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Neuropsychopharmacology Reviews (2016) **41,** 372–373; doi:10.1038/npp.2015.237

Neural Basis of Mindfulness Interventions that Moderate the Impact of Stress on the Brain

The scientific study of mindfulness has skyrocketed. Mindfulness can be defined as 'non-judgmental attention to present-moment experiences' and is thought to comprise several complex processes, including attentional control, emotion regulation, and self-awareness (Tang *et al*, 2015). Although the neuroscience underlying mindfulness is at an early stage, there are some intriguing findings that begin to unravel the effects of mindfulness on mental health, stress, and resilience. For example, those individuals who rated themselves as more mindful, i.e. had greater 'dispositional mindfulness', generally report lower levels of perceived stress (Prakash *et al*, 2015). This is important because the level of stress is strongly related to physical and mental health as well as cortical thinning. In comparison, dispositional mindfulness has been related to structural and functional differences in several neural structures, including the medial prefrontal cortex, hippocampus, amygdala, anterior and posterior cingulate, and orbitofrontal cortex (Tang *et al*, 2015). Therefore, dispositional mindfulness may prove to be an important construct to examine individual differences that can help to predict risk for and relapse to mental disorders.

Mindfulness-based stress reduction (MBSR) has been proposed for almost every psychiatric condition. In a meta-analysis (Sedlmeier *et al*, 2012), mindfulness interventions had medium to large effect sizes for changes in emotionality and relationship issues, medium effect sizes for measures of attention, and small effect sizes for cognitive measures. MBSR has been associated with increased cortical thickness in the insula and somatosensory cortex, which can be associated with reduction of worry, state anxiety, depression, and alexithymia (Tang *et al*, 2015). Moreover, changes after mindfulness training in the insula have been related to increase in interoceptive awareness, i.e. the ability to monitor afferents from inside the body, which is emerging as an important construct for anxiety disorders and addiction (Paulus and Stewart, 2013). Thus, some of the same brain systems that have been implicated in dispositional mindfulness are also affected by mindfulness-based interventions and show a certain degree of plasticity of these systems.

Our understanding of the molecular mechanisms of mindfulness and changes induced by mindfulness-based interventions is at its infancy. Recent studies have reported that MBSR training results in a smaller post-stress inflammatory response (Rosenkranz *et al*, 2013), which includes interleukin-6. MBSR also increased telomerase activity and those individuals with the greatest increase also reported the greatest reductions in chronic stress, anxiety, dietary restraint, dietary fat intake, cortisol, and glucose (Daubenmier *et al*, 2012). These findings suggest that mindfulness interventions affect both inflammatory and epigenetic mechanisms, which are important for mood and stress-related disorders, respectively. Therefore, elucidation of the molecular substrates that underlie individual differences in mindfulness may be one of the most fruitful areas for future research. Taken together, mindfulness and mindfulness-based interventions have profound effects on mental health, affect brain systems that are important for emotion regulation and self-awareness, and alter inflammatory and epigenetic responses, yet much needs to be done to make these interventions a part of precision psychiatry.

FUNDING AND DISCLOSURE

The author declares no conflict of interest.

ACKNOWLEDGMENTS

This study was funded by the William K Warren Foundation.

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Neuropsychopharmacology Reviews (2016) **41,** 373; doi:10.1038/npp.2015.239

Dynorphin, Dysphoria, and Dependence: the Stress of Addiction

The hypothesis that the dynorphin-kappa opioid receptor system may be a key component of the neuroplasticity associated with stress-induced mood disorders and the 'dark side' of