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Issue: *Advances in Meditation Research: Neuroscience and Clinical Applications***The posterior cingulate cortex as a plausible mechanistic target of meditation: findings from neuroimaging**

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There has been an increased interest in mindfulness and meditation training over the past decade. As evidenced by exponential growth in the number of publications since the beginning of the 21st century, progressively more is becoming known about both the clinical efficacy and underlying neurobiological mechanisms of mindfulness training. This paper briefly highlights psychological models of stress that converge between ancient and modern day (e.g., operant conditioning); identifies key brain regions that, with these models, are biologically plausible targets for mindfulness (e.g., posterior cingulate cortex); and discusses recent and emerging findings from neuroimaging studies of meditation therein, including new advances using real-time functional magnetic resonance imaging neurofeedback in neurophenomenological studies.

Keywords: meditation; fMRI; default mode network; mind wandering; task-positive network

Introduction

Based on 2500-year-old Buddhist teachings, mindfulness meditation aims to help individuals identify root causes of stress, and importantly, provides practical tools (including the identification process itself) for the alleviation of these psychological processes. There is growing evidence for the clinical utility of mindfulness training in the intervention of disorders, ranging from addiction to anxiety, depression, and other psychological afflictions.^{1–4} But how does mindfulness actually *work* and what are the underlying brain regions that are involved in this practice? This paper will briefly highlight psychological models of stress that converge between ancient and modern day; identify brain regions that, supported by extant literature, may be biologically plausible targets for mindfulness; and discuss recent and emerging findings from neuroimaging studies of meditation therein, including recent advances using real-time functional magnetic resonance imaging (fMRI) neurofeedback in neurophenomenological studies.

Where does stress come from, and how does mindfulness help with stress?

There are many models of stress (reviewed in Refs. 5 and 6). Recently, we have found a close parallel between early Buddhist models of stress (termed *dependent origination*) and modern models of operant conditioning (positive and negative reinforcement, reviewed in Ref. 7). In brief, as outlined by Skinner,⁸ “Events which are found to be reinforcing are of two sorts. Some reinforcements consist of presenting stimuli, of adding something—for example, food, water, or sexual contact—to the situation. These we call positive reinforcers. Others consist of removing something—for example, a loud noise, a very bright light, extreme cold or heat, or electric shock—from the situation. These we call negative reinforcers. In both cases the effect of reinforcement is the same—the probability of response is increased” (Ref. 8, p. 73). Basically, organisms learn and reinforce behavior through laying down memories associating X (e.g., sex) with pleasant feelings and Y (e.g., being shocked) with unpleasant feelings. This process is

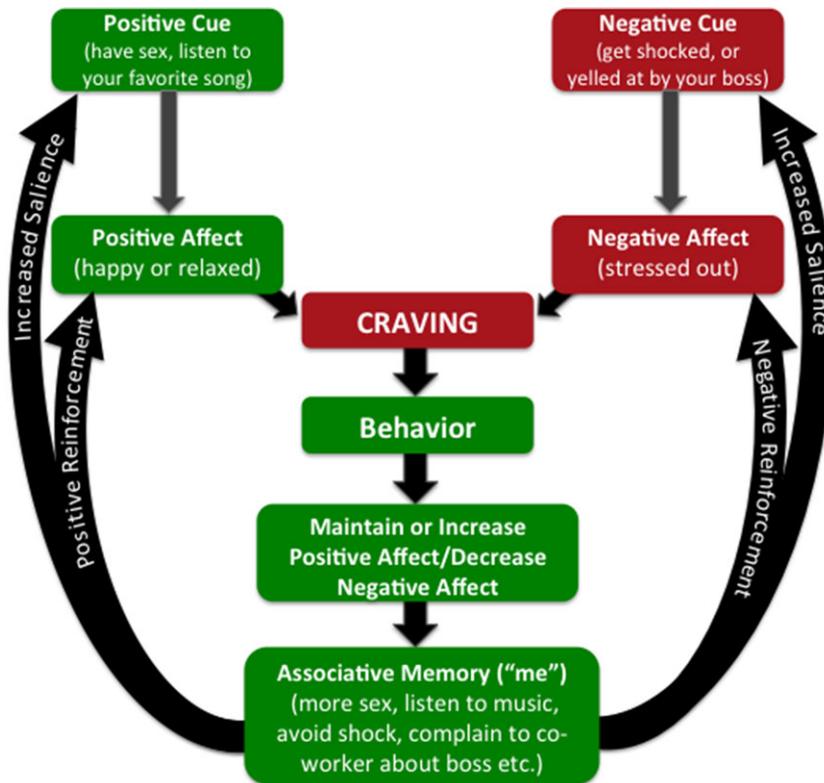


Figure 1. Associative learning “habit loop.” Behavior becomes associated with positive (green) and negative (red) affect through positive and negative reinforcement. Adapted, with permission, from Brewer *et al.*⁷

iterative as individuals engage with their environment in an ongoing manner. Importantly, in humans, given a sense of agency, this associative learning process involves the encoding of self-referential memories—processes become attributed to someone behind the actions—“I” am having sex or being shocked (Fig. 1).

How does mindfulness uncouple the associative learning response?

Studies have highlighted potential psychological components of the associative learning loop and have also started to clarify how mindfulness might act therein. For example, mindfulness training has been shown to decrease affective reactivity, suggesting that it can act on the affective components of this loop.⁹ Also, mindfulness may provide a more accurate view of the sense of self, helping to re-center cognitive distortions.¹⁰ Furthermore, mindfulness training has been shown to directly decouple the link between craving and behavior.¹¹ For exam-

ple, in a study of mindfulness training for smoking cessation, before treatment initiation, participants showed a strong correlation between craving and smoking—the level of their craving predicted the number of cigarettes they smoked. After four weeks of mindfulness training, craving no longer predicted smoking, and this decoupling was directly moderated by the amount of mindfulness practice individuals underwent when cravings were present *in vivo*. These studies highlight the different components of the operant conditioning loops on which mindfulness can act. But where does the brain fit into all of this?

What brain regions are associated with stress?

Taking the operant conditioning model above, one might search for brain regions that are activated during affective states, craving, and self-referential processing. These may serve as sentinels for uncovering larger brain networks that are common to

associative learning processes that may be involved in the larger, complex processes of stress reactions. Furthermore, these may be logical targets for mindfulness, given its psychological mechanisms.

One candidate brain network is the default mode network (DMN). First described over a decade ago by Raichle *et al.*, this network of brain regions has been consistently shown to be activated during the resting state, when an individual is not engaged in a directed task—and relatively deactivated during task-oriented behavior (reviewed in Refs. 12 and 13). Furthermore, the DMN has also been shown to be more active during mind wandering,^{14,15} and specific subregions, such as the posterior cingulate cortex (PCC), have been implicated in self-referential processing,¹⁶ including past and future thinking.¹⁷ Importantly, the PCC has also been shown to be associated with emotional processing,¹⁸ self-referential distortions in depression,¹⁹ and to contribute to anxiety,²⁰ drug craving,²¹ and cognitive distortions in chronic pain.²² These findings suggest that the PCC may be involved in associative learning, as it appears relatively activated during affective, craving, and self-referential components of the operant conditioning loop.

Is the PCC a logical target for mindfulness training? In theory, mindfulness acts to help individuals notice when they are caught up in self-referential processes such as mind-wandering, past and future thinking, rumination, and craving, and to let go or disengage from these processes, bringing their awareness back to the present moment. As PCC activity has been shown previously to be relatively deactivated when individuals are focused on a particular task that does not involve self-referential evaluation (which essentially is what mindfulness trains individuals to do), one might expect similar PCC deactivation with meditation, which trains individuals to pay attention in a nonevaluative manner.²³ This distinction between paying attention and paying attention in a nonevaluative manner is perhaps subtle yet important. For example, a target detection task decreases PCC activity, and the more difficult the task, the greater the decrease.²⁴ However, evaluating a list of adjectives to determine if they represent one's self is a typical task that increases PCC activity.¹⁶ The critical distinction between these tasks may be related to the degree of self-referential evaluation that is inherent in the task^{25,26} and may be elucidated

by studying meditators, who specifically train to notice and let go of self-referential states. Indeed in early work, monks showed relatively decreased PCC activity compared to novice meditators when presented with distractor sounds in an fMRI scanner, and Zen meditators showed similar responses during pain induction.^{27,28} More recent work has shown that experienced meditators again show decreased PCC activity when mindfully viewing emotional pictures.²⁹ Importantly, these findings have now been shown during blocks of standard meditation itself. For example, in expert compared to novice meditators, we have found relative PCC deactivation that is common among three different types of meditation (breath awareness, loving kindness, and choiceless awareness).³⁰ Furthermore, Pagnoni *et al.* showed that PCC deactivation during meditation correlated with improved performance on the Rapid Visual Information Processing task on a separate day, linking brain to behavior.³¹

Can real-time fMRI neurofeedback improve the link between PCC activity and meditation?

Given the earlier findings of general on-task PCC deactivation, does this convergence of findings suggest anything special about the meditative state or just replicate previous studies by including meditation on the list of cognitive tasks shown to deactivate the PCC? To explore this question, we used real-time fMRI neurofeedback to test the link between PCC activity and the subjective experience of meditation.^{32,33} Previous studies had largely averaged brain activity across meditation blocks with a duration of several minutes, and then asked subjects about their experience averaged across those same blocks. Real-time fMRI neurofeedback affords the ability to gather information on the moment-to-moment correspondence between particular brain regional activation and first-person cognitive processes, in this case between PCC activity and meditation. As the PCC has been shown to have multiple subregions associated with different cognitive processes,³⁴ and we have found that it is relatively specifically deactivated across a number of meditations,⁷ we explored a subregion that showed peak deactivation during breath awareness meditation (see Refs. 7 and 33 for methodological details), which also had strong overlap with regions of interest in other studies of meditation,³¹ and

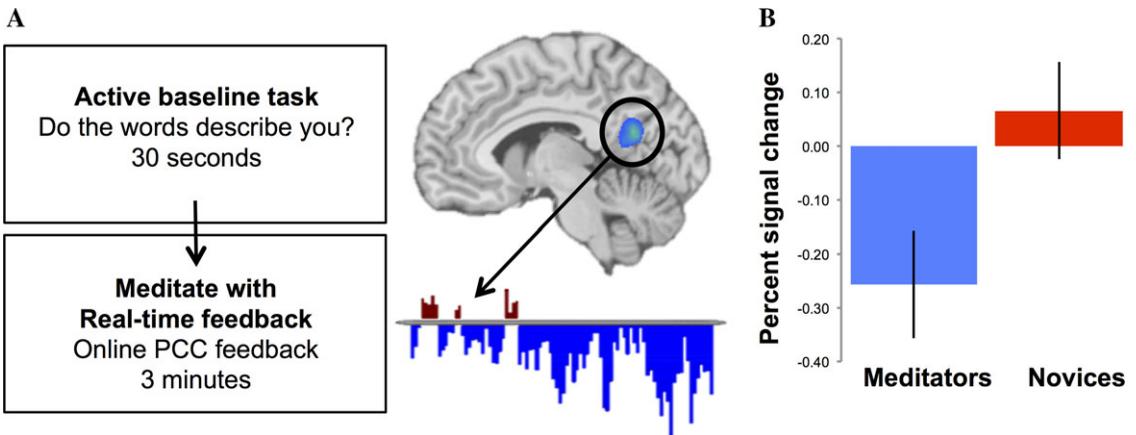


Figure 2. Schematic of real-time fMRI neurofeedback protocol. (A) An active baseline task is followed by meditation with real-time feedback. During meditation, percent signal change in the PCC (corrected for global brain activity) is calculated and plotted in real time. Red = increased activity; blue = decreased activity. (B) Expert meditators show volitional control over PCC activity. BOLD percent signal change for the PCC relative to baseline in meditators (blue) and novices (red). Adapted, with permission, from Garrison *et al.*³³

in contrast, self-referential processing.¹⁶ This was ideal, as in theory, individuals can report on the correspondence between their experience of both self-reference and increased PCC activity, as well as meditation and decreased PCC activity.

Participants were instructed that the PCC is thought to be involved in self-related processing and mind wandering as well as meditation; this instruction was provided in order to anchor them to be able to link PCC activity to particular aspects of experience. They were instructed to meditate with their eyes open while allowing the graph to rest in the background of their awareness during the meditation period, and to look from time to time to see how well increases in the graph (red) corresponded with self-referential thinking or mind wandering, and how well decreases in the graph (blue) corresponded with meditation (Fig. 2A). This was done such that participants could meditate, but also closely link their meditation experience with their brain activity with minimal disruption. After each of six 3-min runs during the fMRI session, subjects were asked how well the graph corresponded to their experience during meditation, using a Likert 10-point scale (0 = not at all, 10 = perfectly). Both novices and experienced meditators reported significant correspondence (8.4 ± 1.8 and 7.8 ± 1.7 , respectively); whereas scores for correspondence with activity in a closely linked default-mode control brain region (posterior parietal cortex) were significantly lower

for all subjects (PCC = 8.1 ± 0.3 ; posterior parietal cortex = 6.9 ± 0.4 ; $t_{(42)} = 3.1$, $P = 0.004$).³³ Thus, subjects could differentiate between feedback from a region involved in meditation (PCC) or a control region, reducing the likelihood of confirmation bias (i.e., favoring information that confirms preconceptions). When, in a separate experiment, participants were asked to volitionally decrease PCC activity, experienced meditators showed significant PCC deactivation (percent signal change from baseline = -0.26 ± 0.1), compared to nonmeditators (percent signal change from baseline = 0.07 ± 0.09 ; $t_{(18)} = -2.40$, $P = 0.028$), which was consistent with previous studies of meditation³⁰ (Fig. 2B).

To mitigate the possibility of confounding confirmation bias or other expectancy effects, we performed a separate discovery study in which experienced meditators took part in a four-step series of fMRI runs progressing from: (1) meditation, (2) meditation with simulated real-time feedback, (3) meditation with real-time feedback from the PCC, to (4) volitional PCC deactivation (Fig. 3A).³³ This protocol was designed to progress from the most naturalistic setting for meditation (1), to learning to meditate on a dynamic graph (2), and then meditating on a graph of one's own brain activity in real time (3), followed by volitional manipulation of the graph (4). Subjects were not provided experiential anchors for the graph, only that increases in the graph (red) indicate increased

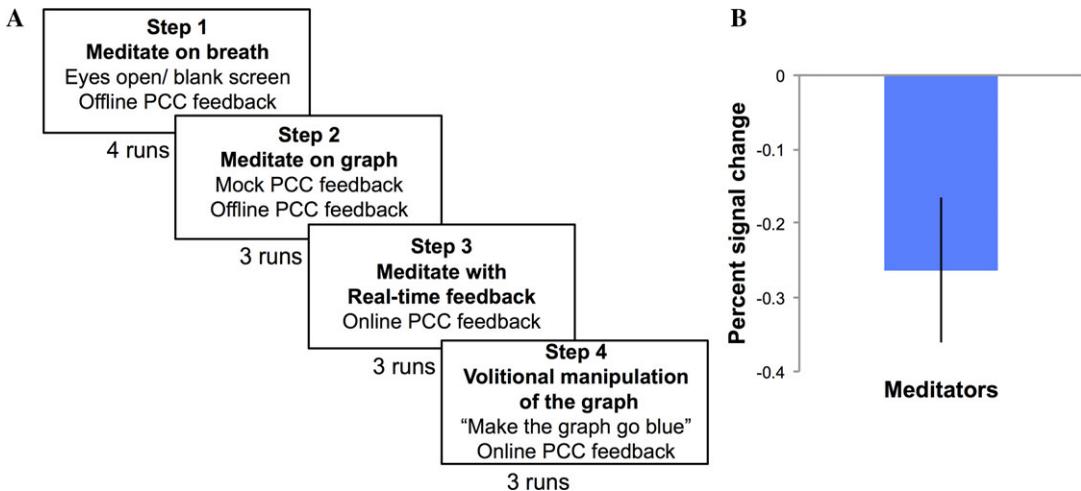


Figure 3. (A) Schematic of novel step-wise real-time feedback discovery protocol. (B) Expert meditators demonstrate volitional deactivation of the PCC during meditation with real-time fMRI neurofeedback in a novel discovery protocol ($P = 0.026$). Mean percent signal change in the PCC \pm SEM. Adapted, with permission, from Garrison *et al.*³³

activity in a particular brain region, and decreases in the graph (blue) indicate decreased activity in that brain region. This allowed subjects to discover over the course of steps 1–4 how their PCC activity corresponds with their subjective experience of meditation, without the bias of specific anchors for that experience. After each 1-min run, subjects were asked how well the graph corresponded to their experience during meditation (0 = not at all, 10 = perfectly). Similar to the previous study, meditators reported a significant correspondence between PCC activity and subjective experience (7.6 ± 0.03 , $P < 0.0001$) and were able to volitionally deactivate their PCC (percent signal change from baseline = -0.26 ± 0.01 , $P = 0.026$). These findings provide an unbiased confirmation that PCC activity corresponds to the subjective experience of meditation (Fig. 3B). While this is an important step forward, these results do not differentiate meditation from other (non-self-referential) cognitive tasks in inducing PCC deactivation.

With which cognitive processes does PCC activity correspond? Toward neurophenomenological studies

There are likely a number of different yet related cognitive processes that occur in any one moment. In the real-time neurofeedback studies described above, participants reported strong correspondence between subjective experience and PCC activity, but which specific processes might this region of

the brain be involved in? Might we be able to use such techniques to more closely home in on specific phenomenological invariants of experience that correspond to PCC activation and deactivation, as has been attempted in previous studies using other methods such as electroencephalography (EEG)?³⁵ To this end, we employed grounded theory methods to identify neurophenomenological invariants of subjective experience corresponding to PCC activity across individuals.³² Participants in the discovery protocol above provided short subjective reports of specific elements of their cognitive states corresponding with PCC activity after each real-time feedback run. In a data-driven manner, these reports were coded by content and grouped into thematic sets. For example, instances when participants reported focusing on the breath were coded and grouped into a bin labeled “concentration.” These sets were then lined up with corresponding PCC activity and secondarily grouped by activation versus deactivation to determine which cognitive processes corresponded with brain activity common across individuals. As one might hypothesize, we found that undistracted and distracted awareness corresponded with PCC deactivation and activation, respectively, across the sample of individuals. Additionally, other themes emerged, including effortless doing (PCC deactivation), contentment (PCC deactivation), and trying to control experience (PCC activation; Fig. 4). As grounded theory provides a framework for deriving

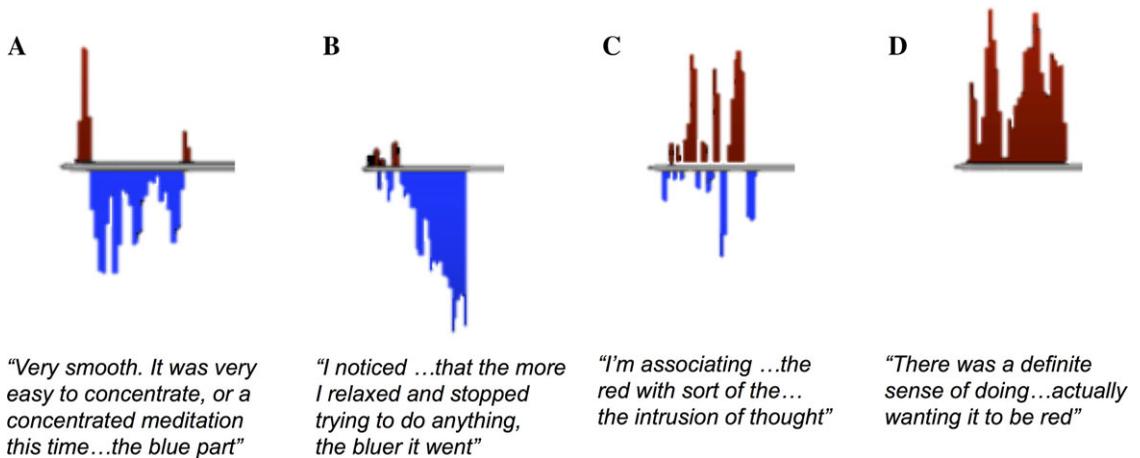


Figure 4. Examples of neurophenomenological invariants of subjective experience corresponding to PCC activity. PCC deactivation corresponded to (A) concentration and (B) effortless non-doing, whereas PCC activation corresponded to (C) distraction and (D) engaging with sensory experience. PCC activity was shown to meditators for 1-min blocks while they were meditating with eyes open. Increases in PCC activity relative to baseline are shown in red; decreases are shown in blue. Meditators reported on their experiences after each run. Adapted, with permission, from Garrison *et al.*³²

data-driven hypotheses, more than confirming that PCC activity relates to meditation or that concentration on an object deactivates the PCC, these data provide a springboard to generate specific experimental paradigms that carefully and deeply probe specific cognitive processes. For example, real-time neurofeedback experiments can be designed to precisely probe equanimity as it relates to PCC activity.

Can real-time neurofeedback help us learn?

Real-time fMRI neurofeedback is unique in allowing individuals to develop voluntary control over activity in specific brain regions that have previously been implicated in neural processes or disorders. Learning to control a brain response may contribute to learning to effectively mediate behavior.³⁶ Recently, deCharms *et al.* found that individuals using real-time neurofeedback learned to modulate activity in the rostral anterior cingulate cortex, with a concomitant change in pain perception.³⁷ Others have demonstrated proof-of-concept of targeted neurofeedback of brain regions implicated in emotion modulation,^{38,39} meta-cognitive awareness,⁴⁰ and speech processing,⁴¹ among others. However, current applications of real-time neurofeedback are limited by requiring individuals to learn to modulate their neural activity by trial and error; this can be time consuming and difficult to stan-

ardize. Similarly, current meditation instruction, while standardized over thousands of years, is typically provided by written and oral instruction augmented by instructor feedback; this can make it difficult for students to describe internal states, and for instructors to interpret students' descriptions. For example, the internal subjective experience of meditation cannot be corrected the way a yoga instructor can correct a student's posture. Might real-time neurofeedback be used to provide feedback for individuals learning to meditate?

In our real-time neurofeedback experiments described earlier, we observed some serendipity: in addition to reporting high correspondence between real-time neurofeedback from the PCC and the subjective experience of meditation, a few novices also reported learning several key premises of meditation practice after receiving real-time neurofeedback from the PCC during meditation. For example, one novice reported learning the difference between paying attention to the breath in a forced rather than a relaxed way (Fig. 5A). Another novice learned the difference between thinking about versus feeling the breath physically (Fig. 5B). In these cases, meditation with real-time neurofeedback from the PCC enabled novices to recognize and learn subtle differences in mental processes that are difficult to convey conceptually, and might otherwise hinder learning meditation, such as the difference between self-referential processes (thinking) and the

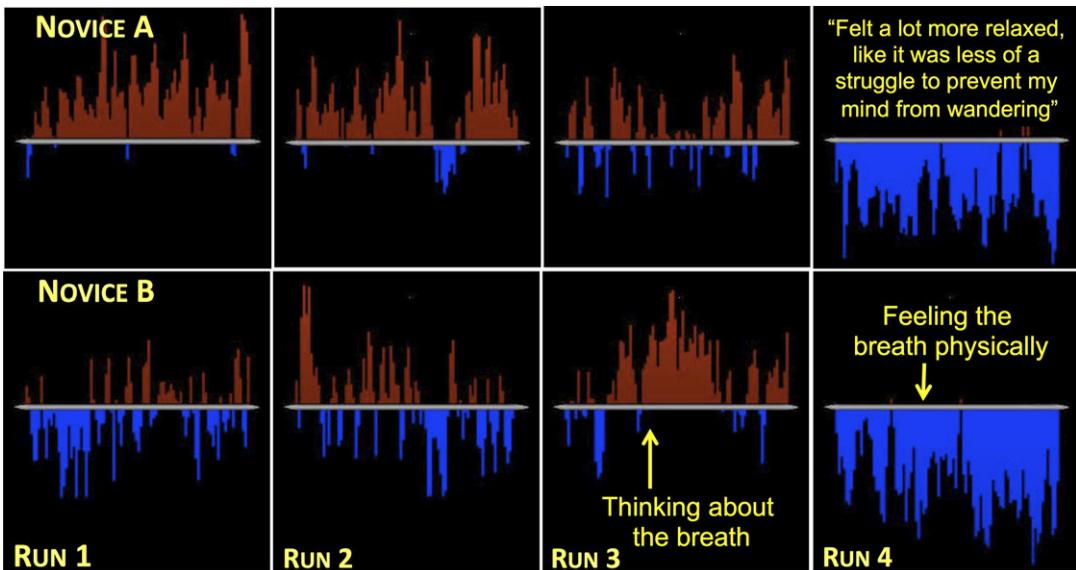


Figure 5. Novices show decreased PCC activity relative to baseline corresponding to learning nuances of meditation through real-time fMRI neurofeedback from the PCC. PCC activity was shown to participants for 3-min blocks while they were meditating with eyes open. Increases in PCC activity relative to baseline are shown in red; decreases are shown in blue. Individuals reported on their experiences after each run. Transcriptions from self-report: Novice A, 3rd run: It just looks like that it tracks exactly . . . I experienced definite blank spaces, mind wandering. 4th run: The run looks like what I exactly experienced feeling. Question from researcher: And what’s the difference between this run and the previous run? A: I felt a lot more relaxed this time. Q: Anything else? A: It felt like less of a struggle to prevent my mind from wandering. Novice B, 3rd run: I felt like that I was really concentrating on my breathing, but it looks like on the graph that I had a lot of wandering thoughts. 4th run: I was able to focus on my breathing, the physical sensation, and not thinking of breathing. But I felt like that I had [two] wandering thoughts. Q: Did you say that you weren’t thinking of breathing? A: Yeah, I was focused more on the physical sensation instead of thinking in and out.

embodied practice of meditation. Though much more research needs to be done to determine optimal brain regions and/or networks that provide accurate readouts of cognitive states that contribute to meditation (e.g., equanimity, attention), these findings suggest that real-time neurofeedback may be able to be used to augment meditation learning. Similar to a yoga instructor watching a student’s posture and giving suggestions about how to pose, neurofeedback may be used as a “mirror” to allow students to receive feedback on particular cognitive states as they practice. Of course this tool will not supplant teachings or teachers, but instead potentially help individuals practice more precisely. As the famous football coach Vince Lombardi once said, “practice doesn’t make perfect, perfect practice makes perfect.”

Conclusions, limitations, and future directions

Much has been learned in the past decade about the clinical efficacy of mindfulness training and its

underlying psychological and neurobiological processes. There is now clear evidence for its utility as a promising intervention for certain psychiatric conditions, such as depression, and growing evidence for others, such as anxiety and addiction, among others. Ancient and modern psychological models are converging, and importantly, specific components of psychological processes are indicating that perturbation therein affects behavior (e.g., mindfulness practice moderates the decoupling of craving and smoking¹¹). Though the field is relatively young with regard to underlying neurobiology, particular brain networks and regions such as the DMN and PCC are emerging as prime candidates for further exploration. New methodologies such as real-time fMRI neurofeedback are helping to home in on particular cognitive processes that these brain networks and regions may be involved in, and also provide the tools for fledgling research programs such as neurophenomenology. Though we focused on the DMN in this paper, other regions such as the insula are also likely critical

players in how networks are both affected in psychological and other disease processes and can change as a result of mindfulness practice.^{42,43} Also, it will be important to compare and contrast other cognitive trainings that affect the associative learning process, such as systematic desensitization, to see if these trainings affect overlapping brain networks with mindfulness training. Furthermore, and more importantly, demonstrating that mindfulness links with PCC activity is only a first step in examining outcomes. Now that we may be able to track meditative states, future studies showing that training these states (and associated changes in DMN activity) translates to changes in neuropsychological function and behavioral outcomes are critical. For example, though PCC deactivation has been linked to improved informational processing in experienced meditators,³¹ does neurofeedback of the PCC augment attention training in novices above and beyond already established mindfulness-based stress reduction programs? Given the emerging armamentarium of tools to track and potentially augment training in cognitive therapies such as mindfulness, the field is well positioned to perform the necessary studies to determine exactly how training in these behaviors (and even training specific brain states, such as systematic deactivation of the PCC) affects meaningful outcomes such as psychological well-being and stress.

Conflicts of interest

The authors declare no conflicts of interest.

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