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The time is now for integrative multilayered stress research and mitigation

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An Editorial on the Frontiers in Science Lead Article

[A multiscale inflammatory map: linking individual stress to societal dysfunction](#)

Key points

- Recent research has highlighted a significant increase in day-to-day stress among midlife adults, underscoring the heightened stress levels in contemporary society.
- Understanding stress as a multifaceted process is crucial, requiring collaboration across disciplines and the development of comprehensive intervention strategies.
- Research efforts should address stress at both individual and population levels, integrating diverse research methodologies and considering various social determinants of health.

Ask almost anyone on the street how they are, and they will probably say that life is more stressful these days. Recent research from my lab (using data from the National Study of Daily Experiences) indicates a significant 19% increase in day-to-day stress in a sample of midlife adults in the United States in the 2010s as compared with a similar cohort in the 1990s (1). This translates to approximately 67 more stressful days per year for contemporary adults. Furthermore, midlife adults in the 2010s exhibited a 17% increase in the perception that stress would impact their future plans and a 27% increase in the belief that their financial status would be affected by stress compared with adults in the 1990s. This research highlights the heightened stress levels experienced by middle-aged individuals in contemporary times, underscoring the need for targeted policy that embraces integrative multidisciplinary research projects and multifaceted intervention efforts.

Stress is a well-recognized risk factor for compromised individual mental, physical, and cognitive health, as well as increased mortality risk (2). At the population level, stress may contribute to public health crises such as vaccine or climate change skepticism. However, defining and measuring characteristics of stress is complex and often treated as a “black box”. Our work has defined stress as a process, distinguishing stressors (environmental demands or events), subjective appraisals of the stressors, stress response indicators

(affective, cognitive, behavioral, and neuroendocrine facets), and the stress response (changes in indicators associated with stressor exposure) as individual components (3).

Our Daily Stress Process Model combines epidemiological approaches that focus on stress as a result of exposure to events with psychological theories that view stress as a subjective experience. As Figure 1 shows, this model introduces five components of the stress experience: exposure, diversity, appraisal, reactivity, and residue (4, 5). Stressor exposure assesses the likelihood and frequency of daily stressors, while stressor diversity measures the variety of stressor types. Stressor appraisals refer to the subjective meaning of the stressors in terms of perceived control and domains of risk due to the stressor. Reactivity captures emotional, behavioral, or biological reactions to stressors, and residue reflects prolonged stress responses extending into the following day. These components are influenced by individual resources and environments, contributing to differences in how people experience and cope with daily stressors. Overall, this model offers a nuanced and comprehensive account of the micro-level processes through which daily stressors contribute to long-term health (6).

However, our model only gets us so far in establishing how stress affects health and vice versa. To gain actionable insights into stress as a risk factor for individual and population-level well-being, it is crucial to consider policies that target overarching mechanisms that underlie these stress-health associations at both levels.

Vodovotz et al.'s "Multiscale inflammatory map", published in a *Frontiers in Science* lead article (7), proposes an explanation of how the brain regulates inflammation and how inflammation, in turn, impairs various aspects of human experience, including perception, emotion, cognition, consciousness, and behavior. They argue that this interplay of inflammatory and neural processes, coupled with the transmission of stressors through social media and global communications, creates a multiscale, runaway process that could significantly impact human decision-making and behavior at a large scale.

The hypothesis presented in their thought-provoking and important article suggests that inflammation serves as a multiscale driver linking individual stressors to societal dysfunction and, ultimately, to environmental impacts on a planetary scale, creating a positive feedback loop. Understanding the interconnected relationships among stress, inflammation, mental states, and behavior is, thus, crucial for both human and planetary health. To address these challenges, the authors propose a bold and expansive mathematical model to elucidate and test the links between stress, inflammation, neural control, cognition, and health. The model has implications for understanding stress transmission, potential interventions, and the promotion of resilience.

Testing and implementing this model will require an interdisciplinary and international effort to undertake stress assessments and interventions at the individual and societal levels. This involves implementing multilayered, multiscale stress measurement and mitigation strategies (8). The goal to improve lives at both levels requires a complex interplay of factors influencing stress and health. Here are three broad steps to achieve this goal.

First, there is a clear need for a coordinated, interdisciplinary, and international research effort. Most stress research is siloed between

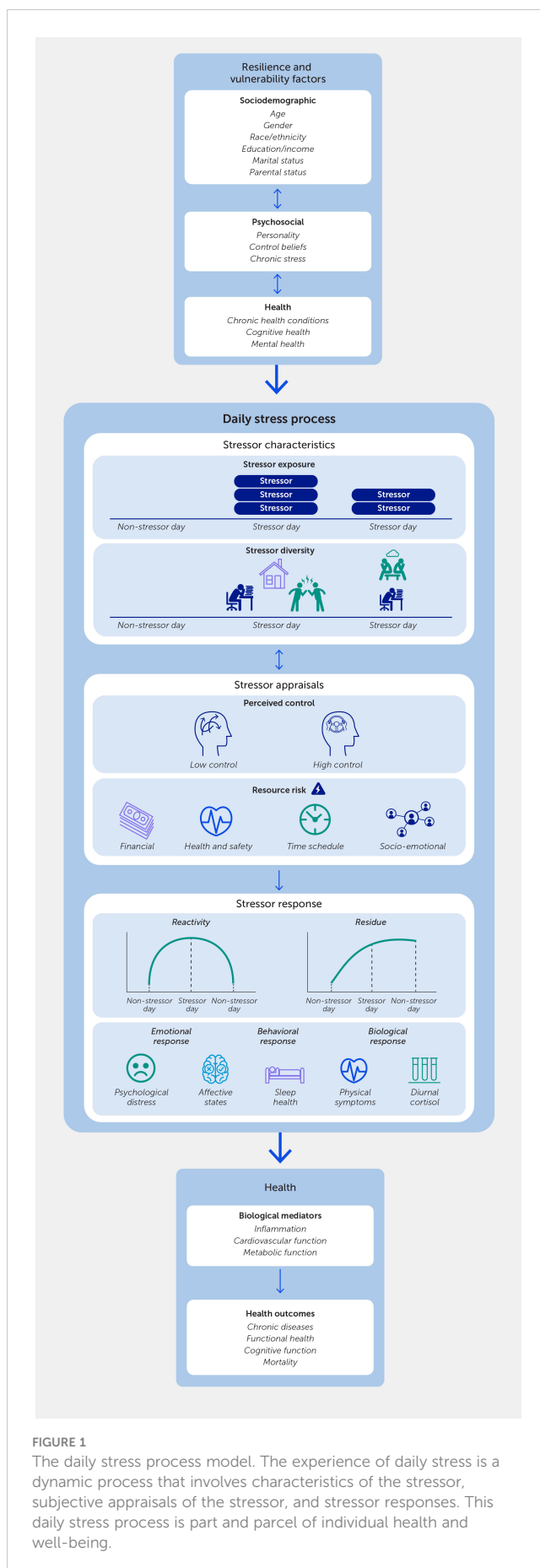


FIGURE 1

The daily stress process model. The experience of daily stress is a dynamic process that involves characteristics of the stressor, subjective appraisals of the stressor, and stressor responses. This daily stress process is part and parcel of individual health and well-being.

social, behavioral, and biological sciences, each targeting different layers of stress experiences, from society to individuals to cells. Each discipline uses different methods, research designs, and analytic strategies. To understand the multiscale nature of stress and capitalize on it for improving well-being, researchers from diverse fields need to collaborate. This collaborative effort should aim to validate assumptions, expand variables, and integrate methods and designs to test the proposed integrative theories across multiple populations.

Second, policymakers and funding agencies should support and prioritize interdisciplinary and integrative research to validate the assumptions of the presented multiscale model. This includes expanding the factors and variables considered and ensuring the model's alignment with real-world observations. A validated model could provide a foundation for developing targets for effective interventions. For instance, due to systemic racism, socioeconomic status (e.g., education and income) is not equivalent across racial groups. African Americans tend to have lower earnings at similar education levels, as compared with White people. These interactions among multiple social determinants of health probably have significant implications for individuals' emotional and physiological responses to stress, including inflammation (9).

Policies for understanding and alleviating stress require a nuanced perspective in assessing how stress processes contribute to social gradients in health across the lifespan. Therefore, future research should focus on examining the intersectionality of social categories, such as gender identity, sexual identity, race, and socioeconomic status, to understand how they confer advantages or disadvantages. It is crucial to conduct additional research exploring this intersectionality to enhance and refine prevention and intervention efforts.

Third, researchers and policymakers should focus on implementing multilayered, multiscale stress mitigation interventions. This includes not only traditional approaches, such as lifestyle changes, but also macro human ecosystem design and micro precision interventions. Mitigation strategies need to include social-structural considerations, such as access to medical care and caregiving, as well as individual lifestyle behavioral interventions such as diet, sleep, and exercise. Such strategies should be combined with person-centered therapeutics and temporally sensitive interventions such as real-time delivery of cognitive-behavioral mitigation during stressful episodes.

Structural barriers from funding, academic, and clinical institutions, which have a history of focusing on only one area of stress, are hindering the implementation of these multidiscipline interventions. Implementing these would require a shift in focus and

collaboration between researchers, policymakers, and practitioners. This holistic approach recognizes the interconnectedness of stress and health at various ecological and temporal scales.

In summary, the '*Multiscale inflammatory map*' (7) underscores the need for a comprehensive and nuanced approach to stress assessment and management that considers the multiscale nature of stressors, response, and health at the individual and population levels. This involves collaboration across disciplines, validation of theoretical models, and the development of interventions that address stress at all levels.

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Author contributions

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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