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PSYCHOSOCIAL AND SUPPORTIVE CARE: RESEARCH ARTICLE

Meditation reduces brain activity in the default mode network in children with active cancer and survivors

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Abstract

Background: Mounting evidence demonstrates that meditation can lower pain and emotional distress in adults, and more recently, in children. Children may benefit from meditation given its accessibility across a variety of settings (e.g., surgical preparation). Recent neuroimaging studies in adults suggest that meditation techniques are neurobiologically distinct from other forms of emotion regulation, such as distraction, that rely on prefrontal control mechanisms, which are underdeveloped in youth. Rather, meditation techniques may not rely on "top-down" prefrontal control and may therefore be utilized across the lifespan.

Procedure: We examined neural activation in children with cancer, a potentially distressing diagnosis. During neuroimaging, children viewed distress-inducing video clips while using martial arts-based meditation (focused attention, mindful acceptance) or non-meditation (distraction) emotion regulation techniques. In a third condition (control), participants passively viewed the video clip.

Results: We found that meditation techniques were associated with lower activation in default mode network (DMN) regions, including the medial frontal cortex, precuneus, and posterior cingulate cortex, compared to the control condition. Additionally, we

Abbreviations: ACCEPT, mindful acceptance; BOLD, blood oxygen level-dependent; BREATH, focused attention to breath; CAMM, Child and Adolescent Mindfulness Measure; CEN, central executive network; DISTRACT, distraction; DMN, default mode network; fMRI, functional magnetic resonance imaging; FWE, familywise error; LOOK, passive viewing; MFC, medial frontal cortex; MNI, Montreal Neurological Institute; SCARED, Screen for Child Anxiety-Related Emotional Disorders; VAS, visual analog scale.

found evidence that meditation techniques may be more effective for modulating DMN activity than distraction. There were no differences in self-reported distress ratings between conditions.

Conclusion: Together, these findings suggest that martial arts-based meditation modulates negative self-referential processing associated with the DMN, and may have implications for the management of pediatric pain and negative emotion.

KEYWORDS

adolescents, functional magnetic resonance imaging, martial arts, mindfulness

1 | INTRODUCTION

The ability to regulate emotion develops across the first two decades of life, corresponding with maturational changes in brain networks supporting emotion processing and self-regulation.[1] Emotion regulation is central to developmental outcomes.[2–4] Deficits in emotion regulation can increase risk of mental disorders in adulthood (e.g., depression).[5] Therefore, strategies that are effective for bolstering emotion regulation during childhood may have long-term benefits, such as ameliorating adverse outcomes during adulthood.[6]

Emotion regulation strategies that involve forms of *mindfulness and meditation* originate from ancient practices.[7] Meditation refers to an umbrella of mental practices that involve the monitoring and regulation of attention and emotion.[8,9] Mindfulness is a form of meditation that involves focusing attention to and accepting thoughts and emotions in the present.[10] There are also individual differences in the tendency toward mindfulness (i.e., trait mindfulness) that can change over time through deliberate meditation practice.[11] Trait mindfulness is defined as an individual's innate ability to maintain attention to the present moment and is thought to be a critical factor contributing to overall psychological health.[12–14] Trait mindfulness is also relevant for meditation-based interventions, wherein individuals with high levels of trait mindfulness at baseline may be more responsive to interventions.[9] State mindfulness, on the other hand, refers to more transient or temporary periods of mindfulness.[9] Repeated practices of mindful states may induce more stable or trait-level changes in mindfulness.[15] Meditation techniques are now integrated into established treatments for psychological disorders involving emotion dysregulation, including depression.[16] Meditation programs have been shown to be effective for reducing stress, anxiety, depression, and pain among clinical[17] and nonclinical[18] adult populations. They show promise for reducing disease- and treatment-related distress among patients with chronic conditions, such as cancer.[19] Active engagement in meditation has also been shown to lower self-reported pain and negative emotion.[20,21]

Although most research has been conducted in adults, emerging evidence suggests that mindfulness and meditation are beneficial for children. A meta-analysis of 33 randomized controlled trials reported benefits of meditation programs on attention, depression, and stress among clinical and nonclinical pediatric samples.[22] Mindfulness and meditation-based programs are popular in school settings,[23] and increasingly used to help children cope with stressful experiences, such as chronic conditions (e.g., cancer)[24,25] or trauma.[26] Meditation as an emotion regulation strategy is promising for preventing mental disorders, given that nearly half of all mental disorders begin during childhood and adolescence.[27] However, the neural mechanisms supporting meditation as an emotion regulation strategy in children remain unclear. Insight on these mechanisms could help validate and improve interventions for at-risk pediatric populations exposed to high stress and trauma.

Meditation strategies are distinct from other forms of emotion regulation, such as distraction. Rather than controlling attention away from emotional experiences, meditation strategies involve noticing and accepting emotional reactions as they arise.[8] Meditation also appears to be neurobiologically distinct from other forms of emotion regulation that rely on "top-down" (i.e., prefrontal-based) modulation of emotional responses. These forms of emotion regulation, such as distraction, commonly engage brain regions in the central executive network (CEN), including regions of the prefrontal cortex.[28,29] Meditation emotion regulation strategies do not appear to engage the CEN. Rather, these techniques have been shown to reduce activation in regions of the default mode network (DMN), including medial frontal cortex (MFC) and precuneus/posterior cingulate cortex, during deliberate meditation and exposure to aversive stimuli.[20,21,30] The DMN is associated with self-referential thought and depressive rumination.[31,32] Prior research suggests that individuals with depression fail to downregulate DMN activity when exposed to negative emotional stimuli.[33] Taken together, existing research suggests that meditation can modulate DMN activity, and these effects do not rely on prefrontal-based control mechanisms. This is important because children might not be able to employ complex regulatory strategies due to underdevelopment of the CEN.[34,35] Further, simple meditation strategies, such as focused attention to the breath, may be more accessible to children in stressful situations.

To our knowledge, only two functional magnetic resonance imaging (fMRI) studies have examined the neural correlates of meditation training in children. These studies report lower amygdala response to fearful faces and lower resting-state functional connectivity between the DMN and CEN in children (mean age = 11.75 years) following an 8-week mindfulness-based school program relative to a control computer programming course.[36,37] These finding support the notion that meditation can modulate brain activity (e.g., DMN) in children. These patterns are consistent with our prior fMRI study showing that more trait mindful youth spent less time in a dynamic functional connectivity state characterized by higher DMN–CEN connectivity.[38] However, no studies to our knowledge have examined neural activity in children actively engaged in meditation emotion regulation.

To address this gap, we examined the within-subject effects of meditation on brain activity in a sample of children with cancer, who may be prone to experiencing significant disease- and treatment-related distress.[39] Participants received minimal meditation training (4 hours) through a well-established martial arts-based meditation program[24,25] prior to undergoing an adapted version of an established fMRI emotion regulation task in the scanner. The 4-hour minimum was to improve feasibility and fidelity to the mindfulness conditions during scanning. Our goal was to ensure that participants were able to reliably enter and maintain a mindful state at the time of scanning, so that brain responses were robust. We compared two meditation emotion regulation techniques (i.e., focused attention and mindful acceptance) with a control condition (i.e., passive viewing) and with a non-meditation emotion technique (i.e., distraction). Participants were asked to engage in one of the four conditions while they were exposed to aversive video clips (e.g., a child receiving an injection), and rated their negative emotion after each trial. This design allowed us to test (a) whether meditation techniques can reduce brain activity in the DMN, and (b) whether meditation emotion regulation techniques are more effective than a non-meditation technique (distraction) at reducing DMN activity. We also (c) compared brain activation during the two meditation techniques, based on evidence that different meditation techniques have different effects on brain activity.[40]

2 | MATERIALS AND METHODS

2.1 | Participants

This preliminary study reports on 12 childhood cancer patients or survivors (ages 5–17 years; five female) recruited from the Children's Hospital of Michigan Hematology/Oncology clinic (Detroit, MI, USA) and from local cancer support groups and organizations (e.g., Kids Kicking Cancer, Gilda's Club of Metro Detroit). Data were collected from August 2017 through January 2019 as part of a larger prospective study examining the effects of a martial arts-based program, Kids Kicking Cancer (www.kidskickingcancer.org), on pain, emotional distress, and health-related quality of life among children with cancer (Supporting Information). Eligible participants were ages 5–17 (inclusive), English-speaking, and previously diagnosed with any form of pediatric cancer that did not include the central nervous system. Youth were excluded if they had MRI contraindications (e.g., claustrophobia, braces, non-MRI compatible port), major sensory impairments (e.g., severe vision loss), comorbid neurological disorders (e.g., epilepsy), gross neuropathologies (e.g., ventriculomegaly), pervasive developmental disorders, or other severe psychopathology (e.g., schizophrenia). The study was approved by the Wayne State University Institutional Review Board. Written informed consent and assent were obtained from participating primary caregivers (i.e., parent or legal guardian) and youth, respectively. Participant demographics and clinical characteristics are provided in Table 1.

2.2 | Questionnaire measures

Prior to the MRI scan, youth were assisted by a trained member of the research staff in completing standardized self-report measures of anxiety and trait mindfulness.

2.2.1 | Anxiety symptoms

Anxiety symptoms were measured using the 41-item Screen for Child Anxiety-Related Emotional Disorders (SCARED)[41] that shows good reliability, as measured via internal consistency and test–retest reliability. The SCARED demonstrates good discriminative validity between anxiety and non-anxiety disorders.[42,43] Total possible SCARED scores range from 0 to 82, with scores of ≥25 recommended for differentiating anxious from nonanxious youth, and may indicate the presence of an anxiety disorder.[44] In the present sample, 25% ($n = 3$) of participants exceeded this threshold for detecting potential anxiety.

2.2.2 | Trait mindfulness

Youth completed the Child and Adolescent Mindfulness Measure (CAMM), a 10-item measure of trait mindfulness.[14] Possible scores range from 0 to 40, with higher scores indicating higher mindfulness. The CAMM shows adequate internal consistency (Cronbach's alpha = .81–.88), reliability, and validity in youth samples.[13,14] Here, we report trait mindfulness in our participants, as trait mindfulness is thought to be relevant for responses to meditation-based interventions and predicts overall psychological health.[9] We explored whether trait mindfulness was associated with neural activity. Although we ask participants to go into a transient mindful *state* during the scan, capturing state mindfulness during the task would have interfered with task demands.

2.3 | Emotion regulation task

Participants completed an adapted emotion regulation task[45,46] during fMRI scanning. During the task (Figure 1), participants viewed distress-inducing stimuli and rated their current emotional distress after each trial. Participants rated their distress on a 1–6 visual analog scale (VAS; 1 = "No distress at all," 6 = "Worst possible distress") using an adapted version of the FACES scale.[47,48] The FACES scale was previously adapted by Trentacosta and colleagues to capture emotional distress related to children's cancer treatments, rather than pain levels.[47] We used the adapted version here, given our interest in

TABLE 1 Participant demographics and clinical characteristics

Variable	*n* (%)	*M* (SD)	Range
Age (years)		10.33 (3.26)	5–17
Age at diagnosis (years)		5.48 (4.49)	1–17
Biological sex (females)	5 (42%)		
Length of treatment (years)		3.06 (0.73)	2–4
Cancer diagnosis			
Acute lymphoblastic leukemia (ALL)	8 (67%)		
Acute promyelocytic leukemia (APML)	1 (8%)		
Neuroblastoma	1 (8%)		
Wilms tumor	1 (8%)		
Juvenile myelomonocytic leukemia	1 (8%)		
Active cancer patients	5 (41.7%)		
Types of treatment			
Chemotherapy	11 (91.7%)		
Surgery	3 (25%)		
Radiation	1 (8.3%)		
Blood transfusion	1 (8.3%)		
Bone marrow transplant	1 (8.3%)		
Approximate time since last treatment, in years (survivors)		3.4 (1.8)	1–5
Race/ethnicity			
White, non-Hispanic	7 (58.3%)		
African American, non-Hispanic	3 (25.1%)		
Other	1 (8.3%)		
Not reported	1 (8.3%)		
Annual household income			
$0–10,000	1 (8.3%)		
$10,000–20,000	1 (8.3%)		
$20,000–30,000	2 (16.7%)		
$30,000–40,000	1 (8.3%)		
$40,000–50,000	1 (8.3%)		
$50,000–60,000	0 (0%)		
$60,000–80,000	3 (25%)		
$80,000–100,000	1 (8.3%)		
$100,000–120,000	0 (0%)		
$120,000–140,000	1 (8.3%)		
Not reported	1 (8.3%)		
Trait mindfulness (CAMM)		30 (10.4)	3–40
Anxiety symptoms (SCARED)		25.6 (17.7)	6–60

Abbreviations: CAMM, Child and Adolescent Mindfulness Measure; SCARED, Screen for Child Anxiety-Related Emotional Disorders.

emotion regulation. Task stimuli consisted of 10 validated 30-second video clip vignettes depicting various realistic, salient stressors (e.g., child receiving an injection) that have been shown to induce transient distress in children.[49] Negative stimuli were used to test for differences in brain response to distress-inducing stimuli. Participants were explicitly instructed to pay attention to the movie as if it were real, pretend they were the child in the movie, and react as if they were in that situation. Prior to each video clip, participants were given instructions for one of four conditions: (a) focused attention to breath, BREATH; (b) mindful acceptance, ACCEPT; (c) distraction, DISTRACT; or (d) passive viewing, LOOK. During BREATH, participants were instructed to focus their attention on their breathing in a

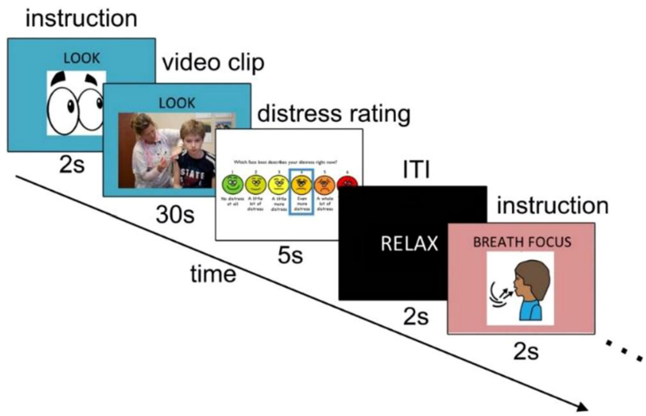

FIGURE 1 Emotion regulation task. Participants received one of four instructions prior to watching the video clip. After each clip, participants rated their level of distress (1 = no distress at all, 6 = the worst possible distress) on a visual analog scale (VAS), which is an adapted version of the Wong and Baker's FACES scale. Instructions consisted of (i) LOOK, a control condition during which participants were instructed to passively view the video clip; (ii) DISTRACT, a non-meditation condition during which participants were instructed to count backwards from 10; and two meditation emotion regulation techniques: (iii) BREATH, during which participants were instructed to focus their attention on their breathing in a nonjudgmental context; and (iv) ACCEPT, during which participants were instructed to pay attention, in a nonjudgmental manner, to the emotions they were experiencing and accept them

nonjudgmental manner, and during ACCEPT, participants were instructed to pay attention to the emotions they were experiencing and just accept (or "be okay with") them. During DISTRACT, participants were instructed to count backwards from 10 in their head. DISTRACT was selected as the non-meditation emotion regulation technique, because distraction is the most commonly used technique to manage children's pain and distress in clinical settings.[4] DISTRACT differs from BREATH in that DISTRACT involves directing attention away from emotional experiences, whereas BREATH involves noticing and accepting emotional reactions and focusing on an internal sensation (the breath) in a non-judgmental manner. During the control condition, LOOK, participants were instructed to passively view (or "just watch") the video clip. More details about how these were instructed in class and during the pre-scan mock scanner training session are provided in the Supporting Information. Participants were cued using the text and visual cue during the task in the fMRI scanner. Each trial lasted 37 seconds, and included a 2-second instruction slide, a 30-second video clip, and a 5-second emotion rating period (Figure 1). The inter-trial interval (2 seconds) was a "RELAX" screen. There were five trials of each of the four conditions, for a total of 20 trials (total time = 13 minutes 21 seconds). Video clips were counterbalanced across conditions. Presentation software (Neurobehavioral Systems, Inc.) was used for stimulus presentation and behavioral data acquisition. The task was displayed on a back-projection screen affixed to the head coil and behavioral responses were registered using a 2×2 MR-compatible response device.

2.4 | Emotional distress ratings

Distress ratings were averaged for each condition (BREATH, ACCEPT, DISTRACT, LOOK) and submitted to IBM SPSS software v.26 for within-subject analysis. Overall effects of condition were examined using a one-way nonparametric Friedman test for repeated measures ($p < .05$). Post hoc repeated measures Wilcoxon signed-ranks tests were used to further examine differences in distress ratings between conditions. Behavioral data were missing for one subject due to errors in data collection.

2.5 | fMRI data acquisition and analysis

Details regarding blood oxygen level-dependent (BOLD) imaging fMRI data acquisition, preprocessing, quality assurance, and first-level analyses are provided in the Supporting Methods.

2.5.1 | Second-level analysis

Group-level random effects analysis was performed in SPM8 to examine within-subjects differential activation patterns based on instruction, using one-sample *t*-tests. First, to identify regions modulated by meditation emotion regulation techniques versus a control condition, we examined the contrasts BREATH versus LOOK and ACCEPT versus LOOK. To identify regions modulated by the non-meditation emotion regulation condition, we examined DISTRACT versus LOOK. Then, we compared the two meditation conditions (BREATH vs. ACCEPT) and compared the meditation versus non-meditation instructions (i.e., BREATH vs. DISTRACT, ACCEPT vs. DISTRACT).

2.5.2 | DMN analyses

To identify the effects of different emotion regulation techniques on brain activity, we focused on a priori regions of interest in the DMN: MFC, posterior cingulate cortex, dorsal frontal cortex, and supplementary motor area. Small-volume familywise error (FWE) correction was used to identify significant results ($p_{FWE} \leq .05$ and five-voxel minimum).

2.5.3 | Whole-brain analyses

A complementary whole-brain analysis was performed using a whole-brain FEW-corrected threshold ($p_{FWE} < .05$). See Supporting Information for details.

2.5.4 | Exploratory analyses

Of note, although our sample consisted of patients undergoing active treatments and survivors, our main focus was on within-subjects effects. We did not perform between-subjects analyses given the relatively limited sample size and the potential confounding factors between groups. However, we did explore associations with age (older vs. younger, median split), anxiety symptoms (SCARED scores, continuous), and trait mindfulness (CAMM scores, continuous).

3 | RESULTS

3.1 | Distress ratings

There was no main effect of condition (BREATH, ACCEPT, DISTRACT, LOOK) on distress ratings following negative video clips, Friedman's two-way analysis of variance by ranks, df = 3, test stat = 2.35, p = 0.5 (Supporting Information, Table S1). Post hoc repeated measures Wilcoxon signed-ranks tests also revealed no significant differences between conditions; $p > .1$.

3.2 | fMRI results

3.2.1 | Effects of meditation emotion regulation strategies (vs. passive viewing)

A whole-brain BREATH versus LOOK contrast revealed lower activity in several regions of the DMN, including the precuneus, parahippocampal gyrus, and posterior cingulate cortex, and also the cuneus and lingual gyrus (Table 2, Figure 2B). There were no regions showing the opposite pattern (i.e., higher activity for BREATH relative to LOOK; Table 2) and no significant effects for the BREATH versus LOOK contrast in any DMN region ($p_{FWE} > .05$). There were also no significant effects for the ACCEPT versus LOOK contrast at the whole-brain threshold (Table 2) or in any DMN region ($p_{FWE} > .05$).

3.2.2 | Effects of a non-meditation emotion regulation strategy (vs. passive viewing)

There were no significant effects for the DISTRACT versus LOOK contrast at the whole-brain threshold (Table 2) or in any DMN region ($p_{FWE} > .05$).

3.2.3 | Comparison between meditation emotion regulation strategies

Region-of-interest analyses showed differential DMN activity for the BREATH versus ACCEPT contrast in the MFC, such that MFC activation was lower during the BREATH relative to the ACCEPT condition (xyz = 0, 58, 18, 9 voxels, Z = 3.73, p_{FWE} = .02; Figure 3A). No other regions were significant for the BREATH versus ACCEPT contrast, and there were no significant results for this contrast at the whole-brain corrected threshold (Table 3).

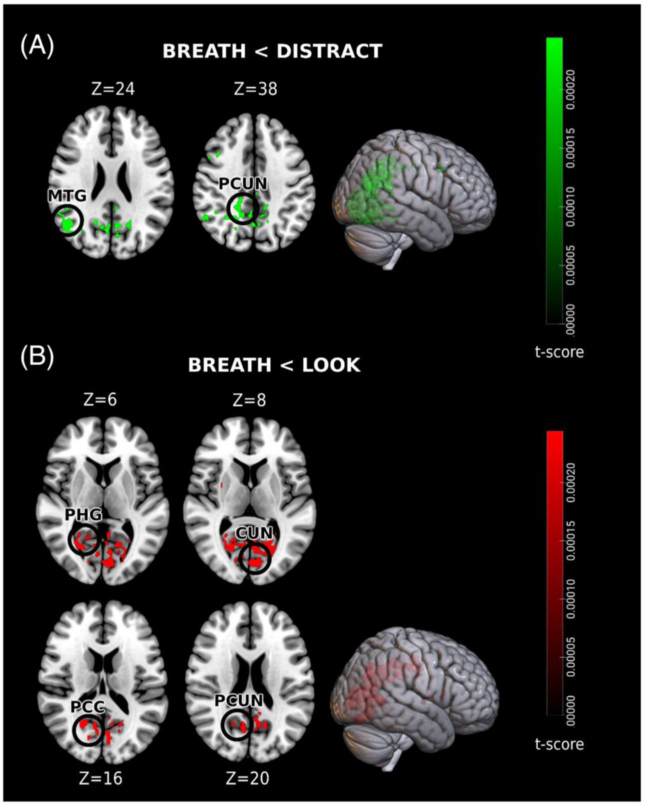

FIGURE 2 Whole-brain results. Effects of meditation emotion regulation techniques on activation in the default mode network (DMN). (A) Differential DMN activation associated with meditation (BREATH) versus non-meditation (DISTRACT) instructions. Green colors indicate lower BOLD response in the DMN for BREATH versus DISTRACT. (B) Differential DMN activation during meditation instructions (BREATH) versus a control condition (LOOK). Red colors indicate lower DMN activation during meditation instructions (BREATH) relative to a control condition (LOOK). Results significant at whole-brain threshold ($p < .001$, >6 voxels) and shown at $p < .005$ for display purposes. BOLD, blood oxygen level-dependent; CUN, cuneus; MTG, middle temporal gyrus; PHG, parahippocampal gyrus; PCG, posterior cingulate cortex; PCUN, precuneus. x, y, and z are Montreal Neurological Institute (MNI) peak coordinates

3.2.4 | Comparison between meditation and non-meditation emotion regulation strategies

A whole-brain BREATH versus DISTRACT contrast revealed lower activation in the precuneus and middle temporal gyrus at the whole-brain corrected threshold (Figure 2A, Table 3). No region showed significant activation for the BREATH versus DISTRACT contrast. For the ACCEPT versus DISTRACT contrast, there was lower DMN activation in the MFC (xyz = 2, 48, 22, 6 voxels, Z = 3.5, p_{FWE} = .05; Figure 3B). No other regions were significant for the ACCEPT versus DISTRACT contrast, and there were no significant clusters for this contrast at the whole-brain threshold (Table 3).

TABLE 2 Whole-brain results for regions showing differential activation while participants are engaged in meditation and non-meditation emotion regulation techniques versus the control condition

Regions of activation	BA	Laterality	*x*	*y*	*z*	Voxel extent (k_e)	*Z*-score
Meditation techniques (ACCEPT, BREATH) vs. the control condition (LOOK)							
LOOK > BREATH							
Cuneus	17		0	−80	8	32	3.64
Posterior cingulate cortex	30	R	20	−66	8	17	3.59
Posterior cingulate cortex	30	R	8	−64	10	16	3.45
Posterior cingulate cortex	30	L	−22	−68	8	13	3.44
Parahippocampal gyrus	30	R	28	−56	6	12	3.58
Posterior cingulate cortex	30	R	18	−58	16	11	3.81
Lingual gyrus	18	R	8	−70	2	10	3.64
Precuneus	31	R	6	−66	20	6	3.37
LOOK < BREATH: no significant clusters							
LOOK > ACCEPT: no significant clusters							
LOOK < ACCEPT: no significant clusters							
Non-meditation technique (DISTRACT) vs. the control condition (LOOK)							
LOOK > DISTRACT: no significant clusters							
LOOK < DISTRACT: no significant clusters							

Note: BREATH = focus attention to the breath in a nonjudgmental context; ACCEPT = pay attention to emotions in a nonjudgmental way; DISTRACT = count backwards from 10; LOOK = passively view the movie. *x*, *y*, and *z* are Montreal Neurological Institute (MNI) peak coordinates. Voxel extent refers to the spatial extent of each cluster. *R*/*L* refers to lateralization of activation. Results are corrected at the whole-brain level (voxelwise $p < .001$; cluster extent = 6 voxels).
Abbreviations: BA, Brodmann area; BOLD, blood oxygen level-dependent; N/A, not applicable.

TABLE 3 Whole-brain results for regions showing differential activation during different types of emotion regulation techniques (i.e., BREATH vs. ACCEPT vs. DISTRACT)

Regions of activation	BA	Laterality	*x*	*y*	*z*	Voxel extent (k_e)	*Z*-score
Comparison between meditation techniques (BREATH vs. ACCEPT)							
BREATH > ACCEPT: no significant clusters							
BREATH<ACCEPT: no significant clusters							
Comparison between meditation and non-meditation techniques (BREATH vs. DISTRACT, ACCEPT vs. DISTRACT)							
BREATH > DISTRACT: no significant clusters							
BREATH < DISTRACT							
Middle temporal gyrus	39	R	46	−66	24	53	3.32
Precuneus	31	R	12	−50	38	9	3.52
ACCEPT > DISTRACT: no significant clusters							
ACCEPT < DISTRACT: no significant clusters							

Note: ACCEPT, pay attention to emotions in a nonjudgmental way; BREATH, focus attention to the breath in a nonjudgmental context; DISTRACT, count backwards from 10; LOOK, passively view the movie. *x*, *y*, and *z* are MNI peak coordinates. Voxel extent refers to the spatial extent of each cluster. *R*/*L* refers to lateralization of activation. Results are corrected at the whole-brain level (voxelwise $p < .001$; cluster extent = 6 voxels).
Abbreviations: BA, Brodmann area; BOLD, blood oxygen level-dependent; N/A, not applicable.

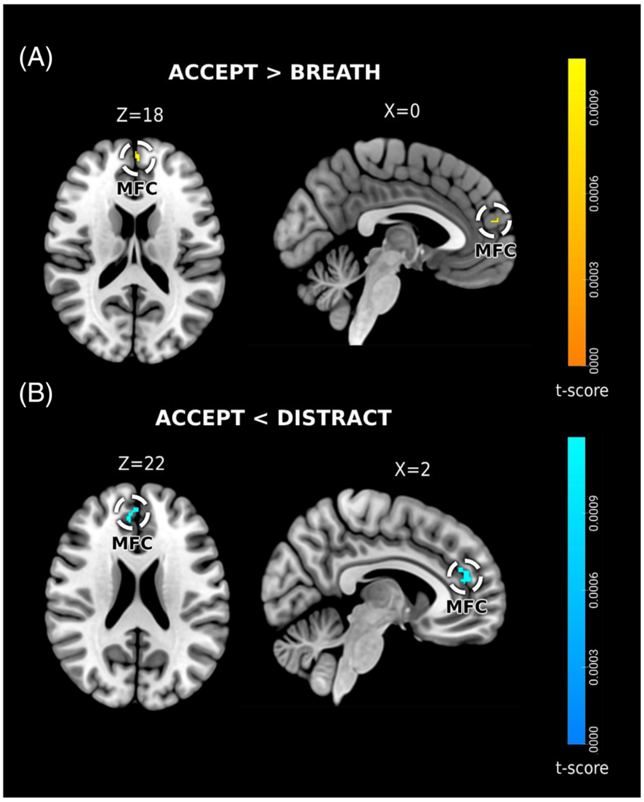

FIGURE 3 Region-of-interest results. Effects of meditation emotion regulation techniques on activation in the default mode network (DMN). (A) Differential DMN activation associated with ACCEPT versus BREATH meditation instructions. Yellow colors indicate greater BOLD response in the DMN for ACCEPT versus BREATH. (B) Differential DMN activation during meditation instructions (ACCEPT) versus non-meditation instructions (DISTRACT). Blue colors indicate lower DMN activation during meditation instructions (ACCEPT) relative to non-meditation instructions (DISTRACT). Results significant at small-volume-corrected threshfold ($p_{FWE} \leq .05$, >5 voxels) and shown at $p < .005$ for display purposes. BOLD, blood oxygen level-dependent; MFC, medial frontal cortex. *x*, *y*, and *z* are MNI peak coordinates

3.3 | Exploratory analyses

3.3.1 | Associations between brain activation and distress ratings

Distress ratings were not significantly associated with activation in any brain region that showed significant results in whole-brain or region-of-interest analyses ($p > .05$).

3.3.2 | Associations between distress ratings and demographic or clinical measures

Spearman correlation indicated that older age at diagnosis was associated with lower self-reported distress following the DISTRACT condition; $r(10) = -.75$, $p = .013$. Distress ratings were not associated with age, anxiety symptoms, nor trait mindfulness ($p > .05$). These findings remained nonsignificant after controlling for age at diagnosis ($p > .05$).

3.3.3 | Associations between brain activation and demographic or clinical measures

Activity in the DMN was not associated with age at diagnosis, anxiety symptoms, or trait mindfulness ($p > .05$). However, older children demonstrated lower brain activation in the posterior cingulate cortex (*xyz* = −22, −68, 8) during the BREATH versus LOOK contrast as compared to younger children; $r(12) = -.58$, $p = .049$. Older children also displayed lower activation in the middle temporal gyrus during the BREATH versus DISTRACT contrast than younger children; $r(12) = -.62$, $p = .032$. Controlling for age at the time of the scan, participants who were diagnosed at an older age showed higher brain activation in the middle temporal gyrus during the BREATH versus DISTRACT contrast, as compared to children who were diagnosed at a younger age; $r = .74$, $p = .035$.

4 | DISCUSSION

This is the first study, to our knowledge, to investigate the neural correlates of active meditation as an emotion regulation technique in a pediatric sample. We examined within-subjects differences in neural activation in children with cancer while they viewed distress-inducing video clips and engaged in meditation (focused attention, mindful acceptance) or non-meditation (distraction) emotion regulation techniques. In the control condition, participants passively viewed the video clip. The following findings emerged: (a) compared to the control condition, mediation emotion regulation techniques were associated with lower activity in several regions of DMN. (b) The non-meditation condition, distraction, was not associated with a similar reduction in neural activation as compared to the control condition, suggesting that meditation emotion regulation techniques may be more effective for downregulating DMN activity. (c) Meditation emotion regulation strategies were associated with lower DMN activity than distraction. Distraction is often used to manage children's pain in clinical settings (e.g., needle-related procedures).[50] Although there were no differences in distress ratings between conditions, evidence that meditation emotion regulation is more effective at quelling DMN activity may suggest longer term benefits—a hypothesis that requires future study with larger sample sizes. These findings may have implications for understanding the neural mechanisms underlying meditation-based emotion regulation in children.

Both forms of meditation emotion regulation strategies examined in this study were associated with lower activity in DMN regions, including the parahippocampal gyrus, precuneus, and posterior cingulate cortex. Lower activity in DMN during active meditation is consistent with prior fMRI studies in adults. For example, a meta-analysis of 78 fMRI studies in adults revealed consistent deactivations in

DMN regions (e.g., posterior cingulate cortex) during focused attention meditation.[40] Another fMRI study in meditation-naïve adults reported that mindful acceptance emotion regulation reduced pain-related activation in the DMN (e.g., posterior cingulate, precuneus).[20] We did not detect activation in the CEN during meditation, consistent with studies showing that meditation does not engage CEN control systems.[51] We also did not observe CEN activation for distraction, which may reflect underdevelopment of prefrontal-based forms of emotion regulation and the CEN.[34,35]

Our whole-brain and region-of-interest analyses revealed lower DMN activation for meditation emotion regulation techniques, but not for distraction. Prior studies on more prefrontal-based forms of emotion regulation (e.g., distraction) did not consistently report activation changes in the DMN,[51,52] and there is evidence that function of the DMN changes across development.[34] Distraction is considered an attention deployment strategy that redirects attention *away from* emotion-eliciting stimuli[53] and engages the CEN in adults.[51] Here, both meditation techniques (focused attention, mindful acceptance) were associated with lower DMN activity than distraction. Specifically, focused attention was associated with lower activation in the precuneus, a DMN region associated with maintaining self-consciousness during self-referential processes.[54] Lower activity in the precuneus during focused attention is consistent with meta-analytic findings in adults.[40] Lower DMN activity in the focused attention condition may reflect a suppression of self-referential thoughts evoked by negative stimuli, and may therefore protect against depressive rumination in children. Relative to distraction, mindful acceptance was associated with lower activity in the MFC, which is consistent with a prior emotion regulation study in adults.[20] Other studies have reported reduced activation in the MFC during sustained meditation,[55] negative autobiographical memory recall, and acceptance of present emotional state.[56] Lower MFC activation observed during mindful acceptance may reflect reduced elaboration and appraisal of emotional experiences. Taken together, although distraction and meditation techniques are both known to be effective for reducing children's pain and distress, the present findings suggest that meditation techniques may be more effective for modulating DMN activity in children with cancer. Given that higher DMN activity is implicated in depressive rumination,[32,56] these findings imply a potential long-term protective role of meditation for helping children cope with stressful experiences.

Although we observed differences in the brain between conditions, there were no differences in distress ratings. We may have been underpowered to detect changes in distress ratings. Prior studies support beneficial effects of meditation on self-reported pain and emotional distress in children over time (e.g., over 4- or 8-week programs)[36] or following a single session.[25] We also observed minimal differences in brain activity between conditions, which should be examined in future studies with larger sample sizes. However, we found preliminary evidence that focused attention may be more effective for downregulating DMN activity than mindful acceptance, which may reflect the fact that paying attention to the breath may be a simpler, anchoring concept for children. This finding is interesting given results of a prior study in healthy adults showing that experienced meditators were better than beginners at downregulating MFC activity in response to emotional images.[21] Therefore, more experience with meditation may improve the ability to attenuate DMN activity. Further, although levels of trait mindfulness in our study were, on average, similar to those reported in prior studies in youth,[57,58] we did not observe associations between mindfulness levels and brain activity during the task in our exploratory analyses. Future studies with larger sample sizes should explore whether these effects are related to baseline mindfulness levels, or whether trait mindfulness predicts response to meditation-based interventions.

4.1 | Limitations

Our sample consisted of a relatively small sample size of children with cancer, and results may reflect the unique neurobiology of this population. Further, our sample consisted of both survivors and children undergoing active cancer treatments, which may confound any group comparisons. However, our hypotheses and analyses focused on a within-subjects approach. Sampling limitations are attributed to the low base rate of childhood cancer, which precluded our ability to examine sex differences in neural or behavioral measures. However, the sample size in the present study ($n = 12$) is consistent with previously published neuroimaging studies in pediatric cancer survivors (e.g., $n =$ 8, 15),[59,60] and we used multiecho fMRI imaging techniques to further increase study power. We focused on children with cancer, because this pediatric population is exposed to disease- and treatment-related stress, is at increased risk of emotion dysregulation,[39] and because martial arts-based meditation programs have shown to be effective for reducing pain and emotional distress in this population.[24,25] In addition, the relatively wide age span (5–17 years) is a limitation due to differences in functional connectivity in young children compared to older teenagers. Another limitation is that we examined two forms of meditation (i.e., focused attention, mindful acceptance) and one non-meditation emotion regulation strategy (distraction), which may not be representative of all available emotion regulation techniques. In addition, we did not have a non-distressing (e.g., positively valenced) condition to compare our activation patterns to, so it is unclear if the resulting neural activation patterns are specific to regulation of negative stimuli. Additionally, all participants had at least 4 hours of meditation instruction. Findings may differ based on meditation experience,[21] as these techniques become more automatized. The brief meditation training may also influence neural activity during the non-meditative conditions, such as distraction. Therefore, future studies should examine different forms of meditation and the impact of meditation experience. Future studies should also integrate measures of both state and trait mindfulness.[15]

4.2 | Conclusions

Mounting evidence indicates that meditation is an effective approach for regulating pediatric pain and emotional distress. Mindfulness- and meditation-based interventions may be particularly well suited for children, because they do not engage CEN control systems, which are underdeveloped in youth, are easily accessible to children, and can be adapted to developmental age. Indeed, the present findings suggest that simple forms of meditation, such as focused attention to breath and mindful acceptance, can reduce activity in the DMN in children with relatively limited meditation training. Given alterations in the DMN are linked to various forms of psychopathology,[61] these results suggest that meditation emotion regulation techniques may be effective for modulating DMN activity in youth. These results also have implications for the management of pain and distress in pediatric healthcare settings (e.g., needle-related procedures), and for mitigating negative effects of stress and trauma in pediatric population that encounters disproportionally high stress (e.g., chronic health conditions).

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CONFLICT OF INTEREST

Elimelech Goldberg is founder and global director and Martin H. Bluth is the global medical/scientific director of Kids Kicking Cancer, a non-profit organization that developed the martial arts intervention. This work was supported, in part, by the St. Baldrick's Foundation and the National Institute of Mental Health to Hilary A. Marusak, and she had previously received grant funding from Kids Kicking Cancer. The authors declare no other conflicts of interest. Funders were not involved in the conduct of the study, data analysis or interpretation, or decision to publish.

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