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At the Forefront of Psychoneuroimmunology in Pregnancy: Implications for Racial Disparities in Birth Outcomes PART 1: Behavioral Risks Factors

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Abstract

Birth prior to full term is a substantial public health issue. In the US, ~400,000 babies per year are born preterm (< 37 weeks), while >1 million are early term (37–38^{6/7} weeks). Birth prior to full term confers risk both immediate and long term, including neonatal intensive care, decrements in school performance, and increased mortality risk from infancy through young adulthood. Risk for low birth weight and preterm birth are 1.5–2 times greater among African Americans versus Whites. Psychosocial stress related to being a member of a discriminated racial minority group contributes substantially to these racial disparities. Providing promising targets for intervention, depressed mood, anxiety, and poor sleep are each linked with exposure to chronic stress, including racial discrimination. A rigorous transdisciplinary approach addressing these gaps holds great promise for clinical impact in addressing racial disparities as well as ameliorating effects of stress on perinatal health more broadly. As will be reviewed in a companion paper, the mechanistic roles of physiological sequelae to stress – including neuroendocrine, inflammatory regulation, biological aging, and the microbiome – also require delineation.

Keywords

psychoneuroimmunology; stress; sleep; depression; anxiety; pregnancy; birth outcomes; racial disparities

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1. Introduction

Birth prior to full term is a substantial public health issue. With an overall preterm birth rate of 12%, the US ranks 130th out of 184 countries globally (Blencowe et al., 2013). Closely linked with length of gestation, the US has had the highest infant mortality rate among high-income countries for decades. These poor rankings are largely attributable to high rates of shortened gestation, low birth weight, and infant mortality among African Americans, among whom rates of these adverse outcomes are 1.5 to 2 times greater than among White/European Americans. It is increasingly recognized that psychosocial factors related to being a member of a discriminated racial minority group, and the accompanying physiological sequelae, contribute substantially to these racial disparities. However, despite widespread recognition that psychosocial and biological factors are closely and bi-directionally linked, data related to these areas remains relatively separate in the birth outcomes literature. A transdisciplinary approach which examines these processes together in a novel and holistic manner represents a critical next step in advancing clinical practice. The current paper will review the existing literature on psychological factors contributing to adverse birth outcomes, while a companion paper will review biological mechanisms implicated in these pathways. Promising directions in relation to understanding mechanistic underpinnings of racial disparities will be explicated, with a focus on opportunities for advancing the literature – particularly moving research toward clinical translation.

2. Delivery Prior to Full Term: Epidemiology and Consequences

As described, in the US, nearly 400,000 babies each year are born preterm, while over an additional 1,000,000 are delivered at early term. Preterm birth (PTB) is the leading cause of infant death and long-term disability in developed countries (Blencowe et al., 2013; Liu et al., 2015). Surviving infants are at immediate risk for respiratory distress, heart problems, brain hemorrhage, anemia, jaundice, and sepsis. Although they represent 9.62% of births, preterm infants account for 57% of the \$12.2 billion in newborn hospital costs annually (Kowlessar NM et al., 2013). Long-term complications include cerebral palsy, cognitive delays, hearing and vision deficits, and poor growth (Mattison et al., 2001).

A relatively new designation, early term birth (ETB; 37–38^{6/7} weeks) has been recognized as a public health concern by the American Congress of Obstetricians and Gynecologists (ACOG) since 2013 (Spong, 2013; The American College of Obstetricians and Gynecologists Committee on Obstetric Practice, 2013). Compared to birth at 39 weeks or later, ETB significantly increases risk for immediate complications including hypoglycemia, need for intravenous fluids, treatment with intravenous antibiotics, mechanical ventilation and intubation, and NICU admission (Sengupta et al., 2013; Tita et al., 2009). Accumulating data from numerous studies link ETB with negative effects on cognitive and motor development in early life, poorer academic achievement in school-aged children, and less efficient brain networks in pre-adolescents (Chan et al., 2016; Chan and Quigley, 2014; Espel et al., 2014; Kim et al., 2014; Noble et al., 2012; Quigley et al., 2012). Effects on physical health are also seen, with increased risk for asthma and wheezing, increased number of hospital admissions, and longstanding illness in childhood (Boyle et al., 2012;

Edwards et al., 2015; Harju et al., 2014). ETB also increases risk for neonatal, postnatal, infant, childhood, and young adult mortality (Crump et al., 2013; Reddy et al., 2011).

Although birth at < 37 weeks (PTB) confers greater risks along this continuum, birth between 37–38^{6/7} weeks (ETB) affects nearly 3 times as many deliveries, thus, the public health implications are substantial. Moreover, women with prior ETB have more than 2X greater risk for both subsequent PTB and repeated ETB (Yang et al., 2016), suggesting that both categorical designations share common etiological pathways and may best be understood as a continuum of the same condition: shortened gestation. While PTB has been studied for decades, data specific to or inclusive of ETB are comparatively sparse. This represents an important gap/future direction in the literature. Of critical methodological importance, the long-standing practice of comparing deliveries occurring at < 37 weeks to those occurring at ≥ 37 results in the inclusion of ETB as part of the “control” group. This is highly problematic; given the evidence that ETB is part of a continuum of shortened gestation (Spong, 2013; The American College of Obstetricians and Gynecologists Committee on Obstetric Practice, 2013), this approach presumably dilutes statistical power to detect predictors of shortened gestation quite considerably.

2.1. Medically-Indicated vs Spontaneous Shortened Gestation.

Cases of shortened gestation can be classified as medically-indicated or spontaneous. Accounting for ~30% of cases, medically-indicated cases are initiated by the provider to protect maternal and/or fetal health, in the context of conditions including preeclampsia and intrauterine growth restriction. These cases are not entirely predictable, but are more common among women > 35 years, smokers, those with hypertension or diabetes, multifetal gestation, and/or obesity (Ananth et al., 2013).

The remaining 70% of cases of shortened gestation are spontaneous, occurring following onset of labor or rupture of membranes. The two strongest predictors of spontaneous shortened gestation are African American race and history of shortened gestation (Yang et al., 2016). Neither of these predictive factors provides mechanistic insight as to causal contributors that can be addressed to mitigate risk. Beyond these two risk factors, clinical prediction of spontaneous occurrence of shortened gestation is remarkably limited. As such, it is widely recognized as an “enigma” and “clinic dilemma” (Menon, 2008; Muglia and Katz, 2010; Norman and Shennan, 2013).

Of note, in studies of etiology of shortened gestation, spontaneous and medically-indicated cases are often pooled together. However, there is considerable debate in the literature with regard to separating versus pooling (Savitz et al., 2005). The central argument for pooling is that both types may share common underlying causes, including psychological stress, inflammation, and vascular dysfunction. If so, pooling increases statistical power. Conversely, arguments in favor of separation of subtypes contend that distinctive pathways will be obscured by pooling. There is currently no consensus on this issue, which requires greater data to determine empirically.

Amongst studies which do focus on a specific category of shortened gestation, spontaneous occurrence is notably underrepresented, even though spontaneous cases are both much more

common and unpredictable than medically-indicated cases. For example, a systematic review of transcriptomics in preterm birth found that 76% of studies focused on medically-indicated cases (Eidem et al., 2015). This disproportionate representation largely reflects greater methodological hurdles to studying spontaneous occurrence. Women with preeclampsia, fetal growth restriction, or other known medical indications can be readily identified well prior to delivery. In contrast, prospective enrollment is required to capture spontaneous cases, contributing to a comparative lack of data on predictors and mechanisms. Thus, to advance the literature in this area, addressing a) the extent to which medically-indicated and spontaneous cases exhibit shared versus distinct etiologies is of importance, as is b) greater focus specific to spontaneous occurrence.

2.2. Prevention of Spontaneous Shortened Gestation.

Corresponding with difficulties in prediction, approaches to mitigate risk for shortened gestation are limited and indicated only for women with specific risk factors (e.g., short cervix). A recent comprehensive review concluded that, in developed countries, systematic implementation of three known interventions - cervical cerclage, progesterone supplementation, and smoking cessation - would prevent *less than 5%* of all spontaneous PTBs (Chang et al., 2013). Because ETB is a relatively new designation, efforts to-date have focused almost exclusively on reducing elective C-sections prior to 39 weeks completed gestation (Richards et al., 2016; Snowden et al., 2017), while efforts to prevent spontaneous cases of ETB are lacking. The lack of preventive strategies for spontaneous shortened gestation – inclusive of early term and preterm birth – is a direct reflection of the inability to predict its occurrence, and thus offer appropriate clinical treatment to mitigate specific risk factors.

2.3. Racial Disparities in Shortened Gestation.

There are remarkable and intractable racial disparities in shortened gestation in the US. Overall, 40.6% of births in African Americans occur prior to full term (13.1% preterm and 27.5% early term) compared to 33.1% of Whites (8.9% preterm and 24.2% early term) (Centers for Disease Control). Racial disparities in shortened gestation contribute to the remarkable two times higher infant mortality in African Americans vs Whites (11.11 vs 5.06 deaths per 1,000 live births) (Rossen and Schoendorf, 2014). Even among births occurring at 37–38^{6/7} weeks (i.e., early term births), neonatal mortality is 40% higher among African Americans than Whites, and postneonatal mortality is 80% higher (Reddy et al., 2011). Thus, African Americans experience both greater risk for shortened gestation, and substantially worse health consequences for their infants when it does occur.

Over the past four decades, researchers have thoroughly examined the role of key potential explanations for these racial disparities in birth outcomes. As detailed below, traditional risk factors, including socioeconomic status, genetics, and health behaviors, do not adequately account for the observed racial disparities. Converging evidence suggests that it is, in fact, the lived experience of being an African American woman in the United States that confers risk to health (Villarosa, 2018).

First – these racial disparities are not explained by socioeconomic status (SES). Lower SES women experience higher risk of shortened gestation, low birth weight, and infant mortality regardless of race. However, the effect of race is super-imposed on top of effects of SES, whereby an African American woman with college education has a greater risk for preterm birth and low birth weight than does a White woman with less than an 8th grade education (National Center for Health Statistics, 2017).

Second, abundant data now demonstrate that racial disparities in birth outcomes and infant death are not adequately explained by differences in health behaviors including alcohol use, smoking, healthy diet, or access to prenatal care (Goldenberg et al., 1996). For example, an estimated 10.5% of White women smoke during pregnancy as compared to 6.0% of Blacks (National Center for Health Statistics, 2018). Moreover, even among women who received early prenatal care, as compared to Whites, African American women experience 3.5 times greater odds of perinatal mortality – defined as loss of a fetus or infant death within 4 weeks of birth (Healy et al., 2006).

Finally, these racial disparities are not driven by genetic differences. Seminal research on this topic, which has subsequently been shown in other cohorts, demonstrated that infants born to black women who were recent immigrants to the US had higher birth weights than infants born to black women of African descent who were born in the US (David and Collins, 1997; DeSisto et al., 2018). Moreover, remarkably, while birth weight *increases* across generations in White/European immigrants, it *decreases* across generations among those of African and Caribbean descent even when women become more educated/affluent (Collins et al., 2002). Increased risk for low birth weight conferred by African-American status was measurable with increased time spent in the US, with significant effects observable after only one generation spent in the US. These findings provide convincing support for a social rather the genetic explanation for racial disparities in birth outcomes.

All considered, “traditional” risk factors for shortened gestation lack adequate power to explain racial disparities in outcomes. There is growing clinical consensus that, as forwarded by the long-standing “weathering hypothesis” (Geronimus, 1992), the psychosocial stress of living in the US as a racial minority plays a primary role in observed racial disparities in birth outcomes. Consistent with this hypothesis, exposure to racial discrimination has been linked with increased risk for preterm birth and low birth weight in multiple studies (e.g., Collins et al., 2004; Mustillo et al., 2004; Rosenberg et al., 2002).

From a clinical standpoint, recognition of the role of racial discrimination in birth disparities presents both an opportunity and a challenge. While changing society to reduce exposure to the objectively stressful exposure to racial discrimination is the ultimate goal, the clinical question remains: *In the context of this societal problem, how can we intervene to affect health at the individual level?*

It is not clinically feasible to prevent exposure to racial discrimination, or other types of chronic stress, at the individual level. However, resulting behavioral and biological sequelae provide promising targets for intervention. In terms of behavioral factors, depressed mood, anxiety, and poor sleep health are each linked with exposure to racial discrimination (Francis

et al., 2017; Grandner et al., 2012; Tomfohr et al., 2012; Williams et al., 2003). These can be effectively assessed in the clinical setting and are amenable to treatment. In addition, the mechanistic roles of neuroendocrine and inflammatory regulation, as well as biological aging require delineation as targets of intervention. While explicating these pathways has particular relevance to addressing the substantial public health issue of racial disparities in birth outcomes, it will ultimately serve to inform understanding of the role of psychosocial stress and physiological dysregulation in perinatal health more broadly, as depicted in Figure 1, with the potential for wide applicability.

3. Behavioral Factors Linked with Shortened Gestation

A relatively large body of literature links psychological distress with preterm birth or shorter gestation (as a continuous measure). Methodology has become more rigorous over time, with concomitant increases in positive (versus null) findings (Staneva et al., 2015; The Institute of Medicine Committee on Understanding Premature Birth and Assuring Healthy Outcomes, 2007). Measures that have been associated with length of gestation include perceived racial discrimination (Collins et al., 2004; Dole et al., 2003; Dole et al., 2004; Giscoombe and Lobel, 2005; Giurgescu et al., 2012; Mustillo et al., 2004; Rankin et al., 2011; Rosenberg et al., 2002), perceived stress (Copper et al., 1996; Glynn et al., 2008; Pritchard, 1994; Tegethoff et al., 2010), pregnancy-specific anxiety (Coussons-Read et al., 2012; Dole et al., 2003; Kramer et al., 2009; Lobel et al., 2008; Mancuso et al., 2004; Rini et al., 1997; Wadhwa et al., 1993), depressive symptoms, (Nylen et al., 2013; Oberlander et al., 2006; Orr et al., 2002; Phillips et al., 2010; Steer et al., 1992; Straub et al., 2012), occurrence of stressful life events (Barrios et al., 2014; Dole et al., 2003; Nordentoft et al., 1996; Wadhwa et al., 1993), and early life stress/adversity (Christiaens et al., 2015; Gillespie et al., 2017; Nesari et al., 2018). Studies differ markedly in measurements utilized including the chronicity, type, and subjective versus objective experience of stress. For example, in relation to racial discrimination, predominant approaches focus on assessing perceived frequency of exposure to everyday discrimination (e.g., poor service at restaurants) and/or major discriminatory events across one's lifetime (e.g., being denied a job), while data on the role of microaggressions or the subjective distress experienced in response to exposures to discrimination are more limited. There is currently no consensus on the best assessment approach with regard to stress exposure and birth outcomes.

As will be reviewed, psychological stress – broadly defined – may contribute to risk of spontaneous shortened gestation via neuroendocrine, immune, and other biological pathways. In addition, stress may also promote gestational hypertension, intrauterine growth restriction, and placental dysfunction via inflammatory pathways (Arck, 2001; Kanayama et al., 1997; Khatun et al., 1999; Kurki et al., 2000; Landsbergis and Hatch, 1996; Ness and Sibai, 2006), thus contributing to medically-indicated cases of shortened gestation.

Explicating the exact effects and magnitude of relationships between particular interrelated stress constructs (e.g., early life stress, racial discrimination, mood) and birth outcomes is of great utility from an empirical standpoint. However, in consideration of clinical translation, assessment approaches that correspond with clinical conditions and for which empirically-supported treatments are available are of particular value. For example, although predictive

of shortened gestation in several studies, screening for exposure to racial discrimination in an obstetric clinic setting is unlikely to be adopted due to lack of acceptability among both providers and patients given unclear treatment options. As reviewed herein, mental health disorders as well as sleep health have defined criteria and established treatments, presenting acceptable targets for screening in clinical settings. Both are strongly linked with exposure to other types of stressors – including racial discrimination – providing modifiable risk factors for addressing racial disparities.

3.1. Depression, Anxiety, and Shortened Gestation.

Over the past three decades, accumulating evidence supports the role of depressed mood and anxiety in risk for adverse birth outcomes, including preterm birth, low birth weight, and intrauterine growth restriction. These effects are considerable. For example, two meta-analyses encompassing 38 separate studies show that depressive symptoms and anxiety are associated with relative risk of PTB of 1.39 and 1.5, respectively (Ding et al., 2014; Grote et al., 2010). These effects are roughly comparable to the magnitude of risk imparted by smoking 10 cigarettes per day.

While the data on associations between depressive symptoms and anxiety with birth outcomes is sizable, the literature to-date has significant limitations. First, existing studies have not included a focus on early term birth (ETB), because ACOG has only recognized this as a public health issue since 2013. As described, it is now understood that ETB incurs significant health consequences. Although the effects of preterm birth are more severe, early term birth affects more than twice as many deliveries. Thus, the public health impact is great. Lack of data on psychological health in shortened gestation inclusive of ETB represents an important knowledge gap.

A second critical limitation of the existing literature is lack of representation of African American women. A large proportion of studies on mood/anxiety and birth outcomes is derived from non-US cohorts, including studies in England, France, Germany, Sweden, and Norway. Among studies conducted in the US which include African American women, race is often highly confounded with socioeconomic status. In addition, race is commonly treated as a control variable, rather than a moderator. This is of methodological importance; as described, exposure to racial discrimination is associated with increased risk for anxiety and mood disorders. Moreover, African American women may experience greater vulnerability to physiological dysregulation in the context of psychosocial stress. For example, our data show that, during pregnancy and non-pregnancy, African American women exhibit exaggerated proinflammatory cytokine responses to acute laboratory stressor exposure as compared to White women (Christian et al., 2013). In addition, as detailed below, our data show that compared to Whites, African American women show heightened risk for shortened gestation as well as greater inflammatory dysregulation in the context of poor sleep during pregnancy as well as postpartum (Blair et al., 2015; Christian et al., 2018). Race may similarly impart enhanced vulnerability to physiological dysregulation in the context of depression and anxiety.

Also of clinical importance, the vast majority of existing data are based on assessment of symptoms, rather than diagnoses. In meta-analyses of psychological factors and birth

outcomes, only 2 of 12 anxiety studies examined clinical diagnoses while only 3 of 29 studies of depression/depressive symptoms did so (Ding et al., 2014; Grote et al., 2010). Other studies have focused on other types of stress and distress, including perceived racial discrimination, general perceived stress, and exposure to events such as natural disasters (for review see Christian, 2012). These data provide valuable context and insight as to pathways by which stress affects maternal-fetal health. However, screening for racial discrimination, general perceived stress, and other related factors is unlikely to be adopted in a clinical setting; these assessment strategies do not provide clinical cut-offs or clear treatment options, limiting utility and acceptability among providers as well as patients. In contrast, clinical mood and anxiety diagnoses are well-defined with empirically-supported treatments. Because clinical disorders present targets highly suitable for screening in the obstetric setting, increased focus on the predictive value of clinical mood/anxiety diagnoses would measurably advance translation to clinical application.

The diagnostic structure provided by the DSM-V provides a beneficial framework for diagnoses, treatment, and related financial support from insurance/health care organizations. However, the conceptualization of mental illnesses as categorical designations has limitations. The burgeoning National Institute of Mental Health (NIMH) Research Domains Criteria (RDoC) framework “explicitly focuses on the complex overlapping multidimensionality of mental illness” (Clark et al., 2017). The RDoC approach recognizes commonalities across mental health conditions, emphasizing underlying multi-causality and co-occurrence of symptoms across traditional categorical dimensions (e.g., DSM-V diagnoses) (Kircanski et al., 2017; Vaidyanathan and Pacheco, 2017). Consistent with the RDoC conceptualization, mood and anxiety disorders share underlying psychological distress dimensions as well as common neurobiological mechanisms which are implicated in inflammation (Kessler et al., 2003; Sharp et al., 2015), supporting an empirical conceptualization that cuts across diagnostic categories. Therefore, while the current diagnostic framework provides a foundational structure to support translation to clinical practice, this research area should also endeavor to generate empirical data to best inform and improve upon the diagnostic system.

3.2. Sleep and Shortened Gestation.

People spend nearly 1/3 of their life engaged in sleep, a critical restorative behavior that is essential to health and highly amenable to intervention. Sleeping < 7 hours per night is associated with increased risk for obesity, diabetes, high blood pressure, cardiovascular disease, stroke, and all-cause mortality (Grandner et al., 2014; Liu et al., 2017; Liu et al., 2013). Thus, the American Academy of Sleep Medicine defines healthy adult sleep duration as 7 hours per night. Per recent data from the CDC, 33.2% of Whites sleep < 7 hours per night, with even higher rates of 45.8% among Blacks (Liu et al., 2016). These data are consistent with numerous epidemiological studies showing that, independent of SES, African Americans have markedly higher rates of short sleep as well as poorer subjective sleep quality than Whites or any other racial/ethnic group (Hall et al., 2009; Petrov and Lichstein, 2016; Ruiter et al., 2011).

Despite compelling evidence that short sleep contributes substantially to chronic disease, all-cause mortality, and racial disparities in health, until recently, sleep has received remarkably little attention in relation to birth outcomes. Emerging data link maternal sleep including sleep quality, insomnia diagnosis, and sleep duration with risk for miscarriage and shortened gestation. Self-reported snoring and sleep apnea diagnoses have been associated with shorter gestation (Felder et al., 2017; Micheli et al., 2011). This warrants further attention, as sleep apnea is closely linked with obesity, which is increasing among women of childbearing age (Deputy et al., 2018). However, causes and consequences of sleep-disordered breathing have been covered extensively elsewhere (Chen et al., 2012; Facco et al., 2017; Pien et al., 2005); the current review focuses on sleep quality and duration.

In relation to sleep quality versus duration, available data in relation to birth outcomes focus predominately on sleep quality (Blair et al., 2015; Christian et al., 2016; Okun et al., 2012; Okun et al., 2011; Strange et al., 2009). Amongst the strongest evidence to-date, retrospective medical record review data from 672 women with diagnosed insomnia compared to 1:1 matched controls showed 1.3 times greater odds of PTB amongst cases (Felder et al., 2017). The primary Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) diagnostic criteria for insomnia is “difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least one month.” Thus, insomnia diagnoses are based on subjectively perceived sleep difficulties, rather than a specific duration of sleep.

Data on sleep duration in relation to birth outcomes are relatively limited (Micheli et al., 2011; Samaraweera and Abeysena, 2010). Of importance, in epidemiological studies in non-pregnant adults, both subjective sleep quality and sleep duration are linked with various health outcomes. However, duration is the most robustly associated with disease, disability, and death (Cappuccio et al., 2010). The limited available data on sleep duration and birth outcomes rely on self-report. While subjective reports often reflect a person’s time in bed rather than time spent asleep, objectively measured sleep duration via wrist actigraphy calculates actual sleep time, excluding difficulty in falling asleep and staying asleep (i.e., sleep disturbances), which are captured as sleep onset latency (SOL) and wake after sleep onset (WASO). Providing evidence for differential predictive validity, a meta-analysis showed that duration measured objectively, rather than by self-report, was a stronger predictor of inflammation (Irwin et al., 2016). Thus, data on sleep duration – particularly utilizing objective measures – are needed to inform our understanding of sleep and perinatal outcomes.

Data on sleep and birth outcomes has focused predominately on non-Hispanic White and/or Hispanic cohorts. Of importance to addressing racial disparities in birth outcomes, data from our group demonstrated that among 138 women (79 African American, 53 White) assessed mid-pregnancy, poor subjective sleep quality (per PSQI) predicted shorter gestation among African Americans ($r_s = -0.35$, $p = 0.002$) but not Whites (Blair et al., 2015). Moreover, when examined using clinical cut-offs, African Americans, but not Whites, scoring > 5 on the PSQI had greater odds of shortened gestation (< 39 weeks), $OR = 3.66$ (95% $CI = 1.36, 9.97$), $p = 0.02$. Taken together, evidence to-date suggests that sleep duration and perceived sleep quality have implications for birth outcomes, with heightened vulnerability among African Americans.

As detailed below, it has been proposed that sleep-induced inflammatory dysregulation may contribute to risk for shortened gestation (Blair et al., 2015; Kajeepeta et al., 2014; Okun et al., 2007; Okun et al., 2013). However, data on inflammatory mechanisms linking sleep and perinatal health remain limited. Moreover, literature in this area would be strengthened by better representation of African Americans, examination of shortened gestation inclusive of ETB, and utilization of objective measures of sleep (e.g., actigraphy) to complement self-report. In addition, concurrent assessment of mood and anxiety disorders would best elucidate the independent versus additive effects of these exposures, given that sleep disturbance is a common feature of these disorders. Elucidation of the role of sleep in risk for shortened gestation and racial disparities in this outcome provides great promise for clinical application, as sleep is clinically assessable and amenable to intervention.

4. Individual Differences in Risk and Resilience

Under similar conditions of objective exposure to stress, individuals vary considerably in their subjective responses and ability to cope, with implications for neuroendocrine and immune dysregulation (Dantzer et al., 2018). Thus, another avenue of investigation is focusing on factors that enhance resilience as well as those that may magnify negative effects of exposures. Key factors include social support and marital satisfaction (Ross et al., 2017; Uchino et al., 2012), religion/spirituality (Cheadle and Schetter, 2017), self-efficacy (Leahy-Warren et al., 2012); emotion-focused coping (Melnik et al., 2006), finding meaning in life (Mitchell and Christian, under review), tendency toward rumination (Zoccola et al., 2014), hostility (Stewart et al., 2008), attachment styles (Fagundes et al., 2011), and personality factors (DeLongis and Holtzman, 2005). Thorough coverage of research in this area is beyond the scope of this review. However, interventions that target the development of personal resilience resources may mitigate the effects of chronic stressor exposure, reducing the risk for experiencing difficulties with mental health and/or sleep in the face of chronic stressor exposure – such as that typified by racial discrimination. In addition, explication of the roles of individual risk factors is needed to target those who can most benefit from intervention.

5. Stress and Birth Outcomes among Hispanic Women

The current review has focused on racial disparities in relation to African American women. Notably, rates of preterm birth among Hispanic/Latina women in the U.S. (12.2%) are similar to non-Hispanic White women (11.6%), despite the fact that the socioeconomic status of Hispanics more closely resembles African-Americans. The relative health of low SES Hispanic women as compared to low SES women of other races/ethnicities has been termed the “Hispanic Paradox”. However, the protective effects of Hispanic ethnicity diminish with greater acculturation (Coonrod et al., 2004). Though not found in all studies (Zambrana et al., 1997), rates of preterm birth have been reported to be 1.5–2 times higher among Hispanic women of high versus low acculturation (Cervantes et al., 1999; Coonrod et al., 2004; Crump et al., 1999; Lara et al., 2005; Ruiz et al., 2008). Thus, it is projected that there will be increases in preterm births among Hispanics as the overall Hispanic population in the U.S. moves towards greater acculturation.

Acculturation among Hispanics may affect preterm birth via both behavioral and physiological stress pathways. Greater acculturation, as defined by greater English usage and preference for American culture, is associated with more smoking, alcohol use, and street drug use as well as poorer diet during pregnancy (Chasan-Taber et al., 2008; Coonrod et al., 2004; Detjen et al., 2007). Greater acculturation has also been linked to greater internalization of ethnic stereotypes, poorer social support networks, greater exposure to stressful life events, and greater depressive symptoms (Alamilla et al., 2010; Davila et al., 2009; Sherraden and Barrera, 1996). In turn, though data are limited, acculturative factors have been linked with neuroendocrine and immune dysregulation in Hispanic pregnant women (Ruiz et al., 2006; Ruiz et al., 2008; Ruiz et al., 2007).

The public health importance of perinatal health among Hispanics is substantial. Hispanics currently comprise 15% of the U.S. population. By 2050, this is projected to nearly triple, from 46.7 million to 132.8 million, thus comprising 30% of the U.S. population. Also by 2050, the number of Hispanic women at childbearing age will increase by 92%, compared to an increase of 10% among African Americans (U.S. Census Bureau, 2009). Thus, inclusion of Hispanic women and consideration of unique psychosocial exposures in this group is needed as research on mind-body health in pregnancy continues.

6. Summary and Conclusions

There is now a considerable amount of data which converges to support an idea that was once rather peripheral – that psychological stress is a key driving factor underlying racial disparities in perinatal health observed in African American as compared to White women (Green et al., 2005; Lackritz et al., 2013). The presence of this effect bolsters the value of thoroughly explicating the perinatal health effects of chronic stress in varied forms across women of all races/ethnicities. In terms of clinical translation, at the individual level, efforts to mitigate effects of exposure to racial discrimination – or other forms of chronic stress – require targets that can be assessed and treated. As reviewed, a clear path moving forward is explicating the role of modifiable behavioral sequelae, particularly depression, anxiety, and sleep. Better understanding of factors that promote resilience and coping including social support, spirituality, and self-efficacy among others will help to inform these intervention efforts. As will be reviewed in a companion paper, underlying biological mechanisms also require further explication, including the role of neuroendocrine function, inflammation, cellular aging, and the microbiome.

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Figure 1: Behavioral and Biological Pathways to Shortened Gestation.

Racial discrimination and other objective stressors are psychosocial exposures that increase the risk for shortened gestation. These are not necessarily clinically modifiable at the individual level. However, as reviewed herein, psychological factors (mood/anxiety disorders, sleep) present promising targets for identifying risk and targeting intervention. In a companion paper, the role of biological sequelae (neuroendocrine function, immune function, cellular aging, microbiome) will be described. These may directly impact delivery length, contributing to spontaneous occurrence of shortened gestation. In addition, these pathways can contribute to medically-indicated shortened gestation by increasing risk for clinical conditions including pre-eclampsia and gestational diabetes. Pathways bolded in red print are emphasized in the current review.