



HOT TOPICS

The critical importance in identifying the biological mechanisms underlying the effects of racism on mental health

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The pervasive and lasting impact of the stress of racism, known as weathering, affects body and brain, and produces an increased risk for mental health disorders in the Black community. Racial health disparities are highly prevalent and have recently been uncovered by the COVID-19 pandemic, where mortality rates are disproportionately higher in Black Americans compared to Whites [1]. Exposure to racism or racial discrimination precipitates a chronic stress state, supported by studies showing higher levels of PTSD and increased disease risk [2]. For example, Black communities in Detroit demonstrated a sharp increase in reporting of distress associated with racism after the killing of George Floyd against the backdrop of the pandemic, suggesting both long-term and acute effects of racism. Recent studies also revealed altered amygdala resting state and functional connectivity and blunted threat response associated with experienced discrimination stress [3]. Therefore, racism-related stress constitutes a double blow of socioenvironmental and neurobiological insults to those who are already most vulnerable. While the association of trauma and lifetime stress with mental health disorders, especially anxiety, PTSD and depression, are well known, there is a critical need for biological mechanisms to be examined.

Identification of biomarkers in human subjects that underlie the lasting effects of racism, and the development of animal models of chronic lifetime stress are key to uncovering this biology. While modeling racial discrimination in a rodent is not possible [2], utilizing methods of chronic stress exposure beginning from a young age and continuing across key periods in brain development may provide unique insight relevant to humans. One marker that may prove translatable is cell-free mitochondrial DNA (cfmtDNA). As a marker of stress and an intermediary signal to the immune system, circulating cfmtDNA is easily obtainable and detectable. Studies show that cfmtDNA levels are increased by stress in humans, and are high in subjects with major depressive disorder and suicidality, and that levels are reduced by antidepressant treatment [4, 5]. Increased levels of cfmtDNA are also associated with increased circulating cytokines, supporting an integration of stress and immune system signals.

A second key biological marker that is abundant in circulation and holds potential in human subject studies is the extracellular vesicle (EV). EV protein and nucleic acid content can be easily assayed, and changes therein are predictive of functionality and tissue specificity, including EV release to and from the brain. New research has demonstrated that EV content is altered by stress, and EVs also act as strong integrators with the immune system [6].

Systemic changes in production of biological stress signals, such as cfmtDNA and EVs and an engagement of the immune system, may be the focal point for an increased risk of mental health disorders by a lifetime of exposure to racial discrimination stress [2]. While racism has had a long-standing and pervasive impact on individuals and society, the combination of the current urgent need for intervention and availability of novel translational tools should spur progress in understanding the biological basis for its role in mental health disorder risk.

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AUTHOR CONTRIBUTIONS

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ADDITIONAL INFORMATION

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