Commentary

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How Racial and Ethnic Discrimination Gets Under the Skin: Inflammatory Outcomes in Adolescents and Young Adults of Color

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Social context strongly shapes child development; for racial and ethnic minority youth, this almost certainly includes experiences of discrimination. Racial and ethnic discrimination is a traumatic, and often chronic, stressor that has been shown to be a major contributing factor to physical and mental health disparities in minorities (1). Because exposure to sustained trauma can influence the development of stress regulatory systems, it is critical to understand the health consequences of discriminatory experiences among minority youth. Several researchers have begun to investigate these issues in older adults by focusing on the associations between racial and ethnic discrimination and immune functioning and inflammatory activity. In these studies, prejudiced treatment has been found to be associated with a proinflammatory phenotype, often measured by higher levels of proteins related to low-grade inflammation (2). Virtually no studies, however, have examined how such discriminatory experiences affect inflammatory signaling among adolescents and young adults of color.

In the current issue of *Biological Psychiatry: Global Open Science*, Chen *et al.* (3) break important ground on this topic by examining associations between peripheral markers of inflammation and experiences of discrimination in two independent cohorts comprised of racial and ethnic minorities (3). Study 1 (longitudinal) included a sample of 419 rural African American young adults, whereas study 2 (cross-sectional) included a sample of 201 urban eighth-grade children of color (53% African American, 44% Hispanic, and 13% other). In both studies, experiences of discrimination were most strongly linked with heightened inflammation in male participants. Specifically, in study 1, male participants (ages 19–20 years) who experienced higher levels of racial discrimination showed increasing trajectories of soluble urokinase plasminogen activator receptor (suPAR) from ages 25 to 29 years. In study 2, whereas reports of experiencing more discrimination did correlate with higher levels of classical monocytes and with greater stimulated cytokine production in response to inflammatory stimuli across both sexes, male participants (ages 12–15 years) who experienced more discrimination evinced a proinflammatory phenotype on a number of other related indices, including higher circulating levels of low-grade inflammation and lower sensitivity to anti-inflammatory agents. Interestingly, in both studies, male participants did not report experiencing higher levels of discrimination compared with their female peers. Together, these results indicate that male adolescents and young adults of color may be especially vulnerable to the inflammatory sequelae of racial and ethnic discrimination.

The authors speculate that one reason for the sex-specific effects they observed is that male individuals of color are more likely than their female counterparts to experience threats of physical harm (4), which are more strongly linked to immediate physiological, and downstream immune, responses compared with other forms of discrimination (2). Exposure to vicarious experiences of discrimination and prejudiced socialization messages surrounding male individuals of color through media may also contribute to greater unconscious threat signaling in this population (5). Certainly, gender is a complex context in and of itself, and the roles of gender expectations and socialization are also processes that warrant deeper investigation in future studies.

It is also important to note that not all effects replicated across the two studies. Whereas female participants from study 1 showed higher levels of C-reactive protein (CRP) and suPAR at 25 years of age compared with their male peers, female participants from study 2 showed lower levels of classical monocytes at ages 12 to 15 years compared with their male peers. Moreover, even though many of the same inflammatory cytokines and proteins that constituted the composite of low-grade inflammation used in the reported analyses for study 2 were also assayed in study 1, these proteins were ultimately not reported due to a poor linear model fit. It is therefore unclear if the same inflammatory markers associated with racial and ethnic in discrimination in study 2 would be associated with the same developmental pattern that was observed in suPAR in study 1.

It is likely that these divergent results may be due to important demographic and developmental differences between the cohorts, as well as the fact that these inflammatory biomarkers are indexing distinct aspects of the immune process: CRP is involved in acute-phase responses and may reflect both acute and chronic inflammation; suPAR is more stable and less sensitive to acute effects (e.g., circadian rhythms) and considered a marker of chronic inflammation; classical monocytes are cellular drivers of inflammatory responses. It will therefore be critical for future studies to clarify the extent to which this sustained effect of racial and ethnic discrimination is specific to suPAR or whether other related immunologic processes (e.g., sensitivity to anti-inflammatory effects) may be key contributors. At least one other study has found that exposure to violence and other related forms of adversity experienced during childhood and adolescence is

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associated with an inflammatory phenotype characterized by elevated levels of suPAR, CRP, and interleukin 6 by 18 years of age (6). Interestingly, in this study, individuals who had higher levels of CRP and interleukin 6 but who had lower levels of suPAR were significantly less likely to have experienced severe early-life adversity (6). These studies raise the intriguing possibility that suPAR is a potentially developmentally sensitive marker of adverse stress exposure and a candidate mechanism by which chronic and stressful experiences, such as discrimination, influence health outcomes in minority youth.

There are also study design differences between the studies that increase the generalizability of the findings but may also represent caveats in terms of interpretation of the data. First, there may be important cohort effects to consider given the significant historical events in the United States that have occurred in the past decade. Second, the measure of discrimination used in study 1, the Schedule of Racist Events, probed past-year experiences; in contrast, the measure of discrimination used in study 2, the Everyday Discrimination Scale, does not explicitly query whether discriminatory acts are perceived as being racially or ethnically motivated and does not cover a specific period. In study 1, only discrimination data from ages 19 to 20 years were analyzed, whereas data related to inflammation were assessed from ages 24 to 29 years. This analytic design is critical for establishing the directionality of the association between discrimination and inflammation; however, it will be crucial for future studies to assess both sets of variables in parallel across development to quantify the differential impact of prior versus ongoing versus cumulative experiences of discrimination on trajectories of immune health.

Overall, this is a timely and rigorously conducted study that significantly advances our understanding of how experiences of discrimination may "get under the skin" of adolescents and young adults of color. The strengths of the study are numerous, including the racial and ethnic diversity of the study samples, the use of two independent cohorts to highlight converging results, and the longitudinal design of study 1. It is noteworthy that prior studies in this area have focused on circulating biomarkers of inflammation, such as CRP, without assessing other immunologic processes that may provide more mechanistic insight into an observed proinflammatory phenotype. By challenging blood cells in vitro to inflammatory triggers as well as anti-inflammatory molecules, as was done in the samples from study 2, Chen *et al.* (3) were able to quantify distinct facets of immune function, including cytokine production and sensitivity to inhibitory signals. As Chen *et al.* have demonstrated in this report, racism has insidious and enduring consequences and the toxic effects can begin early in development—a sobering reminder that far more research is needed in this emerging and critically understudied area.

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