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Imaging stress

Stress affects the brain through a vast array of pathways (Joels and Baram, 2009). These can be observed in neuroimaging in work as expressed in numerous overlapping disorders and neurocircuits (Shin and Liberzon, 2010) in animals and in humans in a way that affects whole life cycle (Lupien et al., 2009). This special issue of the Neurobiology of Stress is called "*Imaging Stress*", and presents a broad canvasing of the literature that touches upon complimentary aspects and understanding of the effects of stress on the brain using imaging and related methods. Effectively combining the literature on such a diverse field can be very challenging, because of differences in approaches, data handling, and construct definition. In "Roadmap for Optimizing the Clinical Utility of Emotional Stress Paradigms in Human Neuroimaging Research," Robin Aupperle and colleagues point to specific methodological practices that should be followed to allow neuroimaging to obtain the level of reliability such that it could be of service to clinical work. This work is augmented by an article by Gregory Fonzo entitled "Diminished Positive Affect and Traumatic Stress: A Biobehavioral Review and Commentary on Trauma Affective Neuroscience." This manuscript calls for methodological rigor and presents evidence of the importance of understanding the diminished reward circuits that augment the fear circuitry. In "The Potential of Calibrated fMRI in the Understanding of Stress in Eating Disorders" Christina Wierenga and colleagues champion a novel methodology for understanding his diminished reward circuitry – specifically focusing on the mechanism by which stress diminishes reward processing and contributes to the development and maintenance of eating disorders in the adolescent brain. The effect of stress on the developing brain is further explored by Tiffany Ho and colleagues in "Network-Based Approaches to Examining Stress in the Adolescent Brain" through the lens of graph theory. In this work, they suggest understanding of conditional network states in the dynamic brain can provide a more meaningful understanding of how stress can affect the developing adolescent brain. The work presented by Rongjun Yu and colleagues in "Stress-induced Changes in Modular Organizations of Human Brain Functional Networks" provides a complimentary understanding of the effects of stress on the brain. In this paper, they look at the effects of a stress induction on a group of healthy individuals to measure the effects on both brain networks and cortisol. In this work, they find that while the overall network architecture remains largely static in the context of stress induction, the architecture between nodes in default network can alter.

In adulthood stress manifests itself in the brain in such a way that it can amplify or interact with other disorders. One of the most common, and clinically problematic, comorbidities of stress disorders is substance use. In "Shared gray matter reductions across alcohol use disorder and posttraumatic stress disorder in the anterior cingulate cortex: A dual meta-analysis," Andrea Spadoni and colleagues point to the dorsal cingulate as a key area that may facilitate the synergy of these disorders. Feng Lin and colleagues find that stress affects how the hippocampus connects to key affective regions such as the insula in "The Mediating Role of Hippocampal Networks on Stress Regulation in Amnestic Mild Cognitive Impairment." This manuscript underscores the broad ongoing effect of stress on the brain through the life cycle.

There are two studies reported here that focus on understanding and mapping stress networks using fMRI-based approaches in awake animals. This includes the study by Yu and colleagues examining functional connectivity between amygdalar subregions in acute stress, alongside the work from the Zhang group which seeks to dissect functional hubs and networks that interact during stress exposure. These types of approaches will help us to better define the systems level changes that mediate behavioral phenotypes following stress. Expanding on this effort is the work of Stout and colleagues whereby they examined trauma-related disorders and the relationship of various neuronal networks across affect, cognition and related modalities. These studies represent and define critical insights into how brain-wide networks on a systems level act directly or indirectly with one another to integrate the animal's response to stress. A key aspect of the experience of stress, especially in disorders such as PTSD is the pernicious effect of prior trauma. Effectively detailing with these traumatic memories is an important part of an effective treatment. In "Pharmacological interventions during the process of reconsolidation of aversive memories: a systematic review," Lívia Bolsoni and colleagues looked into how effective pharmacological interventions have been at controlling these symptoms.

At the more molecular and cellular level, the report from Mantsch and colleagues shows the power of using the immediate early-gene Fos as a neuronal marker for cell and region-specific activity patterns. The use of "fos-mapping" in the basic science of stress has been ongoing for many years. Mantsch and his team nicely highlight the power and utility of the approach as it relates to defining specific clusters, ensembles, engrams, and circuits that mediate stress-induced behaviors, and more specifically behaviors related to substance abuse. The advent of fos-mapping has been further expanded recently with the development of "fos-trap" methods to harness fos-activity to capture neuronal ensembles and engrams which might act to encode specific behaviors (Guenthner et al., 2013). An additional report examines the specific interactions between the locus coeruleus noradrenergic system and the cannabinoid system. A timely review of how these two systems might interact is particularly relevant given the widespread use of cannibinoids for anxiety and stress nationwide. The report also focuses on using electron micrographs for imaging the specific localization of key molecular players in the stress response. The use of this imaging method sits in contrast to the systems-wide imaging methods utilized in other studies in this issue, but nevertheless highlights the importance of cross-disciplinary methods to dissect how stress impacts the brain at

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multiple levels of resolution from molecular, cellular, circuit, and the systems level.

In summary, in this special issue "Imaging Stress", we invited articles to highlight the multi-modal, cross-disciplinary nature of how neuroscientists are working to uncover the mechanisms which underlie stress responsivity and related neuropsychiatric states across animal models and human studies. The issue features novel experimental findings across an array of stress modalities and experiences, from animals to human, as well as, articles reviewing key aspects or technology that continues to facilitate our understanding of stress neurobiology.

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