing. In Part II, we shift our focus to biological mechanisms, as well as promising clinical interventions targeting sleep health to this population. First, we highlight the growing literature linking poor sleep with inflammation and biological aging. Next, we review a burgeoning literature on mind-body interventions to improve sleep disturbances and insomnia. Reflecting the multifactorial contributors to sleep health, these interventions are also multifactorial, with a range including stress reduction, sleep hygiene, family-focused interventions, and nutrition. As highlighted, these interventions may work, in part, by affecting inflammatory pathways. There remains great opportunity to better explicate the role of both behavior and biology in perinatal sleep health, which will ultimately inform individualized treatment approaches.

Inflammatory Mechanisms Linking Sleep and Health

Several lines of research have begun to address the question of what biological mechanisms might be involved in connecting sleep and health outcomes. One key mechanism is inflammation, which is a driver of disease [1] and accelerates aging-related conditions [2]. A substantial body of evidence now demonstrates that sleep impacts inflammatory pathways. For example, a recent meta-analysis of 72 studies with a combined sample size over 50,000 concluded that sleep disturbances are associated with significantly elevated markers of inflammation, including C-reactive protein (CRP) and interleukin (IL)-6 [3]. Acute episodes of sleep deprivation have also been shown to activate intracellular transcriptional control pathways that promote proinflammatory responses [4].

A number of studies in pregnancy and postpartum specifically have also documented links between poor sleep quality and shortened sleep duration with elevations in inflammation [5]. Notably, African-American women may exhibit greater vulnerability to physiological dysregulation in the context of poor sleep. In this work, poor sleep during pregnancy results in a more robust inflammatory dysregulation among African-American women than White women, as well as greater increases in risk for shortened gestation [6]. Similarly, among African-American women assessed during early postpartum, poor sleep was uniquely associated with exaggerated LPS-stimulated cytokine production, an effect not present in Whites [7]. The role of race in linking stress and perinatal health requires continued attention in psychoneuroimmunological models.

In the context of pregnancy, where there is already an enhanced inflammatory state, the additional stimulus of poor sleep quality or short sleep duration may push the inflammatory state into a critical danger zone [6]. Risk for maternal health conditions and birth outcomes, including gestational hypertension, gestational diabetes, intrauterine growth restriction, placental dysfunction, and preterm labor have been linked to dysregulation of inflammatory processes [8–10]. Clinical consideration for the impact of sleep during pregnancy is important, as it might directly impact risk for pregnancy complications and adverse birth outcomes.

In addition, maternal health is impacted by inflammatory pathways. Here, literature links inflammation with anxiety and mood disorders [11], including accumulating evidence in perinatal populations [12]. Further, inflammation could contribute to postpartum weight retention, with evidence that inflammation confers risk for subsequent weight gain [13–17], more difficulty losing weight [18], and greater weight re-gain following dieting [18] independent of BMI. These effects may be partially mediated by effects on appetite hormones; chronic inflammation is associated with reductions in serum levels of leptin, an appetite hormone which induces satiety, as well as leptin resistance [19–21].

Sources of inflammation in the body include both immune cell release of proinflammatory cytokines, along with tissue-specific sources, including aged cells and damaged tissue, which can initiate sterile inflammatory responses (inflammation without an external pathogen) [22]. Cellular aging and tissue damage occur progressively, through accumulated wear and tear. Pertinent to this review, cellular aging dynamics have been identified as a mechanism linking sleep loss with disease risk. Its role in pregnancy and postpartum health outcomes is less well defined. However, given a key driver of aging is inflammation [23], under conditions of higher demand (e.g., higher metabolic load, physical stress), such as pregnancy, cells may accumulate some degree of damage. Cells that become damaged release proinflammatory secretory factors and further promote nearby tissue inflammation and damage. A sustained environment of high demand will lead to the accumulation of damage, cellular aging, and senescence [24]. As senescent cells accumulate and remain in the tissue, the proinflammatory environment is enhanced and contributes to poorer outcomes [25].

Sleep may be a critical window when daytime demands on the physiological system are repaired, leading to lower inflammation. When the critical amount of sleep is not obtained, accumulation of damage may result. Pregnancy may be a particularly vulnerable time when high demands on the physiological system exist, including increased metabolic activity, cardiovascular demand, and generation of sufficient blood volume and nutrients to support the developing fetus. Sleep is vital for protecting health, while the inverse—sleep insufficiency—may promote cellular aging. In support of this, recent evidence has demonstrated that sleep loss promotes a pro-aging micro-environment. Experimental sleep deprivation in humans induced changes in gene expression consistent with an upregulation of DNA damage and cellular senescence [26]. Chronic sleep disruption in rodents parallel these findings, showing accumulation of senescent cells in tissue [27]. Prolonged episodes of sleep disturbances have also been associated with shortening of immune cell telomere length, a marker of aging at the cellular level [28, 29], as well as with an estimated older biological age measured using an epigenetic clock marker of aging [30]. Further research interrogating the role of cellular aging and inflammation in the context of pregnancy and postpartum is warranted [31].

Interventions

Cognitive Behavioral Therapy

Cognitive behavioral therapy for insomnia (CBT-I) is highly effective for treating insomnia, with more favorable long-term remission rates than medication [32]. The three main components of CBT-I are sleep hygiene, which

addresses behaviors that influence sleep (e.g., alcohol use, erratic sleep schedules), stimulus control therapy (e.g., setting a consistent bedtime and wake time), and sleep restriction. Although it may seem paradoxical for someone who is having difficulty falling or staying asleep to restrict their time in bed, mild reductions in time in bed improve sleep continuity; once sleep continuity is improved, they can gradually increase their time in bed. Other components of CBT-I may include addressing dysfunctional beliefs about sleep and relaxation training. CBT-I has been used in many populations and can be delivered individually, in group settings, and via telephone or the internet. Although few studies have been conducted in pregnant women, one study reported that participants indicated a preference for CBT-I compared to either pharmacotherapy or acupuncture [33]. A recent pilot study reported significant improvements in sleep quality and reductions in symptoms of insomnia in a group of 13 pregnant women who underwent CBT-I delivered in a group setting [34].

Mindfulness-Based Stress Reduction

As an alternative to CBT-I, there are a number of treatment options available to help individuals struggling with sleep difficulties due to insomnia symptoms. Mindfulness-based stress reduction (MBSR) and related mindfulness-based therapy for insomnia (MBTI) have recently been tested for efficacy in the context of sleep disturbances [35, 36]. MBSR techniques have traditionally been taught in the context of anxiety and stress, with the goal to help individuals understand their physical and mental reactions to stressors and learn to self-regulate, and ultimately reduce their negative physiological response pattern. However, recent work has tested the efficacy of MBSR techniques for helping treat insomnia, with noticeable and parallel effectiveness to traditional CBT-I treatments for insomnia [37]. This is particularly relevant in the context of pregnancy-specific insomnia symptoms, where the sleep restriction component of CBT-I might be contraindicated. To date, no trials have directly assessed the efficacy of MBSR or MBTI in pregnancy and postpartum sleep disturbances. The application of MBSR/MBTI in the context of pregnancy could have both benefits to sleep and benefits for pregnancy and postpartum health, particularly in light of a growing literature documenting a reduction of inflammatory activity after MBSR interventions [38]. Future interventions designed to test the efficacy of MBSR/MBTI for sleep disturbances in the context of pregnancy and postpartum are needed. These interventions might not only benefit maternal sleep but also provide protective benefit against negative birth and postpartum health outcomes.

Yoga/Tai Chi

In parallel to interventions using MBSR, both yoga and Tai Chi are mind-body-based interventions that have been tested for efficacy in treating sleep disturbances in various patient populations. The efficacy of these interventions have been mixed and seem to depend on the patient population and specific needs being addressed. For example, in survivors of breast cancer, yoga [39] and tai chi [40] provide benefit improving both sleep and fatigue [39]. Older adults with insomnia receiving a tai chi intervention did not experience full remission of insomnia over a control group, however, did report improved sleep quality [40] and lowered intracellular inflammatory signaling [41]. Indeed, a number of yoga and tai chi studies have demonstrated efficacy in distinct patient populations with additional benefit to health through downregulation of inflammatory pathways [38] (See Bower and Irwin 2016, for review). Yoga interventions in the context of pregnancy have been described and reviewed with evidence that these interventions are beneficial to the mental health of women [42]. However, no work to date has assessed the efficacy of yoga for sleep problems in the prenatal period nor examined the inflammatory pathways that might be altered in this context, clearly an area in need of further research. Tai chi has not been tested in the context of maternal health and may prove to be beneficial for pregnancy and postpartum health outcomes, although consideration of physical conditions of the mother will necessitate modifications to the training and practice in this context. Overall, the research to date suggests both yoga and tai chi to be potential new intervention designs that might specifically benefit prenatal and postpartum health, improve sleep, and reduce inflammation. Research in this area is warranted to demonstrate its efficacy in this patient population.

Nutrition

It is well established that long-chain polyunsaturated fatty acids (LC-PUFAs), particularly the ω -3 docosahexanoic acid (DHA; 22:6n-3), are critical to fetal growth, neural, and retinal development. Reflecting transfer of fatty acids from the mother to the developing fetus, maternal plasma and red blood cell (RBC) DHA levels decrease markedly and progressively during normal pregnancy and may not return to normal until several months postpartum [43–45]. Infant DHA levels exceed those of the mother for an extended period, particularly among those who are breastfed [43–45]. This preferential transfer of fatty acids potentiates the likelihood of poor fatty acid status in women during pregnancy and postpartum. However, increased fatty acid intake via supplements or food results in marked and stable improvements in serum DHA within 1 month of initiation can prevent pregnancy-related declines in maternal levels [43, 46].

This is of relevance to sleep; observational and experimental evidence in animals, as well as children and adults, supports a role for LC-PUFAs in subjective sleep quality, objective sleep quality (per actigraphy), sleep architecture, and cardiovascular function during sleep [47–52]. Implicated mechanisms include normalization of melatonin secretion and anti-inflammatory effects [51, 53, 54]. In perhaps the largest study on sleep and ω -3 PUFAs to-date, in 362 children (7–9 yrs), poorer sleep quality was modestly associated with lower serum DHA and a lower DHA:arachidonic (AA) ratio at baseline; following a 16-week supplementation with DHA vs placebo, actigraphy in a subset of 43 children showed considerably fewer waking episodes and longer total sleep duration in DHA-supplemented children, supporting a causal link between DHA status and sleep. However, overall, this literature is relatively small and, despite their unique vulnerability to DHA depletion, data on perinatal women are lacking, providing a promising future direction.

Family-Focused Intervention Strategies

Of relevance at postpartum, infant sleep is rooted in the larger family system and in specific patterns of family interaction, and in family emotional climate, that shape the development of self-regulated sleep. Interventions to reduce infant sleep problems vary widely and, for already established sleep problems, frequently involve some form of graduated extinction that involves working with parents to increase, gradually, their response time to infant crying during nighttime awakenings, with the goal of promoting infants' ability to soothe themselves to sleep [55]. Other family-based approaches, however, that emphasize prevention of sleep problems, have been successfully used that take into account developmental processes in infant sleep consolidation and regulation (in particular, the fact that infant sleep regulation develops very rapidly across the first 6 months of life) and the roles of parenting and family-level processes that proactively shape infant sleep regulation.

One such approach involves the establishment of bedtime routines [56], which has been found to reduce infants' latency to sleep, frequency, and length of infant nighttime awakenings, and mothers' reports of reduced difficulties putting the infant to sleep. Another approach, currently being implemented, draws from empirical findings that coparenting quality at bedtime promotes infant sleep quality [57] and from the evidenced-based transition to parenthood coparenting intervention program, Family Foundations [58]. This program is specifically adapted to promote coparenting in and around infant sleep contexts, with the goal of promoting not only infant but also parent sleep, parental well-being, coparenting, and individual parenting quality, and infant socio-emotional outcomes across the first year. This study, funded by the

National Institute of Child Health and Human Development, awaits its first wave of findings.

Conclusions

The physiological consequences of poor sleep during pregnancy and postpartum are poorly delineated, however, a growing body of work suggests poor sleep increases inflammatory and cell stress pathways raising risk for poorer health outcomes. As a measurable and modifiable health behavior for which effective behavioral interventions are available, empirical focus on sleep health presents a promising direction for improving multiple inter-related perinatal mental and physical health outcomes. Of promise, mind-body interventions such as mindfulness, yoga, and tai chi have proven effectiveness in a number of patient populations, but have not been well studied in the context of pregnancy and sleep. Moreover, pregnancy and postpartum presents unique nutritional burdens, attention to which has relevance to sleep. Finally, postpartum through early childhood represents a unique time during which sleep of family members significantly impacts other members. Future research should aim to explicate the inter-relationship between behavioral and biological pathways in perinatal sleep health and also tailor existing sleep strategies for the perinatal period with consideration for unique vulnerabilities and opportunities for intervention in this context.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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