Biological Psychiatry: GOS

Introduction to the Special Issue on Mindfulness: Measurement, Methods, Mechanisms, & Mental Health

Todd S. Braver and Sara W. Lazar

The term mindfulness refers to an accessible and increasingly popular set of mind-body training practices and skills that can be used to enhance health, wellness, and psychological functioning in a low-cost, nonpharmacological manner. Mindfulness practices originated in Buddhist contemplative traditions more than 2500 years ago, but in just the past 35 years they have undergone a process of adaptation and secularization that has resulted in their widespread adoption by Western popular culture. In the 21st century, mindfulness has become a focus of intense scientific interest and multidisciplinary investigation, engaging researchers in public health, social work, and education, with an increasingly strong emphasis within psychology, neuroscience, and psychiatric medicine. From this work, there is now a growing database of findings documenting beneficial and reliable effects of mindfulness on a range of health outcomes and clinical disorders ranging from anxiety and depression to addiction, chronic pain, insomnia, and others (1). However, despite this abundance of research, both the biology and brain mechanisms of action associated with mindfulness practices, training, and interventions are just beginning to be understood. In this Special Issue (SI) of *Biological Psychiatry: Global Open Science* (BP:GOS), we showcase some of the cutting-edge research in this area, utilizing state-of-the-art methodologies to investigate mindfulness effects in terms of both basic biological mechanisms and their impact on mental health–relevant domains.

The BP:GOS SI came about as an outcome product of M^4, the Mindfulness Mechanisms and Methods Meeting, which was a small-group conference and subsequent workshop that we (TSB and SWL) co-organized at Washington University, St. Louis, in October 2023. The goal of M^4 was to bring together leading cognitive neuroscientists and contemplative neuroscientists focused on mindfulness research, along with expert mindfulness practitioners interested in partnering with neuroscientists. The conference sessions and themes were organized to draw attention to advances within the cognitive neuroscience of mindfulness, focusing on new methods and available tools. Here, we present a broad sampling of exciting new experimental research related to mindfulness, with the opportunity to include a wider range of topics, methods, and research groups than those presented and discussed at M^4. This includes work focused on electroencephalographic (EEG) methods, network neuroscience studies utilizing functional magnetic resonance imaging (fMRI), studies of biological markers, and new measurement approaches. It is also important to note that there is a second, complementary SI connected to M^4, which is published in *Biological Psychiatry: Cognitive Neuroscience & Neuroimaging* (BP:CNNI), the sister journal of BP:GOS. The BP:CNNI SI provides short and topical conceptual reviews that parallel the sessions and key themes of M^4. Because of the complementary and linked nature of the BP:CNNI SI, we will also refer to relevant articles in that journal within this commentary.

EEG as a Highly Flexible Methodology for Mindfulness Studies. A major theme of this SI is a focus on new experimental EEG studies of mindfulness, which fully leverage some of the key advantages and more recent advances in analytic approaches possible with this methodology. As described in the BP:CNNI review by Lin *et al.* (2), studies of the neurophysiology of meditation have been conducted using EEG for decades, but they have only recently have taken full advantage of the power and flexibility of this method to measure neural activity across a variety of timescales and experimental contexts and with a range of measurement approaches (spectral decomposition, event-related potentials, time-frequency analyses, multivariate decoding). The articles in this SI do an excellent job of illustrating the diversity and sophistication of EEG-based approaches to mindfulness.

In terms of spectral decomposition, EEG studies of mindfulness have most commonly examined the effects of different practices or interventions in terms of changes in power within predefined spectral frequency bands (3,4). However, this approach has important limitations in missing out on more complex EEG activity, such as changes to the peak frequency within a narrowband oscillation (e.g., alpha band) or in aperiodic (non-oscillatory) EEG activity, such as 1/f patterns, and in stable spatiotemporal patterns, such as EEG microstates. Addressing these limitations is the focus of Dziego *et al.* (5), who examined resting-state EEG in active-duty military personnel before and after an 8-week mindfulness intervention or active control, focusing on individual peak alpha frequency together with 1/f and microstate parameters. Their analyses revealed that the 1/f and microstate parameters selectively captured some of the neural changes associated with mindfulness training, suggesting the potential richness and additional sensitivity of this analytic approach.

The flexibility of EEG in enabling a range of analytic approaches and research designs is showcased in the work by Ramanathan *et al.* (6). The researchers developed a novel breath monitoring task to assess interoceptive attention, which

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is widely thought to be a skill enhanced in mindfulness training practices (7). The use of a wireless EEG system facilitated monitoring of neural activity during task performance in a large ($n > 300$) lifespan sample under mobile laboratory conditions. Their analytic approach integrated neural source localization with localized spectral power changes and functional connectivity methods to identify key relationships between the activation and connectivity of the default mode network (DMN) and both task performance metrics (breath monitoring consistency) and individual differences in trait mindfulness.

In Lin *et al.* (8), the researchers harnessed the flexibility of EEG to implement a novel, fully within-subjects research design aimed at distinguishing between distinct mindfulness states (open monitoring and focused attention) in terms of their subsequent impact on emotional processing. By examining event-related potentials occurring during an affective picture viewing task performed immediately after mindfulness state induction, the researchers were able to identify opposite effects of open monitoring and focused attention states on well-established neural signatures of emotion processing that were further modulated by subjective arousal.

In 2 other SI articles, multivariate decoding methods were applied to EEG data to address 2 core questions related to mindfulness states: Are there reliable neural signatures that distinguish these from mind-wandering states? Can the depth of the mindfulness state be decoded from neural activity patterns? Aviad *et al.* (9) tackled the first question using well-established machine learning pattern classification algorithms, combined with explainability and feature importance methods, to identify the key components of the best-differentiating EEG signatures. The relatively high accuracy of mindfulness state classification was obtained with a small subset of initially selected candidate EEG features, which reflected the coherence of mostly high-frequency oscillations occurring among frontal and midline brain regions. Reggente *et al.* (10) addressed the question of meditation depth and found that accurate classification was not successful when using traditional univariate assessment of changes in spectral power bands, but could be achieved through a novel machine learning classification approach that combined time-frequency decomposition, spatial source localization, and connectivity metrics.

Using fMRI to Identify Mindfulness Effects on Brain Network Organization. A second theme of the SI was mindfulness studies that have also utilized more recently developed analytic approaches in conjunction with fMRI neuroimaging. As reviewed in the BP:CNNI article by Prakash *et al.* (11), there have been important advances in analytic methods that focus on brain networks and the interactions within and between them rather than on activation or connectivity between localized regions. These network neuroscience approaches provide a new opportunity and vantage point from which to understand how mindfulness impacts brain functioning. For example, as reviewed in the BP:CNNI article by Tripathi *et al.* (12), a key focus in both the mindfulness and broader clinical network neuroscience literature has been on interactions involving the DMN, which tends to be anticorrelated with other brain networks, such as the dorsal attention (DAN) and frontoparietal (FPN) networks. Two studies in this SI exemplify the potentially unique insights that can be gained by a brain network–focused approach to mindfulness.

In Treves *et al.* (13), a key innovation was to not only utilize more traditional static connectivity measures but also examine the dynamic changes between these networks that might differentiate individuals with high trait mindfulness. In a large sample of young adolescents, a surprising finding was that, rather than anticorrelations being predominant, high trait mindfulness was associated with a more frequently occurring state that involved widespread hyperconnectivity among all brain networks (including the DMN, DAN, and FPN). This represents a potentially new neural signature of mindfulness that can be further investigated in future studies.

Czajko *et al.* (14) utilized a different experimental strategy by investigating large-scale features of brain network organization that best differentiated long-term meditation practitioners from novices. The key analytic approach was to focus on connectivity gradients, the primary dimensions of change in connectivity that occur across the brain as a whole. Three primary gradient dimensions have been defined and are treated as an intrinsic coordinate system that characterizes brain network organization. Using this coordinate system together with multivariate decoding methods, long-term practitioners could be differentiated from novices in terms of greater integration among brain regions (reduced eccentricity in connectivity gradients). Interestingly, even though connectivity gradients were measured under both resting-state conditions and during engagement in different mindfulness practices, the gradient pattern appeared consistent and independent of the experimental context, leading to a generalized decoding of expertise suggestive of a more trait-like change in brain organization.

The Biology of Mindfulness. A third theme explored in this SI is the characterization of mindfulness effects in terms of widespread biological changes that impact not only brain function but also other bodily systems. This perspective has a long history, because some of the most influential and early biologically based studies of meditation and mindfulness demonstrated effects on various physiological processes, such as cardiovascular and immune system functioning (15–17). This work can also be highly complementary to cognitive neuroscience–based investigations by helping to elucidate the nature of brain-body interactions and their impact on developmental, aging, and health outcomes. Two studies in the SI nicely highlight this type of complementarity.

In Puhlmann *et al.* (18), the goal was to identify the biological mechanisms underlying mindfulness effects on stress reduction. To investigate this question, the researchers focused on key components of a putative biological stress regulation pathway that impacts brain health, by assessing glucocorticoid markers of hypothalamic-pituitary-adrenal axis function (e.g., salivary cortisol, hair cortisone) and serum BDNF (brain-derived neurotrophic factor) levels together with measures of hippocampal anatomy (e.g., dentate gyrus volume). These factors were found to change in a coordinated fashion throughout a 9-month mindfulness training intervention, with

BDNF increases being linked to increased dentate gyrus volume potentially mediated via changes in long-term cortisol release.

In a second study by Kaliman *et al.* (19), the focus was on whether a long-term training program could promote healthy aging in an older adult sample. Here, rather than focusing on measures of brain aging, the researchers examined cellular aging using the well-established marker of telomere shortening, which has previously been associated with increased risk of mortality and neurodegenerative diseases, such as Alzheimer's disease (20). Interestingly, no effects of the intervention were observed on telomere length in this study, adding to the mixed picture emerging from prior work (21,22). However, Kaliman *et al.* (19) also pointed to potential individual differences in moderating factors, such as personality traits and practice time, which could be followed up in subsequent work.

The Measurement of Mindfulness. A final topic explored in this issue relates to the multidimensional nature of mindfulness, which creates challenges for construct validation via accurate and precise psychometric measures. Although many self-report scales have been developed to assess both trait and state-related dimensions of mindfulness, which are currently in wide usage in the literature, they are subject to widely recognized limitations and reporting biases (23). One of these limitations is related to the dynamic nature of mindfulness, in which practice experiences lead to ongoing changes in both subjective experience and skill development that blur traditional state-trait distinctions.

To address this issue, Abdoun *et al.* (24) developed LAMP (Lyon Assessment of Meditation Phenomenology), a new self-report scale drawing on an influential conceptual framework, which locates different mindfulness practices within a multidimensional phenomenological space (25). A key feature of LAMP was that it was designed to be used in repeated longitudinal assessment contexts, such as intensive meditation retreats or experience sampling, to identify meaningful temporal trajectories. The researchers provided initial validation of the LAMP in terms of clustering among items reflecting the unique temporal trajectories associated with engaging in different meditation practices, individual expertise, and difficulties experienced during a meditation retreat.

The Current State and Future Promise of Biologically Based Mindfulness Research. Our goal for this SI of BP:GOS was to provide readers with an up-to-date sampling of some of the key themes, trends, and technologies currently being used in mindfulness research. The collection of articles presented here provide a nice illustration of how multiple methodologies, including different neuroimaging modalities (EEG, fMRI), biologically based assays, and psychometric measurements, can be integrated to provide a new window into the ways that mindfulness impacts mind-body functioning. From this methodological and mechanistically focused vantage point, it is quite easy to discern the potential of this work to improve mental health outcomes and promote human flourishing, which was a key inspiration for us in organizing M^4. Nevertheless, although the potential is quite clear, in our view, the promise will best be achieved from a translational perspective that builds a clear bridge toward clinical work from the types of studies described in this SI. We look forward with anticipation and excitement to seeing this future realized.

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Article Information

From the Department of Psychological and Brain Sciences, Washington University in St. Louis, St. Louis, Missouri (TSB); Department of Radiology, Washington University School of Medicine, St. Louis, Missouri (TSB); Department of Psychology, Harvard Medical School, Boston, Massachusetts (SWL); and Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts (SWL).

Address correspondence to Todd S. Braver, Ph.D., at tbraver@wustl.edu.

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