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ORIGINAL PAPER

Using fNIRS to Examine Neural Mechanisms of Change Associated with Mindfulness-Based Interventions for Stress and Trauma: Results of a Pilot Study for Women

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Abstract

Objectives This research aimed to examine the mechanisms of change associated with mindfulness-based interventions (MBI) and test the feasibility of using functional near-infrared spectroscopy (fNIRS) to objectively measure MBI-responsive neuro-cognitive functions impaired by stress and trauma: attentional control (AC), emotional regulation (ER), and working memory (WM).

Methods fNIRS data were collected from 31 female participants during AC, ER, and WM cognitive tasks. Measurements were conducted at baseline and follow-up. Half of participants ($n = 16$) engaged in a 6-week MBI, whereas the active control group ($n = 15$) did not. fNIRS measures blood oxygenation (HbO) and deoxygenation (HbR) in specific brain regions as changes in activation of neural networks.

Results After using general linear modeling to isolate the hemodynamic response in the fNIRS data, group-level statistical analyses revealed significant ($p \leq .05$) changes among the MBI group for AC tasks in the frontopolar area (FP), orbitofrontal cortex (OFC), and premotor cortex (PMC); these changes were accompanied by significant improvements in AC performances. Among the control group, there was a significant decline in AC task performance and significant decreased OFC activation. Among the MBI group, there were also significant changes in FP and OFC activation during ER tasks and significant changes in OFC and PMC activation during WM tasks. Performance changes for ER and WM tasks were mixed.

Conclusions fNIRS is a viable means of measuring MBI-related changes in neuro-cognitive activity and MBIs yield significant changes in attentional performance and activation of FP, OFC, and PMC.

Keywords Attention · Cognition · Emotional regulation · fNIRS · Mindfulness · Stress · Trauma · Working memory

Chronic stress and traumatic stress, also known as post-traumatic stress disorder (PTSD), are characterized by psychosomatic symptoms that negatively impact subjective well-being (Creamer et al., 2001), physical health, and aspects of cognitive functioning (Moores et al., 2008; Tang et al., 2015). Compared to healthy populations, individuals impacted by traumatic stress are more likely to exhibit cognitive impairments in attentional control (AC), working memory (WM) (Uddo et al., 1993), and emotional regulation (ER) (Aupperle et al., 2012) particularly when emotionally salient stimuli are involved (Brandes et al., 2002; Morey et al., 2009; Schweizer & Dalgleish, 2011; Vasterling et al., 1998). Such stimuli can result in startle response in people with PTSD; this behavioral hyper-responsiveness is understood to be related to hyperactive alerting of the premotor cortex and attentional networks (Naegeli et al., 2018). Despite recent gains in knowledge regarding the associations between stress, trauma, and cognitive performance, the neurophysiological mechanisms underlying these deficits remain widely unknown (Brandes et al., 2002; Chiesa et al., 2011).

One intervention strategy that may help identify and support the complex associations between cognition, stress,

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and trauma is mindfulness. Mindfulness-based interventions (MBIs) are increasingly recognized as effective treatments for impaired cognitive functioning associated with chronic and traumatic stress. Researchers have demonstrated that MBIs can ameliorate stress and traumatic stress through neurological changes that reduce the physiological stress response and reorganize synaptic connections (Bergen-Cico et al., 2014; Possemato et al., 2016; Tang et al., 2010). Specifically, these neurological changes are associated with increased cognitive functions through improved AC and ER (Jha et al., 2007; Lutz et al., 2014), and WM (Jha et al., 2017; Zeidan et al., 2010) and decreased PTSD symptoms such as the startle response and impaired working memory. Despite the expansion of research on MBIs for treating stress and traumatic stress, the mechanisms of change in stress-related neuro-cognitive processes are not well understood.

Attentional control (AC) enables people to disengage from aversive emotionally generative stimuli through directed attention and skillful regulation of emotions (Goldin et al., 2008; Lutz et al., 2008). Stress and trauma impair AC through the dysregulation of the coupling between the task-positive network (TPN; endogenous attention) and the default mode network/task-negative network (TNN; exogenous attention) (King et al., 2016; Miller et al., 2017; Tang et al., 2015). One mechanism by which MBIs are believed to reduce stress is by improving one's ability to volitionally regulate attention through increased engagement of the TPN (Brewer et al., 2011; Jha et al., 2015; Simon & Engström, 2015; Tang et al., 2015). The TPN is a hub for executive function and attentional networks recruited for attentional control, and research using fMRI has documented increased TPN activation in response to MBIs (Fransson, 2005; Hasenkamp et al., 2012). Thus, measurement of neural networks associated with AC may provide objective indicators of TPN related cognitive and neural changes supported by MBIs (Alfonso et al., 2011; Petersen & Posner, 2012).

Research has shown that MBIs enhance performance on AC and these improvements are correlated with greater activation in brain regions known to be impacted by stress and traumatic stress (Ehring & Quack, 2010; Etkin & Wager, 2007; Hölzel et al., 2007; Jack et al., 2013; Schutt et al., 2015; Shin, 2006; Tang et al, 2007; Zeidan et al., 2010). However, improvements in AC have primarily been demonstrated among long-term meditators and thus, the benefits of mindfulness-based practices among novice meditators are not well studied or understood. Moreover, research conducted with experienced meditators has been confounded by varying degrees of expertise and the heterogeneity of meditation practices among research subjects (see Brewer et al., 2011; Gundel et al., 2018). Thus, research on novice meditators engaged in the same uniform type of practice may enable researchers to gain insight and better understand the mechanisms of change associated with MBIs. Indeed, there is a growing body of research that suggests that even short-term mindfulness meditation practice may help improve the neurophysiological stress response (Bergen-Cico et al, 2014), psychological well-being (Possemato et al., 2016), and executive attention (Tang et al., 2007), with benefits to WM being expressed with continued mindfulness practice (Alfonso et al., 2011).

Neuroimaging techniques have been applied within the field of mindfulness research to help identify the neurological correlates and cognitive processes associated with mindfulness practices. For example, research using fMRI has demonstrated mindfulness practice increases performance on attentional tasks (Tang et al., 2007), response inhibition (Jack et al., 2013), and WM tasks (Mrazek et al., 2013; van Vugt and Jha 2011). Although fMRI represents the gold standard for functional brain measurement, the invasive nature, need to limit subject movement, and high costs are significant barriers to the use of fMRI to study MBI phenomena. Thus, more practical, low-cost, and unobtrusive methods are needed.

One potential solution is fNIRS, a non-invasive means of measuring and monitoring hemodynamic concentration changes in oxygenated (HbO) and deoxygenated (HbR) hemoglobin as an indicator of brain region activation. Yet, few studies have been conducted using fNIRS to measure changes in targeted functional brain regions to examine mechanisms of change in the brain among novice meditators, specifically in relation to stress and trauma. Moreover, the few studies using fNIRS to measure brain differences among meditators (Gundel et al., 2018) or people with PTSD (Tian et al., 2013) are cross-sectional rather than longitudinal and do not provide insight into the processes of change associated with MBI practice.

The non-invasive fNIRS device can provide spatially accurate brain activity information similar to the fMRI (about 2–3 cm lower than that achieved by fMRI resolution), and it can do so in ecologically valid experimental environments that are less restrictive than fMRI (Hirshfield et al., 2011; Irani et al., 2007; Liu et al., 2015; Pinti et al., 2020). Given that individuals with traumatic stress/PTSD may be particularly sensitive to the constrictive and loud fMRI magnet or be physically unable to enter the device due to shrapnel wounds or surgical implants, the portable and relatively comfortable fNIRS device is an ideal candidate for measuring brain function in this population (Matsuo et al., 2003). The basis of fNIRS is the use of near-infrared light, which penetrates through the scalp and skull to reach the brain cortex. Emitter and detector optodes are placed on the surface of the head; the former pulses light into the brain tissue while the latter measures the light that is reflected back out of the cortex, resulting in measurements of the change in oxygenated (HbO) and deoxygenated (HbR) hemoglobin (Chance et al., 1993; Hirshfield et al., 2011;

Irani et al., 2007). The fNIRS has higher spatial resolution than EEG, making it possible to localize specific functional brain regions of activation, as could be done with the more restrictive fMRI (Pfurtscheller et al., 2007). One significant limitation of fNIRS is that, unlike fMRI, it is unable to measure deep brain structures (i.e., amygdala), which can be particularly important in the measurement of raw emotions associated with stress and trauma. Fortunately, the prefrontal cortex is filled with rich information relating to regulation of emotion and attentional control, making fNIRS a viable source of neural data related to cognitive tasks (Hirshfield et al., 2011; Izzetoglu et al., 2004).

There are three specific neural regions of interest (ROIs) in the prefrontal cortex (PFC) which are known to be responsive to MBIs and are also indicated in stress-related cognitive impairment of AC, ER, and WM; these are the frontopolar cortex area (FP) (Brodmann area (BA) 10), orbital frontal cortex (OFC) (BA 11), and premotor cortex (PMC) (BA 6) (see Arnsten, 2009). The PMC plays an integral role in the stress response and is involved in somatosensory input, sensing of peri-personal space, and planning and organizing movements and actions such as preparing to respond to threatening situations. People with PTSD have some noted PMC abnormalities such as decreased volume in the PMC (Rocha-Rego et al., 2012) and increased activation of the PMC in response to stimuli (Naegeli et al., 2018).

The FP and OFC of people with traumatic stress/PTSD are believed to be negatively impacted as evidenced by abnormal activation and decreased inhibitory control, emotional processing, working memory, and executive functioning (Shaw et al., 2002, 2009). Decreased inhibitory control involving the FP and OFC can be measured through response inhibition tasks (e.g., Go/No Go task) and poor response inhibition is correlated with higher levels of PTSD (Swick et al., 2012; Uddo et al., 1993; Wilkins et al., 2011). Moreover, MBIs have been shown to increase performance on response inhibition tasks (Alfonso et al., 2011; Tang et al., 2007) and modulate negative emotional responses through cognitive reappraisal (Doi, et al., 2013; Garland, et al., 2009).

The use of fNIRS has been shown to be a useful modality for measuring the cortical regions implicated in traumatic stress (Etkin & Wager, 2007; Matsuo et al., 2003), and has been used in the past to indirectly measure neural activation in people with traumatic stress/PTSD (Matsuo et al., 2003; Tian et al., 2014). fNIRS has been used to measure attention (Harrivel et al., 2016) and increases in hemodynamic blood flow in the prefrontal cortex (PFC) in relation to mindfulness practices (Deepeshwar et al., 2015; Gundel et al., 2018) and associations between mindfulness meditation and cortical activation patterns associated with emotions and emotional regulation (Gundel et al., 2018), thus suggesting that fNIRS may be a viable means of measuring ER in mindfulness research.

Despite the potential benefits, there are few published studies that have used fNIRS to measure MBI outcomes and to date no fNIRS studies have combined longitudinal outcomes from MBIs on neurocognitive changes associated with stress and trauma. Thus, the goal of the present study was to better understand these mechanisms of change by taking pre and post fNIRS measurements of a treatment (vs. control) group of novice meditators that took part in an MBI. A key exploratory aim of the present study was to determine if fNIRS is an effective non-invasive means of measuring cognitive changes associated with MBIs. Based on the extant literature noted above, we developed the following hypotheses pertaining to attention, emotional regulation, working memory, stress, and traumatic stress.

Our first hypothesis (H1) states that following the MBI, participants in the intervention group would demonstrate significant improvements from baseline in AC as evidenced by AC task performance and fNIRS data associated with changes in activation and cognitive load in regions of the brain associated with directed attention. In hypothesis two (H2), we hypothesize that following the MBI, participants in the intervention group would demonstrate significant improvements in ER as evidenced by ER task performance and fNIRS data associated with changes in activation and cognitive load in regions of the brain associated with ER. In hypothesis three (H3), we hypothesize that following the MBI, participants in the intervention group would demonstrate significant improvements from baseline in the amount of cognitive workload devoted to cognitively demanding WM tasks, as evidenced by WM task performance and fNIRS data–associated WM regions of the brain. In addition to the three main hypotheses pertaining to cognitive resources, our fourth hypothesis (H4) states that participants in the MBI group would have significantly decreased scores in perceived stress (measured by the Perceived Stress Scale) and posttraumatic stress symptoms (measured by the PCL-C) following the MBI.

Methods

Participants

Thirty-one female participants completed baseline and 6-week follow-up data collection. Sixteen participants (age $M = 23$ SD = 5) were assigned to the mindfulness-based intervention group (novice mediators), while the remaining 15 participants (age $M = 21.5$ SD = 3.7) were in the control health education group. All participants were voluntary and were recruited from two health elective courses open to all university students. Group assignment was based on

which course section students had registered for whereby one course included an MBI and one course did not. Recruitment for the study was advertised as a study of college student stress and trauma; only female students volunteered for study participation and thus all research subjects were female. All study procedures were approved by Syracuse University's Institutional Review Board and participants completed written informed consent. The intervention and all data collection were conducted from January 2019 through March 2019.

Procedures

To test our hypotheses, individuals completed a series of cognitive tasks that engaged cognitive resources impacted by stress and traumatic stress to evaluate potential changes related to mindfulness-based intervention, as measured over time. Measures of how well each participant performed, as well as each participant's changes in blood flow (Δ HbO and Δ HbR) in specific brain regions while performing the specified tasks, were captured and analyzed using high-density fNIRS. Due to there being varied research protocols as well as operationalizations of the cognitive resources being studied within the mindfulness meditation literature (Chiesa et al., 2011), it was important that the tasks utilized in this study satisfy three basic criteria. First, the cognitive tasks must elicit a response that utilizes a cognitive resource demonstrated to be impaired by stress and traumatic stress. Second, the neural correlates of the cognitive resource(s) that have been demonstrated to be impaired by stress and traumatic stress must be shown to be measurable utilizing fNIRS. Third, the cognitive resource(s) elicited by the task must have evidence that they are able to show improvement through MBIs. These three criteria were the basis of our research methodology and design and are examined in detail in the "Methods" section.

The longitudinal experimental design is depicted in Fig. 1. First, in the baseline pre-session, all participants completed a battery of self-report psychometric measures using a secure online data collection portal (REDCap). Next, participants engaged in a series of cognitive tasks at a university laboratory, where they were equipped with an fNIRS device while they completed six cognitive computer tasks designed to tax their attention, ER, and WM resources. After the baseline assessments, participants in the intervention group engaged in a 6-week MBI. The control group engaged only in didactic health education content and refrained from participating in meditation, mindfulness programs, and yoga.

After 6 weeks, both groups completed the same self-report psychometric measures and returned to the laboratory for follow-up post-assessment measures, which consisted of the same set of cognitive tasks and protocols as had been completed during the pre-session while wearing fNIRS equipment. The following sections go into further detail on the components shown in Fig. 1, detailing the participant composition, the psychometric measures, the cognitive task battery and stimulus presentation, as well as details about the set-up of the fNIRS apparatus.

The MBI intervention consisted of a validated and abbreviated version of the 8-week MBSR curriculum (see Kabatt-Zinn, 1990) using a brief mindfulness-based program consisting of 6 × 1-h weekly facilitator-led sessions (6 total contact hours) modeled after brief MBI programs that had demonstrated efficacy with non-clinical and clinical populations Detailed information on evidence-based brief mindfulness programs and the curriculum used in this study can be found in published research (Bergen-Cico et al., 2013, 2014; Possemato et al., 2016). The 1-h weekly MBI

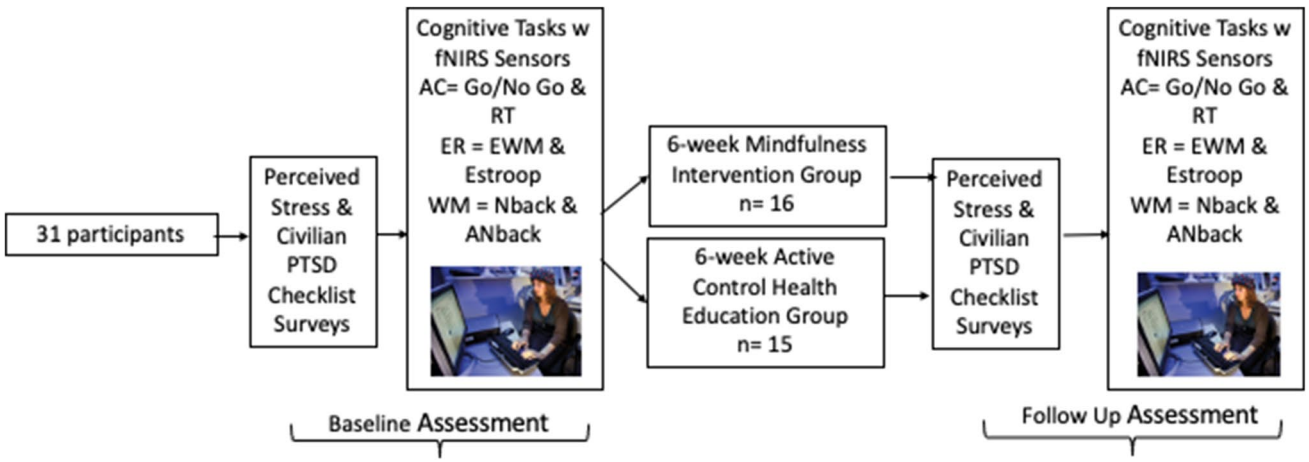

Fig. 1 Overview of experimental paradigm. Key: AC, attentional control; ANback, Audio N-back task; ER, emotional regulation; Estroop, emotional Stroop test; EWM, emotional working memory; fNIRS, functional near-infrared spectroscopy; Nback, N-back task; RT, reaction time task; WM, working memory

program consisted of group practice with all MBI participants engaged in 20 min of mindfulness meditation, 20 min of body scan practice, and 20 min of mindful yoga led by a certified MBSR facilitator. The sessions were rated and assessed by an external independent evaluator for adherence to the principles of mindfulness practice and to core MBSR practices of meditation focused on awareness of breathing, the body scan, and mindful yoga.

Measures

Self-report ratings

Participants completed the Perceived Stress Scale (PSS) and the PTSD Checklist-Civilian version (PCL-C). These self-report measures are associated with the aims of this research and are commonly used in research on examining stress and traumatic stress specifically in relation to mindfulness-based interventions. Traumatic stress was measured with the PTSD Checklist-Civilian Version (PCL-C), a 17-item questionnaire in which civilian respondents rate the degree to which they have been bothered by DSM-IV posttraumatic stress symptoms in the past month using a 5-point Likert scale from 1 (not at all) to 5 (extremely) (Wilkins et al., 2011). The DSM-IV PTSD symptoms are grouped into three symptom clusters of re-experiencing, numbing/avoidance, and hyper-arousal. The PCL-C is used to monitor symptom change and screen individuals for PTSD (Norris & Hamblen, 2004). Scores on the PCL-C range from 17 to 85. Internal consistency of the PCL-C was high for this study, with Cronbach's alpha of 0.92.

Perceived stress was measured using the PSS (Cohen et al., 1983), which is a psychometrically validated measure of the degree to which situations in one's life are appraised as stressful. The PSS is a 10-item scale designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives to be in the past month. Internal consistency of the PSS for this study was good, with Cronbach's alpha of 0.79.

Cognitive tasks

The cognitive tasks designed to measure potential changes related to stress, traumatic stress, and mindfulness were clustered into three measures of cognitive functions: (a) attentional control (AC) measured by Go/No-Go and reaction time taks, (b) emotional regulation (ER) measured by emotional delayed recall task (emotional working memory EWM) and the emotional Stroop test (eStroop), and (c) working memory (WM) was measured by the Auditory N-back and N-back. It is important to note that these classical benchmark tasks are proxies for the cognitive function being examined. They were selected because they have consistently been used to manipulate the target cognitive constructs of attention, working memory, and emotion regulation. For more information on psychological benchmark tasks in the cognitive psychology domain and their targeted functions, please see Kaplan and Saccuzzo (2010).

Prior to each testing session, participants were given practice trials to ensure that they understood how to complete the tasks accurately. The instructions were also displayed on the screen before the start of each task to ensure participants knew which task they were about to begin and to remind them of the protocol. Each participant's response to the stimulus application (correct or incorrect) as well as their response time (in milliseconds) was logged by the application and exported after task completion. More specifically, performance on the cognitive tasks was calculated by scoring each participant's individual task and dividing the number of correct responses by the total number of trials of the task. The experimental materials were developed using the PsychoPy toolkit, an open-source psychological stimulus presentation software sponsored by the University of Nottingham (Peirce et al., 2019).

Research indicates that individuals with high levels of stress experience decreased inhibitory control and attention; therefore, the reaction time task and Go/No-go task were selected as cognitive measures for attentional control (Herrmann et al., 2005; Shucard et al., 2008). The reaction time task displayed a fixation point in the center of the screen at the start of each trial. After a variable period of time for each trial (min = 300 ms, mean = 500 ms, max = 700 ms) a large "X" stimulus replaced the fixation point in the center of the screen. The participant's task was to respond as quickly as possible by pressing the correct key on the keyboard when the fixation point was replaced with the stimulus. The reaction time test yields a time response score. As noted previously, individuals with PTSD often show decreased response inhibition (Uddo et al., 1993) and the Go/No-Go task measures response inhibition as outlined in the protocol of Herrmann et al. (2005) that served as the model for our present study. The task included a red rectangle target stimulus that appeared in the center of the screen and a blue oval distractor stimulus. Participants were tasked with responding as quickly as possible when they were presented with the target stimulus, and with not responding when they were presented with the distractor stimulus. The stimulus appeared on screen for a variable amount of time (1 to 2 s); a variable interstimulus interval was presented between trials, during which a cross fixation point was displayed on the screen before the subsequent test began.

The emotion regulation tasks included the emotional delayed recall task (EWM) and the emotional Stroop test (EST). The emotional delayed recall task is a working memory task validated for individuals with PTS (Schweizer & Dalgleish, 2011). The task followed the basic structure of a

delayed recall task where participants were presented with an array of six letters and asked to memorize the letters in the array. During the delay periods, an image was displayed that was either intended to be neutral and produce no arousal, or an image intended to elicit high negative valence. Participants were then prompted to respond if a certain letter had appeared in the array. Each participant was presented with a combination of emotionally charged and neutral images during the task. Scores were generated both for performance (did the participant correctly remember the letter's presence in the previous array) as well as reaction time. To highlight the emotional effects of the task, correct responses to high valence delay images were weighted by a factor of 1.10 when compared to their non-valence counterparts.

The EST is a variant on the original Stroop task in which a participant is tasked to respond with the color a word is presented in, rather than reading aloud the color the word spells. The EST differs from this original paradigm in the types of words that are presented to the participant. Some of the words presented are valence neutral, such as "pencil," "walk," or "fruit," while other words are associated with high valence or physical threat, such as "weapon" or "fight." Research has shown that there is a significant difference in response times when responding to high valence or threatening words when compared to valence neutral words among individuals with PTS (Cisler et al., 2011). Words were presented to the participant in the colors red, yellow, green, and blue. Participants were instructed to press the key on the keyboard corresponding to the first letter of the color, such as the "y" key for yellow. Similarly, to the emotional delayed recall task, both reaction times and performance measures were obtained from the EST with a similar weight for correct responses on high valence words of 1.10.

We used visual and auditory variation of the well-validated N-back working memory tasks to engage participants' working memory resources. For a detailed description of the standard N-back, see Owen et al. (2005). We included audio N-back (ANB) and N-back tasks; the ANB followed the same protocol of the N-back but used audio rather than visual cues for memory and recall. The audio N-back tasks were created using stimulus materials that were not emotionally salient in an effort to avoid confounding, emotionally laden stimulus materials that have been reported to affect individuals diagnosed with PTSD and other anxiety disorders (Schweizer & Dalgleish, 2011). The ANB task involved participants holding a stream of continually adapting letter values (*b*, *t*, *q*, *v*) in their working memory while simultaneously attempting to recall whether or not a given letter was displayed two presentations prior.

When a participant came in for a pre-assessment or post-assessment, they completed the six tasks in the cognitive task battery; the order of which was determined by the PsychoPy stimulus presentation software. Specifically, as depicted in Fig. 2, each participant ran through the six tasks from the cognitive task battery as previously outlined, where the tasks were presented to participants using a randomized block design format. Figure 2 presents an example of an ordering of the tasks a participant may have received in the baseline (pre) or follow-up (post) assessment, consisting of a randomized block design with two blocks in each test session. The total experiment consisted of two blocks, so that each cognitive task was experienced two times. Each task ran equal to or greater than 60 s and the first 60 s of each task were selected for comparison. Participants rested for 30 s between tasks to allow their brains to return to a baseline state.

fNIRS data were collected using the Hitachi ETG-4000 near-infrared spectroscopy device with a sampling rate of 10 Hz. As shown in Fig. 3, we used a 3×11 probe to cover the frontal cortex region, resulting in 52 channels of data. In order to ensure that the positioning of the optode array remained consistent across all participants, the central channel measurement from the array was positioned directly over each participant's nasion, with the middle bottom probe being placed directly on the Fpz location, to align with the international 10–20 measurement system and to enable us to leverage Tsuzuki's (2006) spatial registration technique for the ETG-4000 3×11 probe. See Tsuzuki et al. (2007)

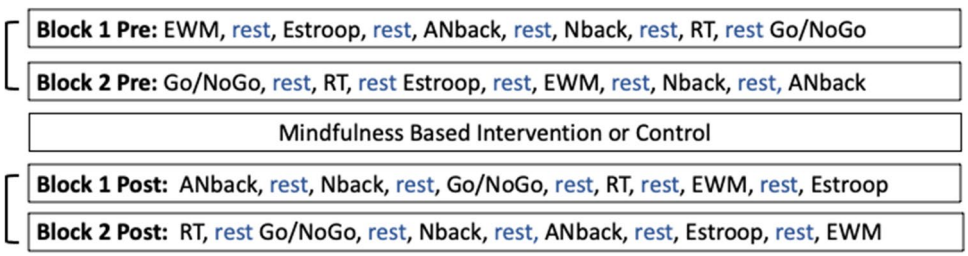

Fig. 2 Cognitive task design: This is an example of the random ordering of cognitive tasks that participants would be presented with during the pre- and post-test. Each pre and post phase of assessments consisted of two blocks with two randomized block designs during each test session. ANback, Audio N-back; ER, emotional regulation; Estroop, emotional Stroop; EWM, emotional working memory; Nback, N-back task; rest, controlled rest in between cognitive tasks; RT, reaction time; WM, working memory

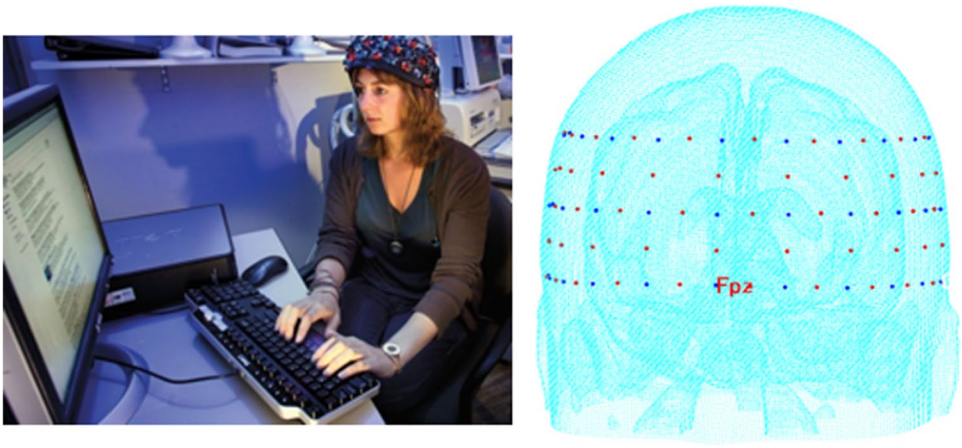

Fig. 3 On the left: the fNIRS device in this study was the Hitachi ETG4000, with the 3 × 11 probe configuration. On the right: spatial registration of the probe on participants' heads was conducted using Tsuzuki's virtual registration (Tsuzuki et al., 2007). All source detector pairings are 3 cm apart in the Hitachi probe configurations

for detailed information on the process used to conduct spatial registration of our fNIRS optodes and channels. Both head size information and 3D-digitized data were collected from the participant using a Polhemus 3D-digitizer, at this time to ensure the probe placements were consistent across participants.

Data Analyses

fNIRS data collection included 52 channels of data collected with Hitachi Medical ETG-4000. The raw fNIRS data was first run through general preprocessing steps provided by the NIRX-toolbox (Santosa et al., 2018). The data was resampled to a rate of 4 Hz, converted to optical density values, and then estimated oxygenated and deoxygenated hemoglobin values were obtained via the use of the modified Beer-Lambert law. After the raw light intensity value output by the device had been converted to Oxy and deOxy hemoglobin, the data was fit to the GLM using the autoregressive model (AR(P)-IRLS) that is used by default in the toolbox. The basis for the model was the standard canonical hemodynamic response which the toolbox also provides (Barker et al., 2013). After fitting to the GLM, a mixed effects model was then generated with individual subjects treated as random effects, and groups (treatment versus control) and conditions (tasks) treated as fixed effects. Next, we condense our channel-wise data into ROIs, where we average across the channel betas for the channels within each ROI. By using the Tsuzuki virtual spatial registration (Tsuzuki, 2007) for the Hitachi 3 × 11 probe, we are able to map our 52 channels of data into MNI space, allowing us to then average our data across three ROIs for analysis, consisting of FP, OFC, and PMC. We then compute group-level statistics by computing paired *t*-tests on the outcome of this mixed effects model, after averaging their values based on the relevant fNIRS data channels that spatially overlapped with those regions. Due to concerns with multiple comparison issues, the fNIRS data results are reported using *q* values, as these values are more conservative adjusted *p*-values which minimize false discovery rates (Lai, 2017). Our analysis produced both *p* and *q* values. Due to concerns with multiple comparison issues, the fNIRS data results are reported using *q* values, as these values are more conservative adjusted *p*-values which minimize false discovery rates (Lai, 2017).

We analyzed and report both ΔHBO and ΔHbR because both provide valuable information about brain activation, especially in contexts when our probe does not cover the entire brain cortex. In general, brain activation in a region is tied to increasing HbO and simultaneously decreasing Hb (Lachert et al., 2017). However, it is worth nothing that HbO and Hb do not *always* co-vary together temporally (Tam & Zouridakis, 2014).

Results

Baseline Comparison Between Intervention and Control Groups

There were no significant differences ($p = 0.39$) in age between the two groups. Differences between the two groups at baseline were explored using independent sample *t*-tests to check for differences in psychometric measures (PCL and PSS) and fNIRS data by brain regions during tasks and we found no significant differences ($p > 0.05$) between groups. Thus, the two groups are considered comparable at baseline.

Within Group Changes in Stress and Traumatic Stress over Time

We conducted within group paired sample *t*-test to assess changes in perceived stress and civilian PTSD symptom scores over time, and the results of the psychometric measures for stress and traumatic stress are presented in Table 1. Although there were no statistically significant changes at the $p \leq 0.05$ level in either group for psychometric measures

from baseline to follow-up assessment, there were clear trends toward improvement for the intervention group but not for the control group. Specifically, participants in the MBI group reported a 2.5 (5.2) point decrease in perceived stress and a 5.7 (12.9) point decrease in PCL scores; during the same time, the control group's perceived stress increased 2.5 (7.3) points and their PCL scores increased 1.2 (9.2) points.

fNIRS and Cognitive Task Performance

We analyze both ΔHbO and ΔHbR fNIRS data and present results in Tables 2, 3, 4. These values do not always covary together and increased HbO values indicate an increase in cortical activation in the specified brain region, whereas increased HbR values indicate reduced cortical activation in the specified region.

Attentional Control

As described previously, we ran group-level statistical analyses for the mindfulness intervention and control groups to measure each group's changes over time in the fNIRS data associated with FP, OFC, and PMC regions while participants engaged in the cognitive tasks that measure the respective cognitive resources. The results of the within-group GLM with fNIRS data measuring

Table 1 Within group paired sample *t*-test changes in psychometric measures

	Intervention ($n=16$)				Control ($n=15$)			
	Pre mean (SD)	Post mean (SD)	*t*	*p* value	Pre mean (SD)	Post mean (SD)	*t*	*p* value
Perceived stress	31.6 (6)	29 (5)	−1.6	.14	28.3 (5)	30.8 (6)	1.2	.26
Traumatic stress PCL	39.7 (15)	34 (10)	−1.4	.17	31.7 (9)	32.8 (11)	.44	.67

Table 2 Brain region activation changes in oxygenated (HbO) and deoxygenated (HbR) hemoglobin for attention tasks using GLM longitudinal outcomes within group by condition

	Intervention ($n=16$)				Control ($n=15$)			
Brain region	Beta	SE	*t*	*q*	Beta	SE	*t*	*q*
FP HbO	19.83	7.39	2.68	**0.02**	4.00	7.64	0.52	0.69
FP HbR	15.19	3.30	4.61	**< 0.00**	−2.07	3.11	−0.67	0.61
OFC HbO	74.28	18.90	3.93	**< 0.00**	−8.63	18.94	−0.46	0.70
OFC HbR	27.92	7.18	3.89	**< 0.00**	28.80	6.06	4.76	**< 0.00**
PMC HbO	−39.35	13.06	−3.01	**0.01**	27.34	14.12	1.94	0.12
PMC HbR	34.54	6.31	5.47	**< 0.00**	−11.36	5.29	−2.15	0.08

GLM, within group general linear modeling; *FP*, frontopolar; *OFC*, orbitofrontal cortex; *PMC*, premotor cortex; *HbO*, oxygenated hemoglobin; *HbR*, deoxygenated hemoglobin

Table 3 Brain region activation changes in oxygenated (HbO) and deoxygenated (HbR) hemoglobin for emotional regulation tasks using GLM longitudinal outcomes within group by condition

	Intervention ($n=16$)				Control ($n=15$)			
Brain region	Beta	SE	*t*	*q*	Beta	SE	*t*	*q*
FP HbO	18.76	7.36	2.55	**0.04**	6.66	7.54	0.88	0.51
FP HbR	4.90	3.30	1.48	0.25	1.85	3.13	0.59	0.65
OFC HbO	−43.24	18.83	−2.30	0.06	28.67	18.82	1.52	0.24
OFC HbR	33.35	7.19	4.64	**< 0.00**	1.63	6.28	0.26	0.82
PMC HbO	17.88	13.04	1.37	0.29	6.57	14.05	0.47	0.70
PMC HbR	−4.59	6.30	−0.73	0.60	5.41	5.26	1.03	0.45

GLM, within group general linear modeling; *FP*, frontopolar; *OFC*, orbitofrontal cortex; *PMC*, premotor cortex; *STG*, superior temporal gyrus; *HbO*, oxygenated hemoglobin; *HbR*, deoxygenated hemoglobin

Table 4 Brain region activation changes in oxygenated (HbO) and deoxygenated (HbR) hemoglobin for working memory tasks using GLM longitudinal outcomes within group by condition

	Intervention ($n=16$)				Control ($n=15$)			
Brain region	Beta	SE	t	q	Beta	SE	t	q
FP HbO	−15.05	7.51	−2.00	0.11	13.65	7.62	1.79	0.15
FP HbR	−4.48	3.40	−1.32	0.31	−0.74	3.12	−0.24	0.83
OFC HbO	37.01	19.21	1.93	0.12	−14.53	13.88	−1.05	0.45
OFC HbR	−26.47	7.43	−3.56	**<0.00**	−6.53	6.29	−1.04	0.45
PMC HbO	16.43	13.38	1.23	0.36	−7.16	19.25	−0.37	0.74
PMC HbR	−21.55	6.51	−3.31	**<0.00**	11.44	5.21	2.19	0.08

GLM, within group general linear modeling; *FP*, frontopolar; *OFC*, orbitofrontal cortex; *PMC*, premotor cortex; *HbO*, oxygenated hemoglobin; *HbR*, deoxygenated hemoglobin

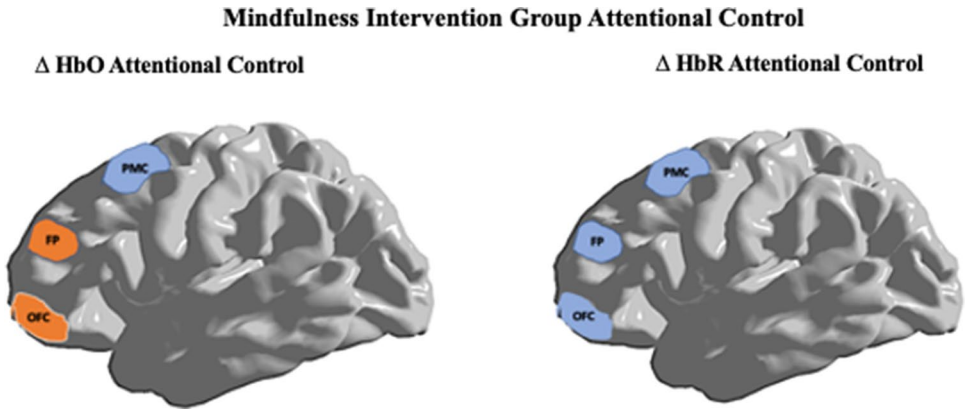

Fig. 4 Significant ΔHbO and ΔHbR changes in brain region during attentional control tasks for Mindfulness group. FP, frontopolar area; OFC, orbitofrontal cortex; PMC, premotor cortex; orange, increased oxyhemoglobin; blue, decreased oxyhemoglobin

attention are presented by group in Table 2, with Fig. 4 summarizing the statistical results of changes in the brain. There were significant changes for the MBI group for the fNIRS data associated with attention tasks in three brain regions with significantly increased activation in the FP area, ΔHbO ($t=2.68$; $q=0.02$) that was also accompanied by a significant decrease in ΔHbR ($t=4.6$; $q\leq0.001$). Similar findings were evident for the OFC with a significant increase in activation indicated by ΔHbO ($t=3.93$; $q\leq0.001$) accompanied by a significant decrease in ΔHbR ($t=3.89$; $q\leq0.001$) values. There was also a significant decrease in PMC activation as noted by ΔHbO ($t=-3.01$; $q=0.01$) and ΔHbR ($t=5.47$; $q\leq0.001$). Figure 4 presents the significant changes for the mindfulness intervention group for both HbO and HbR during AC tasks. The only significant change for the control group during the AC tasks was a decline in activation of the OFC as noted by ΔHbR ($t=4.76$; $q\leq0.01$); the significant control group findings are presented in Fig. 5. Note that increased t values for ΔHbO indicate cortical activation whereas increased t-values for ΔHbR indicate decreased activation. There were no significant changes in the AC task accuracy performance for either group. However, the MBI group demonstrated significant improvements in both the Go/No

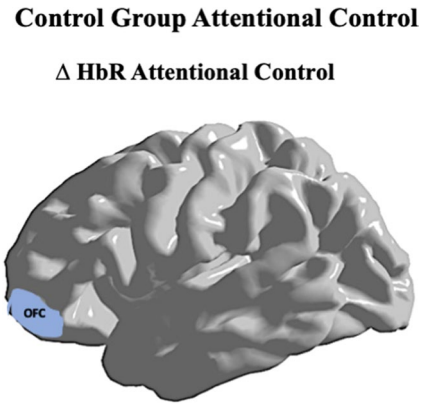

Fig. 5 Significant ΔHbR changes in brain region during attentional regulation tasks for control group. OFC, orbitofrontal cortex; blue, decreased oxyhemoglobin

Go ($t=2.12$; $p=0.03$) and reaction time accuracy performance ($t=2.62$; $p=0.01$); whereas the control group demonstrated significant declines in reaction time accuracy performance ($t=-4.7$; $p<0.01$). All task performance data are presented in Table 5.

Emotional Regulation

Data for the GLM outcomes for fNIRS results of the ER battery of tests are presented in Table 3. The MBI group showed significant increased activation of the FP area, Δ HbO ($t = 2.55$; $q = 0.04$) and significant decreased Δ HbR of the OFC ($t = 4.64$; $q \leq 0.001$). Significant changes in brain regions for the mindfulness intervention group during ER tasks are presented in Fig. 6. There were no significant changes in Δ HbO or Δ HbR for any brain regions during ER tasks in the control group. Paired sample *t*-tests of changes in ER task accuracy performance are presented in Table 5 and reveal significant changes in performance for the emotional working memory (EWM) and emotional Stroop (EStroop) tests for both groups; however, these changes were mixed and inconclusive. The MBI group demonstrated a significant decline in both their EWM performance ($t = -5.56$; $p \leq 0.001$) and EStroop ($t = -2.79$; $p = 0.01$) while the control group demonstrated a significant decrease in EWM performance ($t = -10.23$; $p \leq 0.001$) and a significant increase in EStroop performance ($t = 2.7$; $p = 0.01$). Figure 5 summarizes these statistical results on the brain.

Table 5 Longitudinal changes in cognitive task accuracy performance

	Intervention ($n = 16$)		Control ($n = 15$)	
Task	*t*-test	*p*	*t*-test	*p*
Attentional Control Go/No Go	2.12	**0.03**	1.54	0.12
Attentional Control Reaction Time	2.62	**0.01**	−4.73	**<.001**
Emotional Regulation EWM	−5.56	**<.001**	−10.23	**<.001**
Emotional Regulation EStroop	−2.79	**0.01**	2.71	**0.01**
Working Memory Audio Nback	0.21	0.83	−10.74	**<.001**
Working Memory Nback	−8.56	**<.001**	2.15	**0.03**

Estroop, emotional Stroop, *EWM*, emotional working memory

Working Memory

The GLM outcomes for the battery of tests for WM revealed significant changes in activation as noted by significant decreases in in Δ HbR in the OFC ($t = -3.56$; $q \leq 0.001$) and PMC ($t = -3.31$; $q \leq 0.001$). Figure 7 depicts significant changes in brain region for the mindfulness intervention group during WM tasks. There were no significant changes in any of the brain regions for the control group. Paired sample *t*-tests of changes in WM task accuracy performance are presented in Table 5 and reveal some significant changes in performance for the audio N-back and N-back; however, these changes were mixed and inconclusive. The MBI group demonstrated a significant decline in N-back performance ($t = -8.6$; $p \leq 0.001$) with no significant changes in Audio N-back, while the control group demonstrated both a significant decline in Audio N-Back performance ($t = -10.7$;

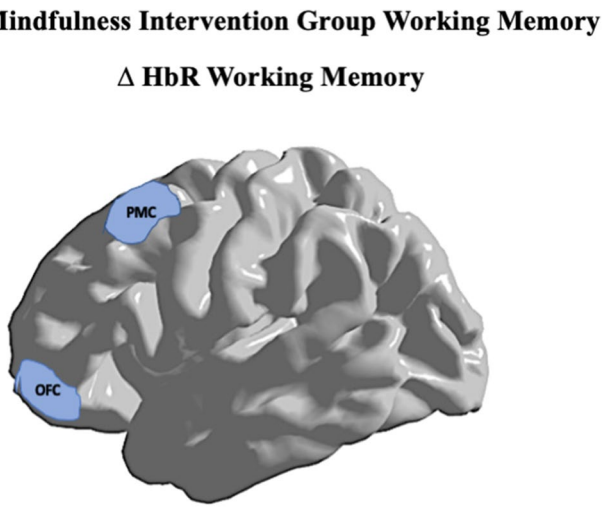

Fig. 7 Significant ΔHbR changes in brain region during working memory tasks for Mindfulness group. OFC, orbitofrontal cortex; PMC, premotor cortex; blue, decreased oxyhemoglobin

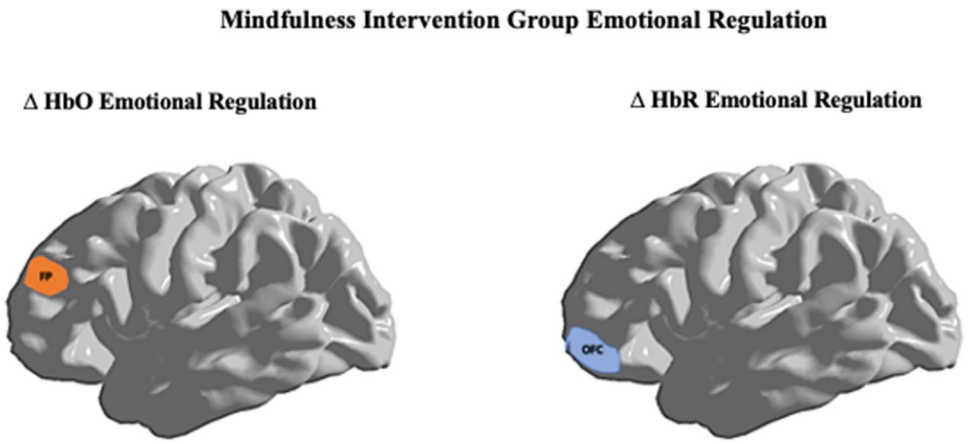

Fig. 6 Significant ΔHbO and ΔHbR changes in brain region during emotional regulation tasks for Mindfulness. FP, frontopolar area; OFC, orbitofrontal cortex; orange, increased oxyhemoglobin; blue, decreased oxyhemoglobin

$p \leq 0.001$) and a significant improvement in their audio N-back performance ($t = 2.52$; $p = 0.03$).

Discussion

Overall, there were three regions of significant change for HbO activation in AC and one for ER in the MBI group and none for the control group. The HbR data revealed three regions of significant change in AC, one for ER and two for WM, while there was only one region of significant HbR change for AC in the control group (see Tables 2–4 and Figs. 4–7). These results demonstrate patterns of significant changes in neural network activation associated with the MBI group that are not evident in the control group. Thus, our exploratory aim to test the feasibility of using fNIRS to measure MBI-related changes in cognitive neural networks supports the use of fNIRS as another research tool to measure changes in the FP, OFC, and PMC. These findings build on prior fMRI research using more invasive neuroimaging methods (Irani et al., 2007; Poldrack, 2007; Solovey, et al., 2015). Next, we discuss our results through the lens of our four primary hypotheses.

With respect to attentional control, in hypothesis one, we hypothesized that following the MBI, participants in the intervention group would demonstrate significant improvements from baseline in AC as evidenced by AC task performance and fNIRS data associated with changes in activation and cognitive load in regions of the brain associated with directed attention. Changes in AC-related activation and task performance provide the strongest evidence of MBI-related improvements in attentional tasks (see Table 5) coupled with significant changes in FP, OFC, and PMC activation for both HbO and HbR that are not evident in the control group (see Fig. 4). Specifically, the intervention group showed increased HbO in FP and OFC. The simultaneous significant decrease in Hb for those regions does indeed suggest increased brain activation in the intervention group during attentional tasks. We suspect that the decreasing HbO in the PMC for the intervention group may be due to a high saturation of HbO being routed toward the FP and OFC regions, which could result in the decrease of HbO we see in the PMC region at that time. This phenomena of oversaturating regions of activation with HbO is often described as "watering the entire garden for a single flower" (Ekstrom, 2021; Fox & Raichle, 1986; Tam & Zouridakis, 2014)). For the control group, the only significant change was a decrease in HbR, which indicates increased brain activation in that region. Thus, we affirmed our first hypothesis that participants in the MBI group would demonstrate significant improvements from baseline in AC as evidenced by fNIRS data and AC task performance.

The FP and OFC areas are indicated in TPN activation and volitional attention (Fox et al., 2014; Hasenkamp et al., 2012). The FP area has extensive networks of executive attentional control system (Petersen & Posner, 2012); thus, increased FP activation may indicate enhanced meta-awareness and attention which researchers have found to be associated with meditation practice; while OFC activation is also known to be related to attentional control (Fox et al.; Tang, et al., 2007, 2010, 2015; 2014; Zeidan et al. 2010) and OFC changes were also noted in WM, these findings are supported by the work of Fox et al. (2014) who identified patterns of structural differences in the FP and OFC of meditators when compared to non-meditators.

With respect to emotion regulation, in hypothesis two, we hypothesized that following the MBI, participants in the intervention group would demonstrate significant improvements in ER as evidenced by ER task performance and fNIRS data associated with changes in activation and cognitive load in regions of the brain associated with ER. Similar to changes evident during AC tasks, changes in FP and OFC activation were evident during both ER tasks; however, the patterns of neural activation changes during ER tasks are less clear than for AC and thus our second hypothesis was not fully supported. During ER tasks, FP activation increased among the MBI group; these findings are supported by research that attributes FP neural correlates with bidirectional interaction of brain regions that help people stay on task while regulating emotion (Kohn, et al., 2014). There was also significant deactivation of the OFC during ER task as measured by HbR, while the HbO changes indicated OFC deactivation that approached significance ($p = 0.06$). The OFC integrates somatic sensations that embody emotions; thus, the OFC plays an important role in emotional processing and related decision-making (Brewer, 2019; Damasio, 1996; Kringelbach, 2005). These characteristics of the OFC in relation to decision-making and emotional processing may indicate that the decreased activation of the OFC reflects reduced cognitive load in the OFC during ER tasks which involve emotional stimuli. However, the decline in ER task performance for the MBI group indicates more research is needed to understand what OFC activation change patterns may signify.

With respect to working memory, in hypothesis three, we hypothesized that following the MBI, participants in the intervention group would demonstrate significant improvements from baseline in the amount of cognitive workload devoted to cognitively demanding WM tasks, as evidenced by WM task performance and fNIRS data–associated WM regions of the brain. Our hypotheses for WM were not clearly supported by changes in WM task performances and the results of WM tasks were mixed for both the control and MBI groups. There were significant decreases in OFC and PMC activation during WM tasks as measured

by HbR data, whereas the patterns of change for the control group were not consistent and showed varying patterns of activation and deactivation. As noted previously, the OFC and PMC influence one another and there were significant decreases in PMC activation for both attentional and working memory tasks.

Lastly, with respect to the perceived stress and traumatic stress self-report measures, in hypothesis four, we posited that participants in the MBI group would have significantly decreased scores in perceived stress (measured by the Perceived Stress Scale) and posttraumatic stress symptoms (measured by the PCL-C) following the MBI. Our fourth hypotheses pertaining to the self-report measures were not supported as they did not show statistically significant ($p \leq 0.05$.) improvements after the 6-week MBI; however, the trends in data were moving towards improvement for the intervention group and worsening for the control group. It is noteworthy that a 5-point decline in traumatic stress symptoms, as measured by PCL-C scores, is considered a reliable change not likely due to chance for determining if an individual has responded to PTSD treatment (Monson, et al., 2008); thus, the mean 5.7 point decline in PCL-C scores among the intervention group may be meaningful; however, the small sample size and large SD make interpretation challenging. This suggests that there may be a temporal ordering of changes that occur in relation to MBIs with neurocognitive changes in AC, ER, and WM evident before changes in psychometric measures may be detected. The questions on the PSS and PCL-C do not directly pertain to AC, ER, and WM and therefore, it is not unexpected that the cognitive changes and these self-report measures are independent of one another.

Limitations and Future Research

Although this study makes several important contributions to the fields of MBIs and cognitive neuroscience, it is not without limitations. The sample population in this study may also present limitations on the generalizability of these findings. Our study was conducted with an entirely female participant pool, and further investigations are needed to replicate these findings with larger sample sizes that include male participants to examine such changes across age groups and sexes. Whereas the majority of the participants in this study scored above the subthreshold score of 30 for PTSD symptoms on the PCL-C, this was not a clinical sample with a PTSD diagnosis; therefore, further research is needed to affirm mechanisms of change in AC, ER, and WM with higher risk participants.

The general lack of significant change in ER and WM activation of the FP, OFC, and PMC brain regions during tasks suggests that more work is needed to understand what ER and WM benefits there may be related to MBIs, particularly brief MBIs. The inconclusive significance in the ER and WM tasks may not be appropriate proxies for measuring these constructs given the inconsistency in performance. For example, the ER tasks include both emotional and neutral conditions and therefore may not adequately reflect ER. It is possible that AC mediates gains in ER; however, these gains may not be enough to significantly impact ER.

Caution should be taken in interpreting the meaning of our findings because of the large number of variables that were measured with such a small sample size. Furthermore, we tested three hypotheses pertaining to exploratory aims of using fNIRS to measure potential changes in neural networks associated with mindfulness-based interventions, and the testing of each of these hypotheses encompassed statistical measures of HbO and HbR change in addition to task performance which may further increase potential type I error rate.

An additional limitation is that our MBI was a brief (6 h) version of the full 8-week (26 h) MBSR program and although the brief MBI protocol used here has demonstrated effectiveness in diverse populations (see Bergen-Cico et al, 2013, 2014; Possemato et al, 2016), it may not be long enough to affect neurocognitive changes in ER and WM. There is a need for effective brief MBIs that may be more accessible to people unable to participate in the full 8-week program, a factor that has been identified in past research as a barrier to participation (Pigeon et al., 2015; Possemato et al., 2016); however, reducing the length of MBIs may also decrease potential ER and WM cognitive improvements. Therefore, the field may also benefit from future research using fNIRS to measure changes associated with the full standard 8-week MBSR curriculum to enhance understanding of the breadth of neurocognitive changes from longer practice. Future studies may benefit from the collection of fNIRS data at additional and different time points across the intervention to identify the timeframe more accurately for neuro-cognitive changes with follow-up assessments to examine the sustainability of the observed changes or potential sleeper effects.

The primary contributions of this paper are threefold: (1) we demonstrate that fNIRS is a viable method for measuring changes in attentional control neural networks among women with stress and trauma who engage in MBIs, (2) we lend support to the notion that brief MBIs can indeed cultivate neural changes in brain regions associated with volitional attentional control, and (3) we provide a roadmap for future researchers to build on our experimental paradigms in order to further study the effects of MBIs on emotion regulation and working memory, as our results were inconclusive with respect to those functions. Our long-term research goals are to better understand the mechanisms of change associated with MBIs to support cognitive recovery impaired

by stress and trauma. Future research using fNIRS, a lower cost more portable neuroimaging technology, may provide insight into MBI-related cognitive changes and support the identification of objective measures for cross-cultural comparative research beyond the subjective and cultural limitations of psychometric measures.

Author Contribution DBC: designed and executed the study, assisted with the data analyses, and wrote the paper. LH: collaborated with the design and writing of the study. TG: collected and analyzed the data, and wrote sections of the methodology and parts of the results. RR and MC: collaborated with the design, data analyses, and writing of the manuscript. PK: collaborated in the data collection and editing of the final manuscript.

Declarations

Ethics Statement All study procedures were approved by Syracuse University's Institutional Review Board for Human Subjects Research, Syracuse University, Syracuse, NY, USA. The study's methods were carried out in compliance with the Declaration of Helsinki-World Health Organization's standard ethical guidelines.

Informed Consent Statement All participants completed written informed consent prior to enrollment in the study.

Conflict of Interest The authors declare no competing interests.

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