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Taking aim at interoception's role in mental health

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Special issue: Interoception and mental health

When Sherrington first coined the term interoception over 100 years ago [1], it was based on a perceived anatomical distinction between three subdivisions of the body that fundamentally organized the flow of sensory information into the nervous system. While much work in the neurosciences has focused on the exteroceptive and proprioceptive divisions, only recently has interoception appeared on the broader scientific radar. Because interoception encompasses a staggering array of physiological systems (cardiovascular, respiratory, gastrointestinal, nociceptive, immune etc.), understanding its mapping and integration within the nervous system has posed serious challenges. It was only around the turn of the millennium that a series of seminal publications conceptually unified this diverse convergence of visceral information [2–4]. By emphasizing the importance of an integrated mapping of interoceptive inputs, and further, by anatomically localizing this mapping to discrete sectors within the central nervous system, a theoretical underpinning for how the brain senses and responds to threats to bodily homeostasis began to emerge, catalyzing a burgeoning movement of research focused around the theme of interoception (Figure 1). But can we harness the excitement of recent progress in interoceptive science and translate it into meaningful mental health interventions?

Achieving this translational goal will require new tools, new interventions, and new interdisciplinary ways of thinking about body-brain communication. In November of 2016, the Laureate Institute for Brain Research organized the Interoception Summit, a first of its kind gathering of interoception experts from around the world. The aim of the meeting was to unite a multidisciplinary group of leading scientists and thought leaders, with the goal of accelerating progress in interoception research and ultimately improving mental health outcomes. Attendees included mental health clinicians (psychiatrists, psychologists, neurologists), neuroscientists specializing in cognitive, computational, and cellular/molecular processes, and physiologists specializing in the cardiovascular, respiratory, gastrointestinal, nociceptive, and immune systems. Workshops at the meeting were organized around four themes: interoceptive assessment, interoceptive integration,

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interoceptive psychopathology, and the generation of a roadmap that could serve as a guide for future research. During each workshop a panel of speakers provided brief presentations intended to ignite debate within the small group conversations that followed. Keynote presentations and conference-wide discussions focused on consensus-building and identification of clinically meaningful steps forward. The output from each workshop, videos from the meeting, and a comprehensive bibliography of all English language articles published on interoception (the 'Interoception Library') are now freely available online.^{1,2}

The primary output of this gathering of interoceptive minds is the white paper by **Khalsa et al.** [5]. This paper presents an overview of the consensus generated by the meeting. The authors propose a unified nomenclature for the features of interoception and interoceptive awareness, and decompose some of the complexities involved in multisystem and multilevel interoceptive interrogation. They describe the key role of computational theories of interoception in linking the active sensing process with the regulation (or control) of body states. They consider disorder-based and dimensional views of interoceptive psychopathology with the aim of moving the field towards interoceptive tests and/or biomarkers for predicting diagnostic, prognostic, or treatment outcomes. Perturbation approaches are highlighted as one promising strategy for systematically enhancing or altering the flow of information between body and brain as a means to generate novel tests and treatments. Ultimately, the white paper provides a roadmap for future investigations.

This special issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* highlights several new and exciting ways in which interoceptive science is impacting mental health. The papers span a diverse set of approaches including functional neuroimaging, psychophysiology, novel behavioral interventions, and a detailed examination of the link between interoception and inflammation. What unites these papers is their focus on studying clinical issues using a range of different interoceptive tools and approaches, but all for the purpose of improving our understanding of mental illness.

It is well known that individuals with depression have a bias toward recalling negative memories, however what is driving this bias within the brain is unclear. **Dewille et al.** [6] describe a novel test of interoceptive recall focused on the neural correlates of visceral memory for aversive respiratory sensation. Healthy and depressed individuals learned whether neutral visual stimuli predicted aversive interoceptive (inspiratory breathing load) or exteroceptive (loud female scream) experiences, and underwent functional neuroimaging during a surprise test of recall memory. Stimuli associated with the interoceptive experience preferentially enhanced activity in the bilateral insula in healthy individuals but revealed a blunted response in the right insula in depressed individuals. This study supports a new role for the insula in the recall of visceral memories, reminding us that the brain must function to simultaneously monitor current experience while buffering us from the negative consequences of past experiences.

¹Interoception Summit 2016 website: www.iSummit2016.org

²Interoception Library: <https://osf.io/8ygr7/wiki/home/>

Panic disorder has been previously considered to be a prototypical disorder of interoception, based on the primacy of palpitations and dyspnea in the symptomatology of panic attacks. **Meuret et al.** [7] report the results of a secondary analysis from a clinical trial involving capnometry-assisted respiratory training in individuals with panic disorder. This treatment relied on a biomarker-guided approach—patients monitored their exhaled CO₂ levels and learned to pace and slow their breathing. Examining the impact of within-session changes (as opposed to pre vs. post treatment, the subject of the initial study), they found that the degree of dyspnea reported during each session successfully predicted reductions in fear of anxiety-related sensations. These data highlight the potential importance of assessing interoceptive awareness during treatment, and suggest that the experience of dyspnea offers an additional target beyond anxiety during interoceptive exposure therapy.

Interoceptive perturbations are sometimes employed clinically during exposure therapy for anxiety disorders. Here, **Krause et al.** [8] compared physiological and behavioral responses to two types of approaching threats to the body: external (electric shock to the skin) and internal (forced expiratory breathhold). Both threats elicited similar patterns of defensive mobilization with increasing threat proximity, indicating a successful elicitation of dynamic changes in physiology and behavior, while the interoceptive threat elicited distinct changes in minute ventilation. The selectivity of respiratory responses to this task in healthy individuals may help to advance the search for ‘interoceptive stress tests’ capable of assessing threat sensitivity in specific interoceptive channels.

The immune system has been increasingly linked to the pathophysiology of psychiatric disorders. **Harrison and Savitz** [9] remind us that while accounts have traditionally focused on the role of trafficking signals within the nervous system, chemosensory immune pathways disproportionately signal physiological changes from the body to the brain. The authors review current evidence implicating inflammation with changes in brain structure and function, with an emphasis on inflammatory changes in mood disorders, schizophrenia, and autism. Particularly noteworthy is the recent use of inflammatory challenges (another form of interoceptive perturbation) in experimentally probing links between immune signaling, interoception, and psychopathology.

Aversion to the experience of interoceptive sensations is a defining feature of anxiety sensitivity. In the final paper of this special issue, **Feinstein et al.** [10] examine the impact of Floatation-REST (Reduced Environmental Stimulation Therapy) on anxiety in a transdiagnostic sample of patients with high anxiety sensitivity. This novel non-pharmacological intervention, which attenuates exteroceptive sensory input, simultaneously enhanced interoceptive signals while also inducing clinically-significant anxiolysis. This paradoxical effect of anxiety reduction in the context of heightened interoceptive awareness is noteworthy given that individuals with anxiety sensitivity frequently fear interoceptive sensations. However, exposure to these sensations occurred in the context of significant reductions in blood pressure and muscle tension. The unique juxtaposition between physiological relaxation in the face of heightened interoception may confer unique opportunities for helping highly anxious individuals “desensitize.”

Much like the archer depicted on the cover of this special issue, it is now more clear than ever that interoception represents the brain's tightrope act of incorporating what is happening on the outside of the body with what is happening on the inside. In a dynamically changing world, hitting the mark can be quite challenging, and interoception's multifaceted nature only adds to the challenge. We are still in the early phases of identifying how interoception can be parsed across psychiatric disorders. For example, is the same phenotype recapitulated across different psychiatric disorders? Or are there distinct processes or groups of processes which will require unique target-specific approaches for detection, diagnosis, and treatment? Transdiagnostic perspectives may allow for a greater focus on the role of interoceptive signals in the etiology and maintenance of psychopathology. Interoceptive perturbation approaches should provide new perspectives on basic mechanisms of signal processing, potentially leading to new avenues for intervention. Computational models of interoception should provide a linking function between theoretical and experimental approaches, connecting sensation with action. As we embark on the road to understand interoception's role in mental health, these papers and the questions they raise serve as guideposts for where we go from here.

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Figure 1.
The long and winding road of interoceptive science.