Personal Statement
Alexander J. Shackman, Ph.D.

I am an Associate Professor in the Department of Psychology (Clinical and CNS Areas), core faculty in the transdepartmental Neuroscience & Cognitive Science Doctoral Program and Maryland Neuroimaging Center, and Director of the Affective and Translational Neuroscience Laboratory at the University of Maryland (UMD). My multidisciplinary research program has been continuously supported by the NIH since 2016 (> $14M) and led to ~99 publications (h-index: 46; >12,000 citations). I am an Associate Editor at J Psychopathol & Clinical Sci (formerly J Abnormal Psychol); was Co-Editor of The Nature of Emotion (Oxford University Press); served as an Associate Editor at eLife and several other journals; and co-edited 3 special issues focused on emotional states, traits, and disorders. I am a Fellow of the Association for Psychological Science; an active member of the international Affective Neuroimaging Collaboratory, ENIGMA Anxiety, and HiTOP research consortia; and a standing member of the NIH Adult Psychopathology and Disorders of Aging study section. I have been invited to teach and lecture at meetings and institutions around the world. My research has been featured in Discovery Magazine and Newsweek, and I have provided scientific commentary for the BBC and Smithsonian Magazine.

Most of my work is focused on understanding the nature and biological bases of anxiety-related states, traits, and disorders. When extreme, anxiety contributes to a variety of debilitating mental illnesses, including internalizing disorders, substance misuse, and psychosis. To understand this liability, my group uses a broad spectrum of tools—including multimodal neuroimaging, psychophysiology, smartphone digital phenotyping, semi-structured clinical and life-stress interviews, and genetic analyses—in pediatric and adult patients, university students, community members, and monkeys. More recently established secondary lines of research are focused on psychiatric nosology and graduate student training and mental health.

Reconsidering the Neural Architecture of Fear and Anxiety. Anxiety-related disorders are a leading cause of human misery and morbidity, afflicting ~300M individuals annually. In the U.S., nearly 1 in 3 individuals will experience a lifetime disorder, service utilization is surging, and annual healthcare costs exceed $40B. These troubling facts have drawn the attention of the media and policymakers—from the Surgeon General to the White House—and they demand a better understanding of the underlying neurobiology.

It is widely believed that fear and anxiety reflect categorically distinct states, instantiated in segregated neural circuits: that fear, a phasic response to certain-and-imminent threat, is orchestrated by the dorsal Amygdala in the region of the central nucleus (Ce); whereas anxiety, a sustained response to uncertain-and-distal threat, is triggered by the bed nucleus of the stria terminalis (BST). A variant of this ‘strict-segregation’ hypothesis has even been enshrined in the National Institute of Mental Health’s (NIMH) influential Research Domain Criteria (RDoC) framework. With my close friend and collaborator, Drew Fox (UC-Davis), I challenged this canonical view in a 2016 theoretical paper, marshalling evidence that these two regions, while certainly not interchangeable, make similar contributions to fear and anxiety. This work spurred the development and validation of a new fMRI paradigm—the Maryland Threat Countdown (MTC) task—designed to overcome key limitations of existing threat-anticipation tasks. Using the MTC paradigm and a relatively large and ethnoracially diverse sample of university students (n=99), we showed that the anticipation of certain and uncertain threat recruit highly overlapping networks, including the BST, Amygdala, PAG, midcingulate cortex (MCC), and anterior insula/frontal operculum (AI/FrO). We have since replicated this finding in a superset of the original sample (n=220) and an independent sample of community adults (n=75). In head-to-head comparisons, the BST and Amygdala showed indistinguishable responses to certain and uncertain threat, indexed by formal tests of statistical equivalence (‘TOST’). As we later noted in a 2021 AJP retrospective, these findings dovetail with meta-analytic evidence that fear conditioning (the prototypical certain threat) and instructed threat-of-shock (the prototypical uncertain threat) recruit massively overlapping neural networks, including the BST. On-going work in our lab has begun to delve more deeply into the complex dynamics of fear- and anxiety-related neural activity, leveraging new analytic models to decompose threat-anticipation signals into more granular early (onset), middle (sustained), and late (phasic) responses. Results indicate that certain and uncertain threat anticipation recruit a common neural circuit that exhibits context-specific dynamics, including a phasic surge in activation at the conclusion of certain threat anticipation, and persistent levels of heightened activation when the precise timing of threat encounters is unknown. Collectively, this body of work...
underscores the need to revise RDoC and other categorical models of fear and anxiety. Methodologically, this work showcases the value of the MTC paradigm, which we are currently using to probe the neurobiology of acute alcohol and nicotine manipulations (with John Curtin & Megan Piper, Wisconsin; & Daniel Bradford, Oregon State), have adapted for probing adolescent social anxiety (with Andy De Los Reyes, UMD), and have modified for use in the ultra-high field (7T) fMRI environment, with the potential for substantially enhanced resolution of key subcortical regions (Hur, Tillman...& Shackman in prep; Kuhn, Kaplan...& Shackman in prep). The 7T project is a collaboration with Xiaochen Hu (Cologne, Germany) & Ben Becker (University of Electronic Sci. & Tech., China) and supported by the Köln Fortune Programme.

Despite this progress, it is clear that most of the work necessary to understand fear and anxiety remains undone. The literature is fragmented, with different investigators reaching divergent conclusions across disparate tasks, readouts, species, and populations, leading to a proliferation of competing models and hypotheses. Jingle-jangle fallacies and terminological confusion abound. A systematic, integrative approach is lacking. We are tackling this problem in 2 ways. First, from a conceptual angle, we have worked to break down traditional academic silos, and bring experts from different sub-disciplines together to take stock of the state of the science—warts and all—and identify the most important avenues for accelerating discovery. With Miquel Fullana (Barcelona), I co-organized a special issue of *NBR* encompassing 15 reviews from leading international experts. The capstone of the special journal issue is a multidisciplinary roundtable discussion, led by my rising-star Ph.D. student, Shannon Grogans. By design, the discussants encompassed a broad spectrum of expertise, from cutting-edge molecular approaches to pediatric clinical assessment. The side-by-side response format provided a crucial opportunity to sharpen constructs, highlight unspoken assumptions and terminological confusion, and identify key weaknesses in the literature. Second, from an empirical angle, I serve as PI of 2 new NIH projects, both aimed at developing computational models of fear and anxiety (R01-AA030042, R01-MH131264). Leveraging computational-modelling and machine-learning approaches that have been successfully used in other domains, these projects have the potential to clarify the computational functions of the BST, Ce, MCC, and other key regions; adjudicate on-going theoretical debates; and foster a common mathematical framework (‘lingua franca’) for unifying research across approaches and species. Furthermore, because these studies are focused on ethnoracially (>50% BIPOC) and age-diverse samples, they have the potential to provide insights that are more generalizable, clinically relevant, and equitable than is typical of fear and anxiety neuroimaging research.

**The Neurobiology of Dispositional Negativity.** Much of our work is focused on understanding the neurobiology of anxiety-related traits—anxious temperament, behavioral inhibition, neuroticism/negative emotionality, trait anxiety, and so on. This extended family of phenotypes—or what I have termed dispositional negativity—confers risk for a range of mental illnesses and other adversities, from divorce to premature death. Despite its profound importance for health and wellbeing, the nature of dispositional negativity has remained hazy. Beginning with a 2016 theoretical review (cited >200×), I have developed and continued to refine an integrative, multidisciplinary framework for understanding the processes that link dispositional negativity to momentary emotion and, ultimately, to emotional disorders and other adversities. While most work in this area has focused on negative individuals’ well-known tendency to overreact to acute stressors (e.g., Ref. 12), our research highlights the importance of stressors that are remote or uncertain. Uncertain stressors elicit sustained levels of heightened negative affect, and this pervasive distress appears to be most central to daily function and most relevant to the development of emotional illnesses. This conceptual insight guides much of our laboratory’s on-going research.

**An Integrative Model.** Despite its profound importance for health and wellbeing, the nature of dispositional negativity has remained hazy. Beginning with a 2016 theoretical review (cited >200×), I have developed and continued to refine an integrative, multidisciplinary framework for understanding the processes that link dispositional negativity to momentary emotion and, ultimately, to emotional disorders and other adversities. While most work in this area has focused on negative individuals’ well-known tendency to overreact to acute stressors (e.g., Ref. 12), our research highlights the importance of stressors that are remote or uncertain. Uncertain stressors elicit sustained levels of heightened negative affect, and this pervasive distress appears to be most central to daily function and most relevant to the development of emotional illnesses. This conceptual insight guides much of our laboratory’s on-going research.

**Primates.** Our work demonstrates that core features of dispositional negativity—including heightened behavioral inhibition and elevated cortisol—can be successfully modeled in macaques. Monkeys provide a useful model of extreme early-life anxiety; children and monkeys share similar genes, homologous brains, and a shared repertoire of defensive responses to potential threat. Work that I began as a postdoctoral fellow and have continued with collaborators at the Wisconsin and California National Primates Centers provides evidence that variation in anxious temperament—a key facet of dispositional negativity—reflects heightened activity in
a circuit encompassing the central extended amygdala (EAc), including the Ce and BST. Key components of this circuitry (e.g., Ce) are commonly recruited by individuals with radically different presentations of their extreme temperament, reinforcing the possibility of developing ‘broad-spectrum’ treatments for individuals with different clinical presentations. Leveraging ‘resting-state’ fMRI, our work also highlights the importance of functional connections between the prefrontal cortex (PFC) and EAc. For example, monkeys with an anxious temperament and children with anxiety disorders show a strikingly similar pattern of reduced connectivity between the Ce and prefrontal regions implicated in the regulation of emotion, highlighting the importance of this evolutionarily conserved circuit for extreme early-life anxiety. More broadly, this observation teaches us that core features of early-life temperament can be discerned in the spontaneous, ongoing activity of the brain in the absence of trait-relevant challenges. More recently, we have begun to identify the molecular and genetic underpinnings of anxious temperament.

**Humans.** Like many anxiety patients, individuals with a negative disposition are prone to pervasive distress in the absence of acute threat. Our work suggests that this is partially rooted in the misallocation of working memory (WM) to threat-related cues. WM is the ‘blackboard of the mind,’ a limited-capacity workspace where information is transiently stored and used to guide goal-directed cognition. Once lodged in WM, threat-related information is poised to bias thoughts, feelings, and behavior when it is no longer present in the external world, promoting pervasive distress. Building on work that I conducted as a Ph.D. student with Greg Hancock, Danny Pine (NIMH), & Chris Conway (Fordham). Building on work I conducted at Wisconsin with Richie Davidson, Lyn Abramson, Marika Kovacs, & Robin Nusslock, several on-going projects in my laboratory will let us test whether BST reactivity to a genuinely distressing threat is enhanced among individuals with frank DSM-5 internalizing diagnoses at the time of scanning (R01-AA030042, R01-MH131264), something that could not be addressed in our earlier work focused on internalizing risk, and something not addressed by...
biobank studies (e.g., ABCD, HCP Extensions, UK Biobank) focused on emotional face tasks (for a review, see Ref. 34). Answering this question is crucial for determining the relevance of BST threat reactivity for treatment development.

**Using Smartphones to Understand Real-World Emotion.** Laboratory studies of emotion have intensively focused on a limited number of well-controlled, but highly artificial manipulations—emotional faces, shocks, and so on—presented under unnatural conditions. Aside from their impoverished ecological validity, these manipulations are typically less intense than those encountered in daily life. The widespread dissemination of smartphones affords new opportunities for objectively, efficiently, and unobtrusively quantifying moment-by-moment fluctuations in context, emotion, and motivated behavior. Because data are repeatedly captured in the real world, smartphone-ecological momentary assessment (EMA) circumvents the mnemonic biases that distort daily diaries, clinical assessments, and other retrospective ‘snapshots.’ We have used smartphone-EMA to understand the dynamics of everyday emotional states, the social factors that govern the momentary expression of emotional traits, and the relevance of threat-related brain circuits to real-world distress. We have shown that individuals at risk for internalizing illnesses derive greater emotional benefits (e.g., larger dips in distress) from positive daily events and from the presence of close companions (e.g., friends), motivating the hypothesis that close companions serve as a regulatory ‘prosthesis’ for at-risk individuals (with Ed Lemay, UMD; & Todd Kashdan, GMU35, 36, 37, 38). We have shown that individuals at risk for social anxiety disorder spend more time alone and exhibit heightened distress during periods of solitude, in the absence of objective threat or social scrutiny39. By fusing EMA with fMRI assessments of the MTC paradigm, we have shown that heightened activation in the cingulo-opercular network under threat in the scanner is associated with dampened reactivity to stressors in daily life, suggesting a regulatory role40; and that diminished safety signalling in the ventromedial prefrontal cortex (vmPFC) is associated with pervasively elevated distress in the absence of acute stressors41. These observations provide a novel conceptual framework for understanding the nature of emotional traits, for determining the larger significance of brain circuits identified in the lab and important clues about how alterations in the function of threat and safety circuits might promote psychopathology, and for informing the development of new intervention strategies, including the kinds of scalable, tailorable, and cost-effective mHealth interventions recently highlighted by the White House. **Other Work.** Smartphone-EMA is incorporated into all of my prior and on-going NIH-sponsored projects. As part of an on-going MPI collaboration with Jack Blanchard (UMD), we are using smartphone-EMA to understand the factors governing paranoia in psychosis (R01-MH121409)45, and are beginning to extend this approach to passive data-streams (e.g. GPS/geolocation tracking), which may prove more useful for monitoring and intervention than traditional EMA. I have gladly served as an expert EMA consultant and Co-I on several NIH awards and applications led by my UMD colleagues (R01-MH125370, Elizabeth Redcay; F31-AA027937, Lauren Ondo; and R01-AA031261, Derek Iwamoto).

**The Adaptive Control Hypothesis (TACH).** Like many anxiety patients, individuals with extreme dispositional negativity often show an inhibited, threat-avoidant profile of choices and behaviors. Our work motivates the hypothesis that this reflects alterations in a circuit centered on the mid-cingulate cortex (MCC). In a highly cited (>500×) meta-analysis, Jim Cavanagh (UNM) and I showed that control-sensitive electrophysiological signals generated in the MCC (ERN, FRN, N2) are exaggerated in individuals with a more negative disposition and prospectively predict increased behavioral inhibition and instrumental avoidance in the lab44. In related work, I showed that negative affect, pain (which is typically associated with robust negative affect), and cognitive control consistently recruit an overlapping territory in the MCC45. As part of an on-going collaboration with Luiz Pessoa (UMD), Dave Seminowicz (Western Ontario), Tor Wager (Dartmouth), and Wani Woo (Sungkyunkwan University, South Korea), we have replicated this pattern using more recently developed meta-analytic tools. Furthermore, the same pattern emerged in a sample of subjects that alternated between negative affect (uncertain shock-threat), thermal pain, and cognitive control tasks in a single fMRI session, ruling out the possibility that the observed 3-way overlap is an artifact of the spatial blurring inherent to neuroimaging meta-analyses. Remarkably, this overlap was apparent even for spatially unsmoothed fMRI data in individual participants. In short, negative affect, pain, and cognitive control are anatomically co-localized in the MCC. Of course, we want to infer that this neural overlap provides evidence of mental overlap—that negative affect, pain, and cognitive control reflect a shared psychological process, such as salience or arousal. But this is hardly guaranteed; it could be that negative affect, pain, and cognitive control engage fundamentally different
processes that are encoded in distinct (albeit overlapping) patterns of MCC activation. To address this, we used machine learning to show that ‘brain signatures’ (multi-voxel pattern-based classifiers) trained on each of the 3 tasks show robust cross-classification performance (5-fold CV.). Using these data, we also developed a successful domain-general signature, providing additional evidence of representational similarity. Together, these observations provide compelling evidence that negative affect, pain, and cognitive control are anatomically co-localized and functionally integrated in the MCC, enabling us to decisively reject prominent claims that the ‘dorsal ACC’ is specialized for cognition or pain. Based on these observations, I proposed and have continued to refine The Adaptive Control Hypothesis (TACH), which suggests that MCC is a hub, where threat- and punishment-relevant signals are integrated and used to regulate regions involved in expressing fear and anxiety, executing aversively-motivated behavior, tuning attention, and biasing learning in the face of action-outcome uncertainty. This work provides a neurobiological framework for understanding the mechanisms underlying exaggerated avoidance and aberrant punishment learning in dispositionally at-risk individuals and internalizing patients. More broadly, these observations teach us that that emotion and cognition are assembled from partially overlapping neural ‘ingredients’ and, hence, should not be conceptualized as fundamentally different mental faculties.

The Nature and Measurement of Psychopathology: Moving Toward Rigorous Data-Driven Phenotypes. Billions of research dollars have failed to provide useful assays or biomarkers, let alone cures for mental illness. There is a growing recognition that this abysmal record reflects the limitations of categorical DSM/ICD diagnoses, including rampant co-morbidity, marked diagnostic heterogeneity, low symptom specificity, poor reliability, and arbitrary boundaries. Addressing these limitations requires a fundamentally different approach. As an active member of the international HiTOP consortium, I have been involved in several efforts aimed at promoting data-driven dimensional approaches that have the potential to overcome these hurdles, including methodological primers and reviews focused on psychiatric genetics, neuroscience, and clinical practice. Building on work that I conducted as a Ph.D. student, I have also been involved in recent efforts to promote more reliable clinical phenotypes.

Graduate Student Training, Mental Health, and Wellbeing.

Training. Addressing the staggering burden of mental illness on global public health demands new etiological insights and the development and implementation of more effective, scalable, and equitable approaches to disease prediction, prevention, and treatment. Clinical psychology is poised to serve as a transdisciplinary hub for this work, but rising to this challenge requires an honest reckoning with some uncomfortable truths about current training practices and systemic barriers, from growing concerns about the alarming state of student mental health and systemic racism to hypercompetition for faculty jobs and research dollars. In a 2022 article (co-authored with trainees, Rachael Tillman & Kathryn DeYoung), we leveraged a variety of new data—including the results of our own national survey of students and faculty—to identify the most significant training challenges and to provide actionable recommendations for the full spectrum of stakeholders. A follow-up article focused more narrowly on the challenges of clinical internship (for a commentary, see Ref.). Impact: Along with a 2021 report led by Howard Berenbaum, our 2022 Annual Review article helped spur the Academy of Psychological Clinical Science to coordinate the first national summit focused squarely on clinical psychology training since the 1949 Boulder Conference. Efforts to implement key recommendations from the May 2023 summit at UMD are already underway.

Mental Health and Wellbeing. On-going work in the laboratory is focused on clarifying the true depth and breadth of what the media and policymakers have framed as a crisis of graduate student mental health. Using data from the American College Health Association-National College Health Assessment II—which encompasses surveys acquired from 187,054 graduate students across 358 institutions between 2008 and 2019—Kathryn DeYoung, Dr. Matthew Barstead, and I showed that mental distress, psychiatric diagnoses and treatment, and suicidality have all significantly worsened over the past decade (DeYoung et al. in prep). Follow-up analyses used the National Survey on Drug and Health—which includes nationally representative data from 443,894 adults over the same 11-year span—to show, for the first time, that the mental health of U.S. graduate students is significantly worse than both the general population and their demographically matched peers.
**Affective (Neuro-)Science.** Beyond my core program of research, I have also worked to nurture the broader disciplines of Affective Science and Affective Neuroscience. As detailed in my CV, I served as Co-Editor of *The Nature of Emotion* (OUP) and 3 special issues focused on emotion and the brain. I served on the editorial boards of the Psychonomic Society's CABN; the American Psychological Association’s (APA) Emotion; and the Society for Affective Science’s (SAS) Affective Science. I have gladly shared my expertise in affective (neuro-)science with my colleagues at UMD (Blanchard, Bennett, Hamilton, & JC Smith) and Virginia (Jim Coan), including published and on-going projects focused on the impact of sleep and exercise on the emotional brain in elders, the brain bases of temporal discounting in adolescents, and the consequences of reward deficits in adults with psychosis.

**Rigor and Reproducibility.** My team is committed to transparent reporting practices and to sharing our published imaging results (NeuroVault) and raw data (NIMH/NIAAA Data Archives.) De-identified MRI data are routinely shared with the Affective Neuroimaging Collaboratory and ENIGMA Anxiety consortia (e.g., Ref. 88). Manuscripts are shared via PubMed Central and nonprofit pre-print servers. We have also begun to selectively share our code, preregister our hypotheses and implement registered reports (selected as a Best of 2022 paper). I have worked to nurture the adoption of reproducible practices in my service to the Department's Open Science Workgroup, which developed the Open Science Impact Award to recognize exceptional examples by UMD faculty and trainees; and in my service to the Department’s Appointment, Promotion, & Tenure (APT) Committee, which developed the first revision of department APT policy since 2006, with the aim of mitigating known biases, encouraging reproducible scientific approaches, and facilitating the inclusion and promotion of women and BIPOC faculty. The resulting policies has been adopted as a best-practices template by the HELIOS consortium.

**IT Leadership.** Since 2020, I have served as the Director of NIMBUS, which provides secure, cost-effective, off-site back-up data storage for UMD neuroimaging labs spread across 3 colleges (BSOS, SPH, and Education; Bernat, Blanchard, Fox, Gard, Hamilton, Redcay, Riggins, Shackman, & JC Smith).

**Summary.** The overarching mission of my laboratory is to have a deep impact on the intersecting fields of Affective, Translational, and Clinical (Neuro-)Science. My team strives to perform innovative studies that can lead to significant discoveries, to disseminate our discoveries as widely as possible, and to mentor our trainees to become top-notch scientists. From a basic science perspective, our work begins to address fundamental questions about the nature and the origins of emotional states and traits. Clinically, our work promises to enhance our understanding of how emotional states and traits promote a spectrum of often-debilitating mental illnesses and set the stage for developing more effective psychological and biological interventions—which, ultimately, is the most important challenge of all.