Factors contributing to racial differences in neurogenic orthostatic hypotension

Nisha Charkoudian¹ · Austin T. Robinson²

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Neurogenic orthostatic hypotension (nOH) is a characteristic manifestation of the alpha-synucleinopathies (multiple system atrophy, pure autonomic failure, Parkinson disease and dementia with Lewy bodies) [10, 14]. However, nOH can occur in other disorders as well, including people with diabetic autonomic neuropathy or rare genetic disorders like familial dysautonomia. nOH can exacerbate the negative consequences of any of these conditions by confining the individual to a wheelchair for most of their waking hours. In some patients with baroreflex dysfunction, nOH coexists with supine hypertension, thus resulting in the negative sequelae and risks of both ends of the blood pressure spectrum in a single individual [14].

It has become increasingly clear in recent years that we have historically limited our understanding of mechanisms of cardiovascular and neurological diseases by conducting research primarily in groups of white men [7, 8], limiting our insight into the pathophysiology of diseases that occur in a diverse population. In this context, what we call “race” is primarily a social construct [2, 22]. However, it is also important to evaluate biological mechanisms that might be statistically more or less prevalent in one racial group than another, and to evaluate potential reasons why this might be the case. In the United States and other countries, a history of chattel slavery, redlining, and racism have, at least in part, contributed to racial and ethnic minorities facing wealth inequality and being more likely to experience poverty and live in disadvantaged neighborhoods [2, 3, 6, 15]. These social and environmental factors influence cardiovascular disease risk by limiting access to healthful foods, safe

spaces for physical activity, environmental exposures, sleep, and access to healthcare [11, 16, 19]. For example, there are racial disparities in dietary potassium intake, namely Black Americans consume less than other racial/ethnic groups [4]. Importantly, lower dietary potassium is associated with higher resting blood pressure [13]. At the other end of the blood pressure continuum is nOH, which has been understudied in Black Americans.

In this issue of *Clinical Autonomic Research*, Giza and colleagues provide novel biological insight into nOH in non-Hispanic Black men [12]. The investigators studied cardiovascular and neurohumoral data in nine non-Hispanic Black individuals with nOH and compared to non-Hispanic White individuals with nOH and to a group of 8 non-Hispanic White healthy control subjects. They report that many of the variables relevant to nOH, including hemodynamic and plasma norepinephrine changes with upright posture, were similar in non-Hispanic Black and non-Hispanic White patients with nOH. However, there were marked differences between non-Hispanic Black and non-Hispanic White patients in terms of plasma renin activity and aldosterone responses to upright posture. Whereas non-Hispanic White patients and controls had marked increases in plasma renin activity and aldosterone when upright, non-Hispanic Black patients had only very small changes, and these were not statistically significant [12]. In terms of volume regulation, it is intriguing that Wenner and colleagues also reported a diminished responsiveness (reduction) in plasma renin activity and aldosterone response to sodium loading in healthy non-Hispanic Black, compared to non-Hispanic White, individuals [21].

In terms of the bigger picture of autonomic physiology research, there is evidence to suggest altered autonomic function in healthy non-Hispanic Black compared to non-Hispanic White individuals [8]. Some of these data suggest that autonomic dysfunction might contribute to the increased risk of hypertension and other cardiovascular disorders that is often reported for Black communities in

✉ Nisha Charkoudian
nisha.c.simmons.civ@mail.mil

¹ Thermal and Mountain Medicine Division, United States Army Research Institute of Environmental Medicine, 10 General Greene Avenue, Natick, MA 01760, USA

² School of Kinesiology, Auburn University, Auburn, AL, USA

the US and other countries [1, 5]. For example, Vranish and colleagues showed that the transduction of sympathetic noradrenergic nerve activity into vascular resistance was augmented in healthy young non-Hispanic Black men compared to non-Hispanic White men [20]. Similarly, Wenner and colleagues showed that the pressor response to a given increase in plasma sodium concentration (caused by hypertonic saline infusion) was augmented in young healthy non-Hispanic Black compared to non-Hispanic White men [21]. In contrast, Fonkoue and colleagues reported smaller sympathetic neural and blood pressure responses to mental stress in non-Hispanic Black men [9]. These data are consistent with the idea that “stress” is context-specific, and that chronic stressors of everyday life may result in differential neurovascular responsiveness to sympatho-excitatory stimuli associated with an acute laboratory-based mental stressor.

It is not immediately clear, for any biological variable, the extent to which biology is “inherent” or the result of external influences. What is clear is that social determinants play a large role in health outcomes influenced by biology, including blood pressure regulation [17, 18]. In the context of areas such as epigenetics, within-life modification of the genome by a range of environmental influences, it is unclear what the term “inherent” even really means. Nevertheless, this should not hold us back from studying biological variability as one of a constellation of factors that contribute to the biomedical disparities that we are hoping to address, and mitigate, by studying differences between racial groups in the first place [2]. For our community of autonomic researchers and clinicians, the new study by Giza and colleagues provides a helpful step in this direction.

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Compliance with ethical standards

Conflict of interest The views, opinions, and/or findings contained in this article are those of the authors and should not be construed as an official United States Department of the Army position, or decision, unless so designated by other official documentation. Approved for public release; distribution unlimited. Citations of commercial organizations and trade names in this report do not constitute an official U.S. Department of the Army endorsement or approval of the products or services of these organizations.

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