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Future Leaders in Stress: the next generation of stress neurobiology

We are living through one of the most volatile periods in recent memory. Wars, pandemics, climate disruption, political polarisation, and the always-on demands of digital life. This has made chronic stress a defining feature of modern existence, particularly for the young. It is no coincidence that this is also the moment in which stress neurobiology has become one of the most consequential frontiers in biomedical science, nor that the generation of researchers now entering independence is approaching the field with a different set of tools, frameworks and ambitions than those that came before.

The questions that defined stress research for decades, such as how the HPA axis is wired, how glucocorticoids reshape neurons, and how early adversity gets "under the skin", remain central (Lopez, 2025; Hartmann, 2025). But the methods used to answer them have changed quickly. Single-cell and spatial transcriptomics, *in vivo* imaging of defined circuits, organoid and placental models, AI-enabled behavioural tracking, and large longitudinal human cohorts have collapsed long-standing boundaries between molecular, cellular, circuit and population-level approaches (Parekh, 2025; Cruceanu, 2026; Matosin, 2026). At the same time, the populations that this generation of researchers is working with (e.g., children growing up through a pandemic, young people with risky substance use, mothers and their infants in an increasingly stressful world, sexual and gender minorities, communities exposed to collective trauma) are pushing the field to be more translational, more developmentally aware, and more honest about the limits of any single-model system (Halldorsdottir, 2025; Sampedro-Piquero, 2026; Rincón-Cortés, 2025).

This special issue, “Future Leaders in Stress”, captures that shift. We invited early-career investigators who are leading independent programs and shaping the new directions where stress neurobiology is headed. Each was asked to write the article they most wanted to write: a synthesis of their research program, the questions driving it, and the directions they believe the field must take. The resulting twelve contributions span genomics to organoids, infant rats to postmortem human brain, single synapses to population-level mental health, and together offer a portrait of a field that is simultaneously more mechanistic and more integrative than it has ever been. We have organised the special issue to move from the most basic and preclinical contributions through to the most clinical and human, while recognising that almost every article refuses to sit cleanly on one side of that divide – a sign of the multidisciplinary boundary-pushing that defines the next generation of future leaders in stress.

1. Molecular and cellular mechanisms of stress

The opening cluster of papers works inward from the genome to the synapse, and then outward again into circuits, advancing a shared claim: that the molecular grammar of stress can only be read at cell-type and cell-state resolution. Cuarenta (2025) begins at the level of the genome itself, examining how early-life stress engages mobile genetic elements such as the LINE-1 retrotransposon, and arguing that these elements are not genomic curiosities but active regulators of stress-responsive transcription with mechanistic relevance to anxiety, depression and substance use disorders. Cutting-edge genome-wide and genome editing technologies, she notes, are finally making this layer of biology tractable.

Hartmann (2025) then builds upward from the intracellular machinery that translates a stress signal into a transcriptional response. Drawing together rodent and human postmortem evidence, he reframes the canonical glucocorticoid receptor (GR) signalling cascade around its co-chaperones FKBP5 and FKBP4 and the regulatory partner SKA2, and identifies a previously unrecognised GR-independent role for SKA2 in microglial secretory autophagy. The result is a vision of stress signalling as fundamentally cell-type-specific, with direct implications for major depression, PTSD and bipolar disorder, and providing the mechanistic bridge to Shin (2025), who moves from intracellular signalling to receptor dynamics in defined stress circuits. Synthesising work in the nucleus accumbens, lateral hypothalamus and lateral septum, Shin traces how stress at different life stages reshapes mGluR5, leptin receptor, GR and dopamine D3 receptor signalling to produce maladaptive coping behaviours such as social withdrawal, emotional overeating and blunted reward, mapping these onto transdiagnostic features of psychiatric illness and making the case for receptor-level mechanisms as one of the most druggable entry points into stress biology.

Parekh (2025) takes these circuit-level questions into the behaving animal. Using *in vivo* approaches such as fibre photometry, two-photon calcium imaging and spatial transcriptomics, she shows how chronic stress dysregulates synapse formation, maturation and pruning to produce a uniquely vulnerable brain state, and argues that only longitudinal, real-time recordings can capture the dynamic trajectories of stress adaptation that cross-sectional work necessarily misses. Read together, these four contributions describe a vertically integrated molecular biology of stress: from retrotransposon to receptor, from receptor to circuit, from circuit to behaving brain. They also lay the mechanistic groundwork for the developmental questions that follow.

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2. Development, caregiving and the social brain

The second cluster shifts the temporal frame. If the molecular layer asks what stress does to a cell, this group asks when it does so, and to whom. Opendak (2025) anchors the developmental thread by using awake, behaving infant rats combined with optogenetics, microdialysis and targeted microinfusions to dissect the dopaminergic amygdala circuits that produce age-appropriate social behaviour, and to show how adversity at distinct developmental windows disrupts those circuits in distinct ways. Her work is a reminder that "early-life stress" is not a single phenotype but a developmental trajectory, and it provides the conceptual scaffold for Peña (2025), who extends this logic across species and across the lifespan. Reviewing behavioural, circuit-level and molecular evidence that early-life stress sensitises individuals to future stressors and elevates lifetime risk for mood and anxiety disorders, Peña integrates rodent epigenetic and RNA-sequencing data with human population studies to provide a mechanistic scaffold for latent vulnerability and to identify plausible intervention points for childhood stress and trauma.

Where Opendak and Peña focus on the developing offspring, Rincón-Cortés (2025) reframes the analysis around the mother-infant dyad. Synthesising rodent and human evidence that disrupted caregiver-infant relationships alter behaviour and brain function in both offspring and mothers, she argues that maternal neurobiology, historically a peripheral concern in stress research, deserves to be central. Cruceanu (2026) pushes this dyadic logic back one developmental step further, introducing neuroplacentology as an emerging frontier. By positioning the placenta as a stress-responsive organ that actively shapes fetal neurodevelopment, and by drawing on placental organoids and single-cell multi-omics, she opens a tractable experimental window into how maternal mental health, genetic susceptibility and environmental exposures converge to influence offspring psychiatric risk before birth.

Together, these four papers describe a developmental neurobiology of stress that is no longer organised around a single age, a single brain, or even a single body. They also set up the translational and human-level questions that close the special issue.

3. Translation, populations and the human brain

The final cluster carries these mechanistic and developmental threads into translation, asking how the biology described in earlier sections actually plays out in human populations and in the human brain itself. Lopez (2025) provides the conceptual bridge by framing stress as a biological "echo" that propagates from molecules to cells to circuits to social behaviour, and arguing that single-cell technologies and AI-driven behavioural phenotyping are bringing the long-promised goal of precision mental health into genuine reach. Sampedro-Piquero (2026) takes one of the most pressing translational questions of the moment, namely how exercise modulates stress responses, craving and emotional functioning in adolescents and young adults with risky alcohol use, and integrates animal and human evidence with particular attention to female vulnerability and interoceptive function. The result is a model of what a developmentally sensitive, sex-aware translational stress neurobiology can look like in practice.

Halldorsdottir (2025) widens the lens to the population level. Reviewing the rise in child and adolescent mental health problems over the past two decades and the further deterioration during the COVID-19 pandemic, she argues that the pandemic, for all its harms, has created an unprecedented natural experiment for studying stress vulnerability and resilience at scale, and outlines how gene-environment interactions and epigenetic embedding during sensitive periods can be tested within it. Matosin (2026) closes the issue at the level of the human brain itself. Using single-cell and spatial transcriptomics in the postmortem human brain, she maps how HPA axis activation and glucocorticoid signalling reshape distinct cell populations in coordinated molecular and morphological ways, and argues that cell-type-resolved human data are now an indispensable bridge between preclinical mechanism and clinical phenotype.

Taken together, these four contributions show how the molecular and developmental insights of the earlier sections can be translated into testable questions in human populations and human tissue, completing the loop from cell to society.

4. A field redefining the boundaries

Read together, the twelve articles assembled here describe a stress neurobiology that is no longer organised around a single level of analysis or a single model system. They are deliberately more than the sum of their parts. Each paper is mechanistically self-contained, but each also borrows assumptions, tools or populations from the others, and the field they collectively describe is one in which genes and molecules, placentas, infant social circuits, postmortem brain and population mental health data are no longer separate enterprises. Several themes recur across the issue, especially the centrality of developmental timing, the irreducibility of cell-type and circuit specificity, the need to take sex, caregiving context and lived adversity seriously as biological variables, and the view that precision approaches to mental illness will not come from any one discipline alone.

We are grateful to the contributors for the generosity and ambition of their work, to the reviewers who engaged so substantively with each manuscript, and to the editorial team at *Neurobiology of Stress* for the opportunity to curate this issue. We hope the collection serves not only as a snapshot of where stress neurobiology stands in 2026, but as evidence that the field is entering its most generative phase, and that the people leading it (both the authors in this issue and those beyond it) have both the tools and the appetite to meet the moment.

Declaration of competing interest

The authors declare no competing interests.

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Jessica L. Bolton[a,*], Natalie Matosin[b,c,d,**]
[a] Georgia State University, Neuroscience Institute, USA
[b] The University of Sydney, School of Medical Sciences, Faculty of Medicine and Health, Australia
[c] The University of Sydney, Charles Perkins Centre, Australia
[d] The University of Sydney, Brain and Mind Centre, Australia

[*] Corresponding author. Georgia State University, Neuroscience Institute, USA.

[**] Corresponding author. The University of Sydney, School of Medical Sciences, Faculty of Medicine and Health, Australia.
E-mail addresses: jbolton@gsu.edu (J.L. Bolton), natalie.matosin@sydney.edu.au (N. Matosin).