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Introduction to the Special Issue: Using neuroimaging to probe mechanisms of behavior change

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Identifying the neural correlates of behavior change and predictors of treatment response with neuroimaging has potential to drive radical changes in current approaches to diagnosis and treatment of mental health conditions (Chung et al., 2016; Potenza et al., 2011). Improved understanding of the neural mechanisms underlying changes in cognition and behavior could spur the development of novel neuroscience-based interventions that amplify the effect of "active ingredients" of treatment, optimize dosing and intervention duration, and foster sustained behavioral outcomes (Fisher and Berkman, 2015; Naqvi and Morgenstern, 2015; Riggs, 2015). Neuroimaging methods could fundamentally change our understanding of "how" and "for whom" treatment works, and under what conditions behavior change occurs (Gabrieli et al., 2015; Potenza et al., 2011), in moving toward a personalized medicine (Calhoun et al., 2017; Prendes-Alvarez and Nemeroff, 2016). As a step toward this goal, this Special Issue, which includes systematic literature reviews and innovative empirical studies, addresses the use of neuroimaging to refine theories of disease mechanisms, and provides an inspiring glimpse into how interventions have effects on brain circuits, cognition, and behavior.

Dr. Dagher's thoughtful commentary (Dagher, 2017) for the Special Issue focuses on the key role of brain circuits as a basic level of analysis for understanding mechanisms of behavior change across the continuum of health to illness, and in different domains of functioning (e.g., response to threat or reward). In contrast to traditional symptom-based approaches (American Psychiatric Association, 2012; World Health Organization, 1992), transdiagnostic approaches, such as Research Domain Criteria (Insel and Cuthbert, 2015), are proposed to more parsimoniously capture features that are "shared" versus "distinct" across symptom-level phenotypes. For example, in the article by Landin-Romero et al. (2017), across two disorders with overlapping symptoms, neuroimaging revealed significant changes in brain

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structure that effectively distinguished Alzheimer's Disease from behavioral variant fronto-temporal dementia. Regarding substance use, Vergara et al. (2017) found a general pattern of resting state hypo-connectivity among substance users compared to controls, as well as substance-specific patterns of resting state connectivity that may serve as targets for different types of intervention. Likewise, the systematic review of neural mechanisms involved in cognitive reappraisal by Zilverstand et al. (2017) identified features that were shared across disorders involving mood, anxiety, and addiction, in addition to disorder-specific aberrations. These pioneering reports show how neuroimaging, in contrast to symptom-level phenotypes, can uncover both shared and disorder-specific signatures that can guide differential diagnosis and personalization of treatment.

Several articles in this issue examine the predictive utility of brain-based biomarkers (Calhoun et al., 2017; Gabrieli et al., 2015), particularly in addictions research. Specifically, Zelle et al. (2017) found that during cue exposure, greater functional connectivity, but not mean level of activation, of left anterior insula with dorsolateral prefrontal cortex was associated with an adult's ability to resist smoking during a quit attempt. Among adolescent cannabis users, Feldstein Ewing et al. (2017) found that greater orbitofrontal cortical network connectivity in response to client language in favor of change ("change talk") was associated with poorer treatment response (more cannabis-related problems) one month later. In a study of adult smokers that compared mindfulness and cognitive behavioral therapy (CBT), Kober et al. (2017) identified mindfulness-specific effects on stress reactivity in several brain regions (e.g., amygdala) that were not observed for CBT, and that, importantly, predicted post-treatment reductions in smoking. These intriguing studies support the use of neuroimaging biomarkers to predict clinical outcomes, as identified in other studies (Courtney et al., 2016; Feldstein Ewing et al., 2016). These initial, formative studies pave the way for future efforts integrating neural targets for mechanisms of change, and biomarkers into applied clinical practice (Gabrieli et al., 2015).

Another theme in this Special Issue involves investigating the effects of cognitive training and behavioral treatment on brain circuitry across a variety of disorders (e.g., schizophrenia, mood, addiction), and intervention types (e.g., cognitive enhancement therapy, cognitive bias modification). In this regard, Keshavan and Eack, (2017) found that cognitive enhancement therapy showed effects through increasing the efficiency of prefrontal circuitry, which was associated with cognitive improvement in patients with schizophrenia. The systematic review by Wiers and Wiers, (2017) indicated that cognitive bias modification training was found to impact fronto-amygdalar circuitry for the disorders of anxiety and addiction, but instead influenced functional connectivity between frontal gyrus, anterior cingulate, and insula for depression. Using a cue approach training paradigm, Bakkour et al. (2017) found that the training shifted choice preferences through differential engagement of task control networks (e.g., lateral prefrontal cortical areas), which interacted with value networks. Importantly, these studies provide first insights into "how" a behavioral intervention can affect brain circuitry, and boundary conditions at the level of brain functioning that delimit "for whom" specific types of treatment protocols may be most effective.

Nascent efforts in the new field of computational psychiatry (Huys et al., 2016; Stephan et al., 2016, 2015; Teufel and Fletcher, 2016), as described in the commentary (Dagher, 2017)

and compelling review article by Heinz et al. (2017), apply mathematical models to neuroimaging and behavioral data with the goal of obtaining quantitative *in vivo* markers to predict potential individual expressions of behavioral outcome. In particular, Heinz et al. propose the use of a computational model that predicts relapse to alcohol use; this model is individualized using non-invasive assays, such as neuroimaging biomarkers that quantify changes in key learning mechanisms (e.g., an individual's trial-by-trial learning rate or pattern of responses) (Stephan et al., 2017). Ideally, the computational model would provide a mechanistically interpretable prediction of individual outcomes, which could have profound implications for the personalization of neuroscience-informed treatments by identifying specific deficits that could be addressed with more precisely targeted intervention (Paulus et al., 2016; Wang and Krystal, 2014).

Tailoring neuroscience-based interventions to an individual remains challenging, but possibly within reach, as demonstrated by two Special Issue articles on the use of neurofeedback to facilitate meditation training, and neuro-navigation to optimize repetitive transcranial magnetic stimulation (rTMS). As an aid to meditation training, van Lutterveld et al. (2017) demonstrated that EEG neurofeedback can provide an objective measure of brain activity that individuals could use, in tandem with their subjective experience, to maintain a brain state consistent with meditation. Other work, by Luber et al. (2017), explored the use of fMRI guided neuro-navigation to directly, and in a personalized way, locate targets for bilateral prefrontal cortical locations used in rTMS, delivered in combination with cognitive therapy for depression. These thought-provoking studies open up new possibilities for personalizing treatment based on an individual's strengths and specific needs.

The goal of this Special Issue was to present state-of-the-science methods, comprehensive reviews, and cutting-edge empirical findings from studies incorporating neuroimaging into translational research on behavior change. The issue's twelve articles and commentary showcase the power, as well as limitations and challenges, of using neuroimaging to aid differential diagnosis, predict treatment outcome, track treatment progress, and improve the design of interventions in moving toward personalized medicine. While much work remains to be done in translating neuroimaging results to clinical care, the articles in this issue provide exciting initial steps toward more effective and personalized neuroscience-informed intervention.

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