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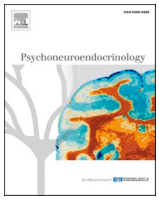

Special Issue: Social Determinants of Health: What we still need to know

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1. Introduction

Life expectancy has dramatically increased in each major world region since 1900 (Bell and Miller, 2005). Nevertheless, within each region worldwide, there are significant health inequities (Aburto et al., 2020). Health inequities reflect preventable differences in the burden of disease, disability, injury, or violence that are experienced or in the opportunities to achieve optimal health. The origins of health inequities are multifactorial (Bailey et al., 2021). The World Health Organization has highlighted a critical need to understand the "non-medical factors" that produce health inequities (World Health Organization, 2017). Social determinants of health are the factors in which people are born, live, learn, work, play, worship, and age that impact health outcomes. Defined by the World Health Organization as "the non-medical factors that influence health problems," social determinants of health impact the development, prevention, and expression of diseases and health problems. A large body of evidence shows that social determinants account for over half of health care outcomes (World Health Organization, 2017).

The field of Psychoneuroendocrinology is well-positioned to answer critical questions related to social determinants by providing a valuable framework to guide basic science and intervention work to elucidate the biopsychosocial mechanisms that underlie health inequities. It is now well established that stressful life events and the negative emotions they generate can dysregulate the autonomic, neuroendocrine, and immune systems in ways that can contribute to disease. For example, although acute rises in glucocorticoids are anti-inflammatory, human and animal work has shown that chronic stress-induced glucocorticoid production can sometimes lead to glucocorticoid insensitivity. Glucocorticoid insensitivity allows immune cells to produce proinflammatory cytokines in an unregulated environment, thereby boosting inflammation (Miller et al., 2002).

By providing the tools and methods necessary to understand how and why biopsychosocial factors interact with the stress response, the discipline can inform prevention and treatment approaches. For example, consider that exposure to chronic stress is omnipresent across each social determinant domain, and a core transdiagnostic risk factor for mental and physical health problems (Hicken et al., 2014; Insel, 2014; Jackson et al., 2010). Key psychobiological factors evaluated within the field of Psychoneuroendocrinology, such as a dysregulated neuroendocrine stress response, could serve as an intermediate transdiagnostic factor linking social determinants to physical health (Beauchaine and Constantino, 2017; Lozupone et al., 2019). In turn, a dysregulated neuroendocrine stress response could provide an intervention target (Biomarkers Definitions Working Group et al., 2001).

The current special issue of *Psychoneuroendocrinology* features examples of scientific studies and review articles within this space. These empirical papers and reviews provide an overview of the field and identify gaps in the literature. Potential individual, community, and society-level interventions are discussed. These studies highlight the importance of measuring and empirically evaluating the effects of social exposures across multiple levels of analysis. Key social determinants of health in this special issue include effects of early life stress, socioeconomic status (SES), race, sex/gender, and sexual orientation on health.

2. Overview of special issue

2.1. Adverse early life experiences

Health inequities begin early in life. The field of Psychoneuroendocrinology has been at the forefront of understanding how adverse early life experiences alter the expression of multiple stress mediators. Recent work suggests that adverse early life experiences can boost disease risk within *and* across generations. In this special issue,

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Vaghef-Mehrabani et al. (2021) present data collected from 340 mothers and 238 infants who took part in the Alberta Pregnancy Outcomes and Nutrition study. They found that maternal nutrition can impact the intergenerational transmission of childhood adversity from mother to child. Specifically, the association between adverse childhood experiences and maternal cortisol awakening response and the association between maternal cortisol awakening response and infant stress-related cortisol reactivity were buffered (moderated) by maternal choline intake. They propose that maternal choline intake may play an essential role in regulating cortisol secretion and in fetal programming of the hypothalamic-pituitary-adrenal axis.

Over the last decade, considerable work has shown that the impact of adverse early life experiences persists into older adulthood (Gee, 2021; Grummitt et al., 2021; Jakubowski et al., 2018). Of course, not everyone who experiences adverse early life experiences is at the same risk. In a sample of older adults who recently experienced the death of a spouse, Chen et al. (2022) found that subjective social status is a critical moderator that predicted risk and resilience patterns among those who experienced early adversity. By identifying risk and resilience factors, intervention scientists will be better able to identify those most susceptible to the negative impact of specific social determinants. Ignoring moderators (risk factors) attenuates the effects of intervention work.

Many studies linking adverse early life experiences to endocrine and immune factors have relied on predominately white samples. Surachman et al. (2021a, 2021b) demonstrated that adverse early life experiences negatively impact adult physiology, regardless of race; however, pathways leading to risk vary across racial groups. Using cross-sectional information on estimated glomerular filtration rate (eGFR) GFR values of middle-aged and older Black and white Americans from the Biomarker Project of the Midlife in the United States (MIDUS) dataset, they found that parental educational attainment, a proxy of early-life SES, is associated with age-related decrements in renal clearance. Mediators linking parental educational attainment to age-related decrements in renal clearance differed between Black and White Americans – findings that highlight the importance of recruiting diverse samples.

2.2. Socioeconomic status

SES is another critical social determinant with well-established impacts on health disparities (Adler et al., 1994). Commonly operationalized as the combination of household income, education, and occupational grade, this social determinant has emerged as a major risk factor for cardiovascular disease (CVD) and preclinical atherosclerosis. Miller et al. (2021) examined 488 midlife adults without cardiovascular disease diagnoses to examine whether HPA activity partially accounted for the association between SES and atherosclerosis. Relative community socioeconomic position was negatively associated with intima-medial thickness. By calculating four different indicators of HPA activity, they found that the association between SES and preclinical atherosclerosis may be partly due to correlated variation in adrenocortical activity.

Perceptions of social status also contribute to biomarkers of physical health. Using a subsample of a larger cohort study and an aggregate score of cardiometabolic risk that included measures of lipids, inflammation, blood pressure, and glucose metabolism, Kempel et al. (2022) examined how subjective social status (SSS), evaluated at 15 years old and again at 28 years old, was related to cardiovascular risk at 28 years of age. Low SSS at 28 years of age but not at 15 years of age was associated with elevated cardiovascular risk at 28 years. Accordingly, in addition to traditional objective markers of SES, future work accounting for SSS may be warranted.

Future research is critical to understand which measures of SES are most relevant for the field of psychoneuroendocrinology. Authors in this special issue evaluated SES and the closely related SSS construct in multiple ways, including an income-to-needs ratio (Johnson et al., 2021), a composite score of individual and community-based characteristics (Miller et al., 2021), and a ladder that asks participants to indicate what "rung" they would place themselves relative to others. While household income is commonly used as an indicator of SES, it is less common to measure savings or wealth. The ability to have a financial safety net is central to the experience of well-being (Panis, 2004). Financial safety differs remarkably by race and ethnicity in the U. S., even among households with similar income (Park et al., 2019), in part due to multi-generational effects of income and savings over time. Further, it is well-understood that income inequality within a society is equally or more important than personal income or wealth alone (Pickett and Wilkinson, 2015). Societies with greater income inequality, including the U.S., United Kingdom, and Japan have worse health outcomes than societies with greater equality (Pickett and Wilkinson, 2015).

2.3. Race & ethnicity

Race and ethnicity are social determinants linked to SES. Racial differences in SES impact racial disparities in health; however, racial health disparities characteristically remain across SES categories (Williams et al., 2016). Racial and ethnic diversity varies dramatically across countries. In the United States and Canada, Black, Hispanic, and Native American people experience considerable health inequities (Baciu et al., 2017). McClendon et al. (2021) conducted a well-powered, racially diverse study of 1577 adults (55–65 years old). They found that Black participants experienced more significant cumulative stress and lower SES than white participants. Importantly both preventative health behaviors and proinflammatory cytokine levels partially explained stress-related Black-White racial health disparities. This study provides valuable evidence that there is a need for culturally relevant interventions on stress and SES to alleviate health disparities experienced by Black Americans.

Surachman et al. (2021a, 2021b) examined whether being low SES and experiencing discrimination differentially impacted markers of systemic inflammation in Black and White participants. Using interview and biomarker assessments from the Midlife in the United States (MIDUS) study to evaluate the association between life course SES trajectories and daily discrimination, the investigators demonstrated that SES trajectories, but not daily discrimination, were associated with all markers of inflammation in White participants. Yet among black participants, daily discrimination, but not SES trajectories, were associated with markers of systemic inflammation.

Experimental designs allow for causal inferences that are not possible with observational designs. Arriola et al. (2021) randomized 52 Black Americans along the kidney disease continuum to recall a race-related stressor or general stressor. Participants who were asked to recall a race-related stressful memory had a greater increase in IL-6 at 45 min and 90 min post recall than those who recalled a general stressor. Furthermore, those who recalled a race-related stressor had lower expectations of racism and had less diastolic blood pressure reactivity than those who had higher expectations of racism. Accordingly, the experience of certain stressors may have differential effects on health-related outcomes.

Racial disparities also exist after disease diagnosis and treatment. In a study of 32 Black and 163 white breast cancer survivors, Madison et al. (2021) demonstrated that Black women experienced higher levels of cancer-related distress and reported greater avoidance of cancer-related thoughts, which remained persistent through 18 months post-treatment, compared to white women who reported less distress and an overall reduction of their distress through 6 months before stabilizing through 18 months post-treatment. Notably, black women generally present with more advanced disease at diagnosis are more likely to experience treatment delay and to die from breast cancer than white women (Gorin et al., 2006; Stapleton et al., 2018). Disparities in the experience and trajectory of distress may contribute to health inequities experienced by Black breast cancer survivors.

In the United States, Latinx accounted for more than half of the population growth in the last decade and now make up approximately 20% of the U.S. population. This special issue highlights a growing literature in Psychoneuroendocrinology focused on the Latinx community, as health inequities are evident. In a study of 84 Latinx adolescents in the U.S., Sladek et al. (2021) showed that those who had experienced more discrimination from adults in high school reported more stress and lower stress-related blood pressure and salivary cortisol reactivity during the first semester of college, while those who had more discrimination from peers also reported more stress. Ethnic-racial discrimination during high school may influence the transition to college and the experience of stress for Latinx college students.

Immigration and acculturation represent unique stressors experienced by some in the Latinx community. While immigrants are more likely to be in poverty than U.S. natives, poverty rates are mainly concentrated within specific immigrant populations (i.e., Latinx, Blacks, and recent arrivals) (Clark and King, 2008). Johnson et al. (2021) collected data from 229 17-year-olds originally from Mexico and examined associations between financial security and cortisol reactivity to social stress. Those who had economically secure families earlier in adolescence exhibited typical salivary cortisol responses to an experimental task evaluating social rejection, while those who had experienced poverty and remained in poverty at 16-years-old exhibited hyporeactivity to the task. Findings suggest that interventions that increase family income during early adolescence may be beneficial to hypothalamic-pituitary-adrenal axis functioning in late adolescence.

The impact of acculturation on psychological well-being and physical health is complex. Assimilating to a host countries culture and language can reduce stress in some contexts. However, the experience of losing one's culture and way of life can be a source of stress and depression. Scholaske et al. (2021) conducted a systematic review of 41 articles on the impact of acculturation on stress biomarkers, dating back to 2010. Although most of the studies reviewed examined acculturation to the U.S from Mexico and South America, there were no restrictions based on country of origin or host country. Acculturation was associated with stress biomarkers, but effects varied across studies. The authors discuss potential reasons for this discrepancy based on third variable influences. Nevertheless, this meta-analysis highlights the need for much more work in this area, as the immigrant population and their descendants are projected to comprise 88% of the U.S. population by 2065. (Pew Research Center, 2015).

2.4. Gender and sexual orientation

Sexually diverse and gender-diverse populations experience unique sources of stress that vary from community to community and country to country. As Diamond, Dehlin, and Alley reference in their review on the biobehavioral mechanisms underlying these disparities, the National Institutes of Minority Health recognized "sexual and gender minorities" as a distinct health disparity population in 2016 (National Institute on Minority Health and Health Disparities, 2016). Diamond et al. (2021) summarize work in this area, highlighting the biobehavioral consequences of sexual and gender stigma. They propose that social safety is a particularly stressful threat confronted by this population and suggest a need for further research. Mijas et al. (2021) present an empirical article that utilizes this framework showing increased cortisol levels in gay men predict various minority stressors.

3. Other factors for future investigation

3.1. Community type

A critical social determinant that was not a focus of any studies in the current issue is residential environment (e.g., urban, suburban, and rural environments). This omission in no way reflects the importance of the topic. Instead, compared with the other social determinants outlined in this issue, few researchers use psychoneuroendocrinology theories and methods to understand this social determinant. Rural residents have higher morbidity and mortality rates than suburban and urban residents (Garcia, 2019; Singh and Siahpush, 2014). Compared with urban and suburban residents, rural residents have higher rates of chronic disease; indeed, diabetes is almost 20% higher in rural America (Callaghan et al., 2020). On average, rural residents are less educated and have lower incomes than urban and suburban residents (Garcia, 2019). However, when researchers account for race/ethnicity, education, and income rural residents still have less access to health information than urban and suburban residents (Chen et al., 2019; Kelley et al., 2016). This includes information about the importance of stress reduction and other "integrative medicine" activities, key topics within the field of Psychoneuroendocrinology (Bhuiyan et al., 2022).

3.2. COVID-19

Of note, social determinants of health have had unique prominence during the COVID-19 pandemic (COVID-19 and the social determinants of health and health equity: Evidence brief, 2021, p. 19). Covid-19 has disrupted education, driven families into poverty, led to job loss, and facilitated discrimination and stigmatization toward certain groups. Adverse childhood experiences such as witnessing domestic violence and experiencing verbal, emotional abuse have also increased since the pandemic, likely due to increased parental stress and mental health challenges within the household (Calvano et al., 2021). These Covid-19 related consequences likely have long-term effects on health and disease, beyond impacting prevention, infection rates, and treatment for the Sars-cov-2 virus. Poorer populations in the United States, Peru, England, Sweden, and France have higher infection and mortality rates than wealthier populations (COVID-19 and the social determinants of health and health equity: Evidence brief, 2021). Longitudinal and sociodemographically diverse research is necessary to characterize disparities and to identify underlying mechanisms of risk accurately; moreover, reporting findings accurately and within context will be important for reducing the spread of harmful stereotypes and myths and for advancing policy and research toward health equity initiatives (Chowkwanyun et al., 2020). More research in this area is forthcoming.

3.3. Micro-level and macrolevel systems of power

Each article highlights that social determinants produce a cascade of chronic stressors that alter physical health indicators. One commonality we observed across social determinants described in this special issue was an implicit power differential. Those of low SES lack the influence to dictate where they live and work. Race, sex/gender, and sexual orientation are significant power categories; indeed, papers in these sections reflect how disparities emerge when not in the dominant group. Finally, children are inherently powerless, susceptible to a wide variety of adversities, and have little control over their environments. In general, those who lack power and control over their environment feel helpless, especially when confronted with significant stressors (Chrousos and Gold, 1998; Friedland, 1992; Hellhammer et al., 1997). Uncontrollable threats reliably trigger a dysregulated cortisol and inflammatory response. Stressors that induce feelings of being negatively evaluated by others in power or authority promote reliably robust inflammatory and cortisol responses (Dickerson et al., 2009; Dickerson and Kemeny, 2004). We propose that those working in the area of Psychoneuroendocrinology and health inequities pay greater attention to how micro-level and macrolevel systems of power and control affect the physiology and health of the individual.

3.4. Multiple minority identities

A myriad of identities and life experiences can affect people's health simultaneously. For example, those who experience multiple

minoritized identities can be impacted in ways that are not just additive but synergistic, as a result of unique stressors and power dynamics. In this special issue, numerous articles and reviews simultaneously focused on multiple social determinates. For example, Chen et al. (2022) examined how adverse early life experiences produce unique health effects when combined with indicators of SES. McClendon et al. (2021) examined how SES and racial/ethnic disparities interacted. Studies such as these are crucial in understanding how multiple patterns of control, oppression, and marginalization impact physiology and health. We encourage more work using this approach. Moreover, when examining various social determinants simultaneously, we encourage scientists to utilize the theoretical insights of intersectionality. Specifically, intersectionality can further advance our field by promoting research and discussion that considers how systems of interlocking power dynamics and social structures can uniquely impact physiology and health.

3.5. Beyond psychological stress

Finally, the special issue is focused on the premise that psychological stressors promote autonomic, neuroendocrine, and immune dysregulation, which boosts risk for health disparities. However, there are a myriad of other factors that negatively alter these physiological systems in ways that contribute to health disparities. For example, air pollution can promote a proinflammatory phenotype that disproportionately impacts those who are socially disadvantaged (Olvera Alvarez et al., 2018). The combination of air pollution and early life stress may synergistically impact a proinflammatory phenotype contributing to the higher rates of asthma exhibited in low SES communities. In a bidirectional feedback loop, the stress-response system and poor health behaviors are interlinked. For a variety of structural reasons, low SES communities are more likely to smoke and consume fast-food-type direct. Research addressing the health impact of the stress-response system, independent of the health behaviors, limits real-world applicability. There is emerging evidence that the harmful health consequences of diet and stress may be multiplicative rather than additive (Stoney et al., 2002). For example, when a fast-food-type meal is consumed in the context of high levels of psychological stress, postprandial rises in triglycerides and inflammation are more profound (Kiecolt-Glaser et al., 2015, 2017).

3.6. Conclusion

In sum, the current issue provides an overview of cutting-edge research on how the field of Psychoneuroendocrinology can be used to understand how social determinants of health impact health disparities. We hope the articles published in this special issue inspire recognition of structural factors that affect individual health and draw attention to the serious work required to move toward health equity.

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