DISSERTATION

MULTI-DIMENSIONAL ASPECTS OF MINDFULNESS: PSYCHOMETRIC EVALUATION, NEUROBIOLOGICAL UNDERPINNINGS, AND EXPERIENTIAL INSIGHTS

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ABSTRACT

MULTI-DIMENSIONAL ASPECTS OF MINDFULNESS: PSYCHOMETRIC EVALUATION, NEUROBIOLOGICAL UNDERPINNINGS, AND EXPERIENTIAL INSIGHTS

Objective: This dissertation aimed to deepen our understanding of mindfulness by exploring a psychometric evaluation of self-report scales, neurobiological underpinnings, and experiential insights in a multidimensional approach. The objective encompassed three specific aims: firstly, to evaluate the psychometric effectiveness of two self-report scales; the Mindful Attention Awareness Scale (MAAS) and the Five Facet Mindfulness Questionnaire (FFMQ) within populations diagnosed with post-traumatic stress disorder (PTSD), ensuring these tools' validity and reliability while addressing the complexity of mindfulness. Secondly, the research intended to synthesize existing literature on brain networks related to mindfulness through an umbrella review (a review of reviews / metanalyses), aimed to clarify the neural mechanisms of mindfulness. Thirdly, the study used functional magnetic resonance imaging (fMRI) to compare brain activity between a control group performing a visualization task (control) and a group engaged in a guided compassion meditation (experimental). This comprehensive framework sought to advance the field of mindfulness research by integrating psychometric analysis, brain network review synthesis, and experimental neuroimaging to enhance theoretical understanding of mindfulness.

Method: We employed a three-pronged methodological approach. Firstly, a psychometric evaluation of the Mindful Attention Awareness Scale (MAAS) and the Five Facet Mindfulness Questionnaire (FFMQ) to assess their reliability and validity in a PTSD-affected veteran population. Secondly, we conducted an umbrella review to synthesize existing research on brain networks and connectivity related to mindfulness to map out neural correlates and their implications. Thirdly, an experimental study using functional magnetic resonance imaging (fMRI) compared neural activation patterns between participants engaged in a visualization task and those practicing guided compassion meditation, aimed to identify distinct neural activities associated with this mindfulness practices.

Results: The psychometric evaluation of the MAAS and FFMQ confirmed their validity and reliability in assessing mindfulness in PTSD populations, highlighting mindfulness as a complex, multifaceted construct. An umbrella review of existing literature demonstrated the significant impact of mindfulness on brain connectivity, particularly in the DMN, CEN, and SN networks. The experimental fMRI study revealed distinct neural activation patterns between compassion mindfulness and a visualization task, with compassion mindfulness showing decreased activity in regions involved in emotional regulation and cognitive functions, such as the medial superior prefrontal cortex and anterior cingulate cortex.

Conclusions: These findings affirm the utility of MAAS and FFMQ reliability and validity, but demand more nuanced research based on a more multifaceted concept of mindfulness. The impact of mindfulness on large-scale brain networks underscores its potential to enhance cognitive and emotional regulation through neuroplasticity. However, significant methodological variability across studies calls for standardized research protocols to ensure consistency and reliability. Future research should address these limitations, explore the long-term effects of mindfulness, and include diverse populations to improve the generalizability of mindfulness-based interventions. Finally, significant differences in neural activation patterns between visualization tasks and compassion mindfulness meditation, indicate that such mindfulness practices may uniquely influence brain regions associated with emotional regulation and cognitive processes. These findings highlight the potential of compassion mindfulness to modulate brain activity in these areas, offering insights into its mechanisms and benefits.

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CHAPTER 1

1.1 Introduction

Mindfulness, a practice rooted in ancient contemplative traditions, has gained substantial attention in contemporary psychological and mental health research due to its therapeutic and overall benefits for well-being (Baer, 2003; Donald et al., 2019; Eberth & Sedlmeier, 2012; Grossman et al., 2003; Khoury et al., 2013a). Usually defined in the literature as the nonjudgmental awareness of the present moment, mindfulness is increasingly recognized for its role in enhancing emotional regulation and cognitive functioning (K. W. Brown & Ryan, 2003; Hülsheger et al., 2013; Kabat-Zinn, 2003; Leyland et al., 2019; Prakash et al., 2017). The applicability of mindfulness across diverse psychological contexts highlights its significance in addressing a range of mental health concerns, from stress reduction to the treatment of complex psychiatric disorders such as post-traumatic stress disorder (PTSD; Grossman et al., 2003; Khoury et al., 2015; Polusny et al., 2015).

This dissertation adopts a multi-dimensional approach to exploring the multifaceted concept of mindfulness, incorporating psychometric evaluation of two self-report measures, summarizing brain network research, and reporting on the results of a mindfulness experiential fMRI study. Through this framework, the dissertation aims to elucidate the psychological constructs, neurobiological mechanisms, and experiential activation dimensions of mindfulness, both in the context of trauma-affected populations such as veterans with PTSD and in healthy adults.

1.2 Background

Central to mindfulness are two key components: present-moment awareness and non-judgmental acceptance. Present-moment awareness refers to the conscious, deliberate attention to one's current experience, encompassing thoughts, feelings, sensations, and the surrounding environment (Cardaciotto et al., 2008). Non-judgmental acceptance involves embracing these experiences without criticism or attaching valence, allowing them to exist without attempting to change or suppress them (Kraines et al., 2020).

The roots of mindfulness can be traced back to ancient Eastern traditions, particularly Buddhism, where mindfulness meditation (Sati in Pali) is a crucial element of the Eightfold Path and a path to spiritual enlightenment and non-self (Brazier, 2013). The practice was primarily spiritual, aimed to cultivate insight, compassion, and wisdom. In the late 20th century, mindfulness was adapted for use in Western psychology, largely through the pioneering work of Jon Kabat-Zinn and the development of the Mindfulness-Based Stress Reduction (MBSR) program (Kabat-Zinn, 2003). Kabat-Zinn's secularization of mindfulness made it accessible to a broader audience, emphasizing its potential for stress reduction, emotional regulation, and psychological well-being.

The integration of mindfulness into contemporary psychological practices has been facilitated by its compatibility with various therapeutic approaches, including cognitive-behavioral therapy, acceptance and commitment therapy, and dialectical behavior therapy (Baer, 2006). This integration has led to the development of numerous mindfulness-based interventions (MBIs) tailored to address specific psychological issues, such as depression (Spijkerman et al., 2016), anxiety (Blanck et al., 2018), and chronic pain (La Cour & Petersen, 2015). The effectiveness of these interventions has been supported by a growing body of empirical research (Cullen, 2011; Goldberg et al., 2017; Hofmann & Gómez, 2017), which has sparked further interest in understanding the mechanisms underlying mindfulness and its potential benefits for mental health.

Different types of mindfulness practices, such as focused attention meditation, open monitoring meditation, and loving-kindness meditation have been identified, each with a unique approach and emphasis (Ainsworth et al., 2013; Chiesa & Malinowski, 2011; Hofmann et al., 2011, 2011; J. R. Martin, 1997). Focused attention meditation involves concentrating on a single object, such as the breath, to cultivate sustained attention and reduce distractibility (Sumantry & Stewart, 2021). Open monitoring meditation, on the other hand, involves observing the contents of one's consciousness without attachment, allowing thoughts and sensations to pass freely (Lohani et al., 2020). A combination of focused attention and open monitoring meditation is typically used in MBCT and MBSR and has been shown to be more effective than treatment as usual for improving major depressive disorder, generalized anxiety disorder, chronic pain, and well-being (Cladder-Micus et al., 2018; Lomas et al., 2019; Spijkerman et al., 2016; Virgili, 2015; Wong et al., 2016; Zgierska et al., 2016). Loving-kindness meditation focuses on cultivating feelings of compassion and goodwill towards oneself and others (Feliu-Soler et al., 2017); this technique has been shown to be effective in increasing compassion (and self-compassion) as well as improving symptoms of PTSD, and can improve the well-being of long-term caregivers (Galante et al., 2021; Hofmann et al., 2011; Kearney et al., 2012).

One of the primary challenges in mindfulness research is the subjective nature of the construct, which complicates its measurement (Davidson & Kaszniak, 2015). Mindfulness is inherently personal and varies between individuals, reflecting internal experiences that are difficult to quantify. This issue is further compounded by the diverse constructs targeted by mindfulness assessment tools, each based on different theoretical foundations and focusing on various aspects of mindfulness (Park et al., 2013). For instance, while the Mindful Attention Awareness Scale (MAAS) predominantly measures the attentional component of mindfulness (Brown & Ryan, 2003), the Five Facet Mindfulness Questionnaire (FFMQ) evaluates five distinct dimensions: observing, describing, acting with awareness, nonjudgement of inner experiences, and nonreactivity to inner experience (Baer et al., 2006). This differentiation in measurement tools leads to inconsistencies in how mindfulness is assessed and poses a significant challenge to attempts to compare and contrast research findings across studies.

Understanding the neural correlates of different mindfulness practices can provide insights into their mechanisms of action and potential therapeutic applications, particularly in the context of mental health interventions (Perestrelo & Teixeira, 2016; Shapiro et al., 2006). The activation of different brain regions during mindfulness practices has been a subject of interest in neuroscientific research. For example, focused attention meditation has been associated with increased activation in the prefrontal cortex, which is involved in attention regulation (Tomasino & Fabbro, 2016), and the anterior cingulate cortex, which is associated with monitoring and resolving conflicts (Zsadanyi et al., 2021). Mindfulness meditation has been linked to decreased activity in the default mode network, a network of brain regions involved in self-referential thinking and mind-wandering (Berkovich-Ohana et al., 2014).

Moreover, a comprehensive understanding of the neurobiological mechanisms underlying mindfulness, particularly during active practices or in-scanner experiments, is critical to gaining deeper insights into these mechanisms, can inform the effectiveness of clinical interventions, and allow for the personalization of treatments (Sanislow et al., 2010; Tang, 2017). For example, understanding that point-of-focus mindfulness practices often increase activity in the prefrontal cortex and decrease activity in the amygdala can explain their effectiveness in managing anxiety

(Taren et al., 2015). Additionally, neurobiological indicators derived from mindfulness research can possibly help predict which individuals are likely to benefit from mindfulness-based interventions (Chiesa & Malinowski, 2011; Donald et al., 2019; Tang, 2017). This predictive role would be invaluable in tailoring interventions and would be in line with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) mission to increase precision medicine in the mental health sphere (Kirmayer & Crafa, 2014; Morris et al., 2022; Sanislow et al., 2010). Furthermore, the intersection of neuroscience and mindfulness encourages cross-disciplinary collaboration, bringing together fields such as psychology, neurology, and artificial intelligence. Such collaborations are essential for advancing our understanding of human consciousness and well-being, fostering a multidisciplinary approach that enriches both theoretical and practical knowledge (Lamme, 2010; Rees & Seth, 2010; Sabbatini & Cardoso, 2002).

The overarching goal of this dissertation is to advance our understanding of mindfulness, utilizing a combination of psychometric analysis of self-report measure, neurobiological synthesis, and experimental neuroimaging. The first specific aim is to evaluate the psychometric properties of the Mindful Attention Awareness Scale (MAAS) and the Five Facet Mindfulness Questionnaire (FFMQ) in assessing mindfulness, particularly within populations diagnosed with PTSD. This evaluation will focus on assessing the validity and reliability of these tools, contributing significantly to the methodologies used for measuring mindfulness and ensuring the accurate interpretation of research findings in this area. Furthermore, this work will address the emerging perspective that mindfulness is not a singular construct but rather comprises multiple facets, each potentially impacting psychological and neurobiological outcomes differently. This nuanced understanding could lead to more sophisticated and effective applications of mindfulness-based practices.

The second specific aim is to conduct an umbrella review of the existing literature on brain networks and connectivity related to mindfulness. This review will synthesize current insights related to large-scale brain networks, aimed to consolidate what is known about the neural mechanisms that underlie mindfulness practices and their impact on brain function and structure. This synthesis is expected to enhance our understanding of how mindfulness can modify neural pathways that underly cognitive and emotional well-being.

The third and final specific aim is to conduct an experimental study using functional magnetic resonance imaging (fMRI) to compare brain activity in participants engaged in two different tasks: a visualization task serving as a control and a guided compassion mindfulness task. This project aims to identify differences in neural activity between these two tasks, providing deeper insights into how specific mindfulness-related practices can influence brain activity and connectivity. Through this experimental approach, the dissertation seeks to reveal nuanced details about the experiential aspects of mindfulness, enhancing our comprehension of its varied effects on the brain.

CHAPTER 2

PSYCHOMETRIC COMPARISON OF THE MINDFUL ATTENTION AWARENESS SCALE AND THE FIVE FACET MINDFULNESS QUESTIONNAIRE IN VETERANS TREATED FOR POSTTRAUMATIC STRESS DISORDER

2.1 Introduction

The practice of mindfulness is increasingly being applied as a treatment for psychiatric disorders, and publication on this topic has been steadily increasing. At the same time, there have been calls for more rigorous research measuring mindfulness and its use in treatment (Creswell, 2017; Ruiz-Fernandez et al., 2019). One concern is lack of consistency in the methods used to measure mindfulness across studies. Namely, two of the most commonly used measures of mindfulness propose very different measurement models. While the Mindful Attention Awareness Scale (MAAS; Brown & Ryan, 2003) is assumed to measure a single mindfulness factor, the Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006) is assumed to measure five aspects of mindfulness.

Research suggests that mindfulness training and practice have positive impacts on clinical outcomes (Hofmann et al., 2010; Khoury et al., 2013b; Li et al., 2017; Poissant et al., 2020). Of particular interest is the relation between mindfulness and posttraumatic stress disorder (PTSD). PTSD is a psychiatric disorder that is caused by exposure to traumatic events with symptoms that include intrusive memories or dreams, dissociative reactions, generalized anxiety, and hypervigilance (American Psychiatric Association, 2013). Unfortunately, many common treatments for PTSD show only modest effectiveness (Benish et al., 2008). Thus, the need for improved prevention and intervention is clear.

Mindfulness has shown promise not only for mitigating the symptoms of PTSD (Bormann et al., 2013, 2018; Heffner et al., 2016), but also for predicting PTSD development and symptom severity (Barr et al., 2019; Boden et al., 2012; Smith et al., 2011; Vujanovic et al., 2020). In particular, mindfulness may be effective for the treatment of hyper-arousal (Crawford et al., 2019; Reffi et al., 2019), anxiety (Schoorl et al., 2015), and depression (Kearney et al., 2012). Moreover, mindfulness appears to mitigate the negative effects of combat experience (Barr et al., 2019). This is true of both brief and primary care based mindfulness training (Possemato et al., 2016), as well as more structured interventions such as Mindfulness Based Stress Reduction, which tend to show better results for depression and anxiety (Davis et al., 2019; Kearney et al., 2012; King et al., 2013; Polusny et al., 2015).

The availability of reliable and valid patient-reported measures of mindfulness is critical to understanding the relationship between mindfulness, psychopathology, and treatment. Although several measures of the construct have been developed, the MAAS and the FFMQ are two of the most popular. Both have been used extensively as measures of mindfulness in research and in clinical settings (Conversano et al., 2020; López-Navarro et al., 2020; Räsänen et al., 2020; Tian et al., 2020; Vilaverde et al., 2020). Less is known about how the underlying constructs assessed by the MAAS and FFMQ relate to each other in the context of PTSD outcomes.

Studies of the reliability of MAAS scores have found acceptable internal consistency, reliability mapping onto a single factor using factor analysis (Baer et al., 2006; Brown & Ryan, 2003; Chiesi et al., 2017; Kotzé & Nel, 2016). The validity of the MAAS has been demonstrated by positive associations with positive traits such as attention, flexibility, engagement, and quality of life as well as negative associations with anxiety, rumination, and self-consciousness (Brown & Ryan, 2003; Cheyne et al., 2006; Rayan & Ahmad, 2018). However, there is some question as to its ability to discriminate between different levels of mindfulness experience (MacKillop & Anderson, 2007). With relation to PTSD, higher MAAS scores have been negatively associated with anxiety, depression, physical symptoms, and alcohol abuse (Smith et al., 2011), lower posttraumatic scale scores (Call et al., 2015), and Clinician Administered PTSD Scale (CAPS) and depression indexes (Barr et al., 2019; Heffner et al., 2016; Possemato et al., 2016).

The FFMQ differs from the MAAS in that it uses a multidimensional approach to measure mindfulness. Specifically, the FFMQ measures the constructs of Observing, Describing, Acting with Awareness, Nonjudgement of Experience, and Nonreactivity (Baer et al., 2006). The scale consists of 39 items (some reverse coded) using an ordered categorical (Likert type) scale and comprising the five facets listed above. Items produce a score for each mindfulness facet, but do not provide an overall mindfulness score (Baer et al., 2006).

The FFMQ has been shown to be predictive of psychological symptoms and negatively associated with depression, anxiety, and obsession-compulsion (Baer et al., 2006). Additional validity studies of FFMQ scores suggest good convergent and discriminative validity with other constructs, such as positive mental health, that were predicted to be either strongly or weakly related to each facet (Bohlmeijer et al., 2011). Notably, FFMQ facet scores have shown generally negative associations with symptoms of PTSD, but less so for the Observe and Describe facets (Kalill et al., 2014; C. E. Martin et al., 2018).

Studies of the MAAS and FFMQ have generally supported the reliability and validity of their scores; however, the relation between scores produced by these measures and their comparative validity as measures of mindfulness in clinical studies is unknown. Moreover, we are aware of no psychometric evaluations that have looked at both measures in a population of veterans with PTSD. Understanding the relations between these measures is critical to advancing our understanding of mindfulness as an intervention in psychiatric research.

This study aimed to evaluate and compare the psychometric properties of MAAS and FFMQ scores using secondary data. Our first aim was to determine whether the measures' factor structures adequately mapped onto the proposed measurement models for each measure in this sample of veterans with PTSD. We hypothesized that the MAAS would be characterized by a single latent factor and that the FFMQ would be characterized by five latent factors. We also aimed to assess the reliability and standard errors of scores produced by both scales. Finally, we aimed to understand how these measures relate to clinical and demographic data from three separate clinical trials that investigated the efficacy of interventions for veterans diagnosed with PTSD. Specifically, we were interested in relationships with intervention and outcomes.

2.2 Methods

Participants

The present study is a secondary analysis with the purpose of psychometric evaluation and comparison of the MAAS and FFMQ scales using data collected from two randomized controlled trials and one non-randomized trial of the Mantram Repetition Program (MRP) compared to control conditions for the treatment of PTSD among veterans. The three studies enrolled a total of *n* = 487 veterans. Across all three studies, veterans were recruited to participate via flyers and provider referrals. In order to be eligible for the studies, veterans were required to be 18 or older, have a diagnosis of PTSD related to military trauma, read and write English fluently, and have a stable psychiatric medication regimen (no changes for at least

6 weeks prior to enrollment). Veterans were excluded from participation if they had active substance abuse, were currently engaged in other complementary or alternative treatments for PTSD, or had cognitive impairments or severe psychopathology that may cause an inability to complete the protocol (e.g., acute suicidality, psychosis, dementia, or untreated bipolar disorder). The subject population is generally representative of the VA populations from which they were drawn. Individuals were not excluded on the basis of age, gender or ethnicity. Demographic characteristics of the samples are provided in Table 1.

Procedure

The MRP is a manualized meditation-based practice of silently repeating a self-selected, sacred word or phrase combined with one-pointed attention to interrupt the stress response and elicit relaxation. It is repeated intermittently throughout the day and prior to sleep at night to support coping with internal and external stressors. The MRP has been shown to increase mindfulness (Bormann et al., 2008, 2014, 2017; Buttner et al., 2016). The three studies mentioned above implemented the MRP slightly differently. Study 1 intervention was conducted over 8 weeks in 1-hour sessions (n = 89 MRP individual vs. n = 84 Present Centered Therapy (PCT) individual, a nonspecific psychotherapy control; Bormann et al., 2018). Study 2 intervention was conducted over 8 weeks in 1.5-hour sessions and occurred at two sites: the VA San Diego (n = 83 MRP group vs. n = 12 “PTSD 101” (psychoeducation) group; Heffner et al., 2016) and VA Loma Linda, CA (n = 37 MRP group vs. n = 36 trauma-focused coping group). Study 3 intervention was conducted over 6 weeks in 1.5-hour sessions at the VA San Diego, CA (n = 146 total, n = 71 MRP + treatment as usual group vs. n = 75 treatment as usual group; Bormann et al., 2013). All were overseen by the San Diego VA IRB, which was the Coordinating Site for all three trials. The MAAS was administered at baseline and posttreatment in study two and study three but not in study one. The FFMQ was administered at baseline and posttreatment in study one and study two but not in study three.

Measures

Mindfulness Measures. Mindfulness measures included the MAAS and the FFMQ,

Clinical Outcome Measures. Clinical outcome measures included the Posttraumatic Stress Disorder Checklist for DSM-IV military version (PCL-4M) designed as a self-report measure for the assessment of the construct of PTSD (Weathers et al., 1993) and the World Health Organization Quality of Life scale (WHOQOL) which is a self-report measure intended to assess the construct of quality of life using global quality of life, physical health, psychological health, social relationships, and environmental health as domains (WHOQOL Group, 1993). The PCL-4M was developed in 1993 by a research team at the National Center for PTSD showing good overall validity and reliability for clinical diagnosis (Blanchard et al., 1996; Weathers et al., 1993). Items in the PCL-4M are rated on a Likert scale with 1 equaling "not at all" and 5 equaling "extremely" (e.g. "Feeling distant or cut off from other people?"). The WHOQOL was developed in 1993 by a research team at the World Health Organization showing good overall validity and reliability (Skevington et al., 2004; The Whoqol Group, 1998; WHOQOL Group, 1993). Items in the WHOQOL are rated on a Likert scale with 1 equaling "very poor" and 5 equaling "very good". Baseline for the WHOQOL was collected for study 1 and study 2 (not present in study 3), where baseline for the PCL-4M occurred for all three studies. Posttreatment for the WHOQOL occurred for study 1 and study 2 (not present in study 3), where posttreatment for PCL-4M occurred for all three studies.

Research suggests that mindfulness increases with age (Shook et al., 2017), there are no observed sex and gender differences in mindfulness (Tasneem & Panwar, 2019), and higher mindfulness is not associated with higher academic achievement (McBride & Greeson, 2021). Mindfulness has been associated with lower PCL scores and higher WHOQOL scores as well (Boyd et al., 2018). Therefore, the validity of these scales should be supported by a positive correlation with age, no differences in sex and gender or education, lower PCL-4M scores and higher WHOQOL scores.

Analyses

Factor Structure. Our first goal was to characterize the measurement model (i.e., factor structure) for each scale. This includes determining the number of latent factors measured using a scree plot and a parallel analysis (Mulaik, 2010). Parallel analysis compares eigenvalues generated from the observed data to eigenvalues generated by simulated data. All observed data eigenvalues that are greater than their corresponding simulated data eigenvalue are retained as factors. Parallel analysis was performed separately on the MAAS item scores and on the FFMQ item scores using polychoric correlations. We also performed a parallel analysis on the FFMQ subscales scores using Pearson correlations to see if the five factors measure a common higher-order factor. Next, we performed a confirmatory factor analysis on baseline observations (CFA; Brown, 2006). We fitted CFA models that only allowed items to load onto latent factors that are consistent with scale interpretations proposed by the tests' developers. That is, for the MAAS, we assumed one latent factor, and for the FFMQ we used item subscale pairings for the Observation, Description, Aware Actions, Non-Judgmental Inner Experience, and Nonreactivity scales. CFA models were fitted to data using the R lavaan package with full information robust maximum likelihood estimation (Rosseel, 2012). All models were identified using the standardized factor approach (i.e., factor means were fixed to 0 and factor variances were fixed to 1). Model fit was based on comparative fit index (CFI), Tucker-Lewis index (TLI), and root mean square error of approximation (RMSEA) statistics. CFI and TLI values of approximately 0.95 or greater and RMSEA values of approximately 0.06 and lower are typically considered excellent, with values of 0.90 and below 0.08, respectively, considered adequate (Brown, 2006; Hu & Bentler, 1999).

Reliability and Error. Our next goal was to characterize reliability and measurement precision for each scale. First, we used the R psych package (Revelle, 2020) to estimate coefficient alpha (McDonald, 1999) a measure of internal consistency using baseline measurements. Alpha values of .70 to .79 are considered adequate, values of .80 to .89 are considered good, and values of .90 and greater are considered excellent (Haynes et al., 2011). Test-retest reliability was examined for both the MAAS and FFMQ by computing correlations between baseline and post-treatment follow-up scores for each. Values greater than .7 over several weeks are considered adequate (Haynes et al., 2011). Only participants randomized to the treatment as usual condition were evaluated in test-retest analyses (study 1, n = 84; study 2, n = 48; study 3, n = 75). Participants with missing scores were dropped from this analysis. Separately, we used item response theory (IRT; Embretson & Reise, 2000) to characterize standard error of trait estimates (SEE) for each scale. In IRT, error is estimated for all trait levels (Thomas & Duffy, 2022). Most often, SEE is a non-linear, “U”-shaped function of trait values. Thus, we aimed to determine the range of mindfulness trait values that are best measured by each scale. IRT analyses were conducted using the mirt package for R (Chalmers, 2012).

Validity Analyses. We aimed to determine how baseline and change scores on the MAAS and FFMQ related to demographic and clinical variables. Specifically, we examined change scores among studies (post-treatment minus baseline). Because patterns of outcomes could vary between studies, we used linear mixed-effects models. We used the R lme4 package

(Bates et al., 2015) and lmerTest (Kuznetsova et al., 2017) packages. Random intercepts were included for the study effect. Otherwise, we regressed demographic or clinical variables onto MAAS or FFMQ baseline and change scores within separate models. Baseline scores were defined at baseline and change scores were defined as posttreatment minus baseline. The data were standardized so that regression coefficients could be interpreted in a standardized effect size metric. The reason for doing so is that this allows the regression parameter estimates to be interpreted on a scale of magnitude that is consistent with the correlation coefficients reported elsewhere in the paper (i.e., magnitude of standard deviation change in the predictor that is needed to produce a 1 SD change in the outcome). In instances where variables were collected within a single study, standard regression was used. F-tests of equality of variances were conducted for MAAS or FFMQ scores across time points. Results indicated no significant differences in variances across time points (all p's > 0.20).

2.3 Results

Factor Structure

The MAAS scree plot and parallel analysis (Figure 1; left panel) indicated that items measure a single latent factor. The FFMQ scree plot and parallel analysis (Figure 1; middle panel) indicated that items measure five latent factors. The scree plot and parallel analysis for the FFMQ subscale scores (Figure 1; middle panel) suggested two latent factors.

Next, we fitted our CFA models to the data. The CFA model for the MAAS provided acceptable fit for the data ($\chi^2(90)$ =180.08, $p < .001$, CFI = .929, TLI = .917, RMSEA = .057). Parameter estimates are reported in Figure 2. The smallest factor loadings were for items 5 ("not noticing tension"), 6 ("forgetting names"), 13 ("preoccupation"), and 15 ("eating without awareness”). The largest loadings were for items 7 (“running on autopilot”), 8 (“rushing activities”), 10 (“doing tasks automatically”), and 14 (“doing without attention”).

The CFA model for the FFMQ provided mostly unacceptable fit for the data ($\chi^2(692) = 1436.89$, $p < .001$, CFI = .834, TLI = .822, RMSEA = .057). The acceptable RMSEA combined with unacceptable CFI and TLI fit indices could suggest that the covariance structure of the data is relatively weak. Indeed, the null RMSEA of model was only 0.149, which is thought to negatively impact the usefulness of CFI and TLI fit statistics (Kenny, 2020). Parameter estimates are reported in Figure 3. The factor loadings relating items to each of the specific factors are generally moderate to large. The most notable features of the model are the relatively small correlations between some factors. For example, the Observing and Acting with Awareness factors have a trivial correlation (r = -.02).

Reliability and Error

Alpha reliability values (internal consistency) for the MAAS and FFMQ scale scores at baseline are reported in the diagonal elements of Table 2 (bolded values). The values ranged from acceptable for the FFMQ Nonreactivity scale (α = 0.77) to excellent for the FFMQ Describing scale (α = 0.90). Despite these high reliabilities, the scales were only modestly correlated. The strongest association was between the MAAS total score and the FFMQ Acting with Awareness scale (r = .68), whereas the MAAS was significantly but less associated with the FFMQ Describe (r = .28) and FFMQ Nonjudgemental Inner Experience (r = .45). It is of note that the MAAS was not significantly associated with either FFMQ Observing (r = 0.11) or FFMQ Nonreactivity (r = 0.15).

Test-retest reliability for MAAS was on the border of adequate (r = 0.78, n = 107). The Observe (r = 0.77, n = 108), Describe (r = 0.75, n = 108), Acting with Awareness (r = 0.68, n =

108), and Nonjudgement of Experience (*r* = 0.68, n = 108) facets of the FFMQ all showed mostly adequate to borderline adequate test-retest reliability. However, the test-retest reliability of the Nonreactivity to Experience subscale was poor (*r* = 0.58, n = 108).

IRT SEE plots are shown in Figure 4 for each scale. The x-axis of each plot represents standardized trait estimates in the population. Thus, approximately 95% of trait estimates should fall between baseline and post-treatment -2 and +2. Consistent with the strong reliability estimates across scales, SEE values (y-axis) were consistently low in the middle parts of the trait distributions for each scale.

Validity

Standardized parameter estimates regressing study variables onto baseline and change scores for the MAAS and FFMQ are reported in Table 3. These effects are reported in standardized regression coefficients from the linear mixed-effects model, meaning that these coefficients are unitless and represent differences in reference to standard deviation. Most scores were generally not associated with age, with the exception of baseline FFMQ Nonreactivity, which demonstrated a small positive association. Sex showed small positive associations with change scores in the FFMQ Acting with Awareness and Nonjudgement of Experience scores indicating higher change scores for females. Education was positively associated with FFMQ Observing and Describing baseline scores, but negatively associated with FFMQ Observing change scores. Treatment using the MRP as compared to the control conditions had a significant positive association with MAAS change scores and with FFMQ Describing, Acting with Awareness, Nonjudging, and Nonreactivity change scores. PCL-4M change scores were negatively associated with baseline MAAS scores and more strongly negatively associated with MAAS change scores. PCL-4M change scores were also significantly negatively associated with

FFMQ Describing, Acting with Awareness, Nonjudging, and Nonreactivity change scores. Perhaps most notably, WHOQOL change scores were positively associated with nearly all MAAS and FFMQ scores, showing broadly small to medium sized associations with both baseline and change scores.

Change Score Correlations

Lastly, we ran MAAS change score and FFMQ change score correlations for MRP participants only. Here, the MAAS change scores were not significantly associated with FFMQ Observing ($r = 0.21$, $p = 0.052$), but were significantly associated will all other facets of the FFMQ change scores including Describing ($r = 0.33$, $p < 0.01$), Acting with Awareness ($r = 0.46$, $p < 0.01$), Nonjudgement ($r = 0.52$, $p < 0.01$), and Nonreactivity ($r = 0.38$, $p < 0.01$).

2.4 Discussion

We completed a psychometric evaluation and comparison of two commonly used measures of mindfulness—the MAAS and FFMQ—in the context of data collected from three separate clinical trials that investigated the efficacy of interventions for veterans diagnosed with PTSD. Specifically, we had three aims: (1) to determine whether the scales' factor structures adequately mapped onto the proposed scoring models for each measure in this population; (2) to assess the reliability and standard errors of scores produced by both scales; and (3) to understand how these measures relate to outcome measures and demographic data from three separate clinical trials.

With respect to aim 1, results generally support the proposed factor structures for each scale. That is, the MAAS measured a single latent factor and the FFMQ measured five latent factors. There remains some ambiguity as to the adequacy of the FFMQ five factor model. Specifically, our confirmatory model fit indices showed disagreement (i.e., acceptable RMSEA combined with unacceptable CFI and TLI). This problem has been anecdotally described in the psychometrics literature as arising from situations where the data show relatively weak covariance; that is, situations where the item correlations are generally weak (Kenny, 2020). Additional psychometric analyses supported this suggestion, as did the model parameters estimates, which suggest weak factor correlations. In plain terms, the proposed measurement model for the FFMQ has poor fit because the FFMQ does not measure highly correlated constructs. This is not a problem *per se*, but it does suggest that the FFMQ does not measure any single construct. This claim is also supported by our parallel analyses of the FFMQ subscales scores, which did not find evidence of a single higher-order factor, suggesting that the FFMQ total score is not very useful. It is possible that these results are due to the veteran population specifically, as there is evidence of more than one higher-order factor in other populations (Tran et al., 2013). Regardless, our analysis strongly suggests that FFMQ total scores based on the sum or average of all subscale scores (or items) are not psychometrically valid. Or, at the very least, these scores are not indicative of a unidimensional higher-order trait, and therefore should not be interpreted as a unitary mindfulness construct.

With respect to our second aim, we found that reliabilities and standard errors for MAAS and FFMQ scores are all generally reliable and precise. Our reliability findings largely replicate previous findings for both measures; that is, high internal consistency (Baer et al., 2006; Bohlmeijer et al., 2011; de Bruin et al., 2012). Test-reliability findings were generally less positive. Most MAAS and FFMQ scores straddled the borderline of adequate. Because test-reliability is highly relevant to statistical power calculations—where poorer test-retest reliability leads to less power—some researchers may find these results concerning for clinical trials that use the MAAS and FFMQ as outcomes. This is especially true of the FFMQ Nonreaction to

Experience subscale, which had poor test-retest reliability. Our IRT analyses of standard error suggest that for most trait levels of mindfulness (i.e., low, medium, and high), scores are comparably precise. Thus, both the MAAS and FFMQ do not appear to be affected by dramatic ceiling or floor effects.

With respect to our third aim, we found that MAAS and FFMQ scores did not produce the same patterns of association with demographic and clinical variables. There are perhaps five key takeaways from our validity analyses. First, the correlation between the MAAS and PCL-4M change scores was -0.32 demonstrating that those who had a greater change on the MAAS are likely to have greater improvement in PCL-4M scores, and thus a reduction in PTSD severity. This demonstrated the high usefulness of the MAAS in this context. Second, the correlation between the PCL-4M change scores and four of the five facets of the FFMQ shows the usefulness of these facets in the context of PTSD (Describing (-0.19), Acting with Awareness facet (-0.31), Nonjudging (-0.23), and Nonreactivity (-0.30)). Third, associations with age, sex, and education were generally small. The only significant associations were found for FFMQ scores. Fourth, mantram interventions were significantly associated with improvements in the MAAS, but with improvement only for the Nonreactivity score of the FFMQ. This is notable given that these two scores had a small correlation; it could suggest that the scales measure unique aspects of change due to the MRP, which teaches one-pointed attention and repetition of a spiritual word, both of which could change Nonreactivity. Lastly, whereas most of the MAAS and FFMQ change scores were weakly, but significantly, correlated with WHOQOL change scores, all but the change in FFMQ Observing scores significantly correlated with the change in PCL-4M. Thus, whereas most aspects of mindfulness that are collectively measured by the MAAS and FFMQ are at least weakly associated with quality of life and improvement in PTSD, only the FFMQ Observing facet does not exhibit change with mantram interventions as evidenced by this facet having the lowest correlations with PCL and MAAS change scores. Future studies are needed to determine whether the FFMQ, as comprised, can be restructured in order to better conform to a higher-order latent construct model, or whether new items are needed.

2.5 Limitations and Future Research

Results of the current study should be considered in light of the limitation that we combined data from distinct studies of silent mantram repetition. Although the characteristics of the samples were highly similar at baseline, it is also likely true that intervention effects are study dependent. The intervention length also varied between studies with study 1 participants receiving 8 hours of MRP, study 2 participants receiving 12 hours of MRP, and study 3 participants receiving 8 hours of MRP. Additionally, this secondary study was not specifically designed to assess the validity of the MAAS and FFMQ. Although a clinical intervention study provides high ecological validity, future studies might be designed that more directly address convergent and discriminative validity of these measures.

Overall, our results suggest a mixed pattern of validity and reliability for the MAAS and FFMQ in veteran populations. On the one hand, the MAAS has a well-established factor structure, while the FFMQ's factor structure is more in question, but both have good internal consistency. On the other hand, the scores have borderline test-retest reliability and are more strongly associated with quality of life rather than posttraumatic stress symptomatology. Additionally, MAAS and FFMQ scores show weak to modest correlations.

Future studies should aim to develop a more comprehensive model that explains how these subconstructs are, or are not, related to the development and use of mindfulness as a treatment of psychiatric disorders in veteran populations. Specifically, one hypothesis might be that lower scores on the FFMQ's Nonreactivity sub-construct will better predict development of PTSD in combat deployed veterans, while another hypothesis might be that higher baseline scores on the MAAS single construct mindfulness scale will predict resilience to developing PTSD for combat deployed veterans.

CHAPTER 3

INTEGRATING MINDFULNESS EFFECTS ON BRAIN NETWORKS: AN UMBRELLA REVIEW

3.1 Introduction

Mindfulness, a practice rooted in ancient meditation techniques, has become a focal point of modern psychological research. In network neuroscience, mindfulness is studied through its impact on brain connectivity, specifically investigating the differences in functional activity within common large scale brain networks and between these networks (Melis et al., 2022). Research suggests that mindfulness practice leads to changes in the structural and functional connectivity within the brain.

The implications of these functional changes extend beyond mental health, potentially influencing physical health by mitigating stress-related physiological processes and enhancing overall well-being (Crowe et al., 2016; Yan et al., 2023). This holistic impact underscores the relevance of mindfulness within network neuroscience, highlighting its potential as a powerful tool in enhancing wholistic human health and understanding the workings of the human brain.

From the perspective of localized function in the brain, mindfulness practices are posited to influence the brain in several specific areas. Regular mindfulness meditation is associated with reduced activity in the amygdala, a region of the brain involved in processing emotional stimuli, which corresponds with decreased stress and anxiety levels (Way et al., 2010). Additionally, increases in gray matter volume in the hippocampus have been observed, which is crucial for learning and memory (Hölzel et al., 2011). These changes not only demonstrate the impact of mindfulness on brain structure and function but also suggest the mechanisms related to therapeutic applications for mental health, such as depression and anxiety, by modulating specific neural pathways (Doll et al., 2015; Farb et al., 2010; Taren et al., 2015). More recently, there has been a shift toward examining brain connectivity related to mindfulness.

The concept of brain connectivity has become increasingly important in neuroscience, shifting the focus from solely examining localized brain functions to understanding how different brain regions interact to facilitate complex behaviors and cognitive processes. Traditional models of brain function emphasized localized activity in discrete brain areas, each responsible for specific tasks. This approach, while useful, often oversimplifies the dynamic and interconnected nature of brain functioning (Friston, 2007).

Brain connectivity encompasses several dimensions, including structural, functional, and effective connectivity, each providing different insights into how brain regions communicate. Structural connectivity refers to the physical pathways, such as axonal connections between neurons, which lay the groundwork for neuronal communication across the brain (Yeh et al., 2021). Functional connectivity refers to the temporally correlated activity between spatially separate brain areas, often measured through synchronous neural activity detected by fMRI or EEG during specific tasks or at rest. This form of connectivity provides insights into the coordinated activity across brain networks, which is essential for understanding complex cognitive functions like memory, attention, and perception (Friston, 2011).

These connectivity approaches highlight the brain's complexity beyond simple location-based functions. They show how cognitive functions are not just localized but depend on the dynamic interactions between different brain regions. This perspective is crucial for more accurately diagnosing and treating neurological disorders, where disruptions in connectivity are often more critical than changes in localized brain function. The shift towards connectivity analyses helps in crafting interventions that can modulate these networks, potentially leading to better outcomes in clinical applications.

The growing interest in mindfulness within the scientific community (Baminiwatta & Solangaarachchi, 2021) has led to a proliferation of systematic reviews and meta-analyses examining its effects on brain connectivity. This surge in literature stems from the increasing recognition of mindfulness as a potent therapeutic tool, capable of altering the neural pathways associated with various cognitive and emotional processes CITE. However, the number of findings reported across individual reviews presents a challenge for researchers and practitioners seeking to understand mindfulness' brain network impacts (Bursky et al., 2022; Gu & Zhu, 2022; Melis et al., 2022). An umbrella review is crucial in this context as it aggregates findings from multiple systematic reviews and meta-analyses, providing a higher-order synthesis that can offer a clearer, more comprehensive understanding of the available evidence (Belbasis et al., 2022; Fusar-Poli & Radua, 2018).

Network neuroscience research in mindfulness has demonstrated certain networks are likely to have distinct roles in mindfulness. The triple-network model outlines a relationship between the Default Mode Network (DMN), the Central Executive Network (CEN), and the Salience Network (SN). In this model, the CEN is noted as the task positive network, the DMN is thought of as the task-negative (or self-referential / mind-wandering) network, and the SN is thought to be the switch between the two. These networks and other functional connectivity is thought to contribute to both the mindfulness process and thought to improve with practice.

The need for an umbrella review is further underscored by the heterogeneity in methodologies, populations, and types of mindfulness interventions included in the existing reviews. This variability can lead to conflicting conclusions that complicate the formulation of evidence-based guidelines for the application of mindfulness. By systematically evaluating the breadth of reviews and meta-analyses, an umbrella review can identify consistencies and discrepancies in the data, assess the robustness of reported effects, and highlight areas requiring further investigation. Ultimately, such a review serves not only to refine the scientific narrative surrounding mindfulness but also to inform clinical practice and guide future research directions, helping assure that interventions are both scientifically grounded and optimally effective.

The primary objective of this umbrella review is to systematically evaluate and synthesize the existing evidence from systematic reviews and meta-analyses concerning the effects of mindfulness practices on various aspects of brain connectivity. Specifically, this review aims to explore how mindfulness influences structural connectivity, functional connectivity, and effective connectivity within the brain. By examining these topics, this dissertation seeks to clarify the extent to which mindfulness practices alter brain networks involved in processes such as attention, emotion regulation, cognitive task-related functioning, and self-referential thinking.

The broad aim is to identify and discuss characteristics of existing reviews, such as the type of review, the conceptualization of mindfulness’ effect on brain networks (both within and between connectivity), the interpretation of these effects (what are the practical implications of these network changes), and identify what gaps exist in the current literature with proposed future directions.

3.2 Methods

Article inclusion criteria included reviews and metanalyses related to mindfulness and large-scale brain network connectivity as these were the specific focus of this umbrella review.

Identical searches were completed in Web of Science, PubMed, and PsychInfo. Web of Science was chosen because it provides broad multidisciplinary coverage with extensive citation indexing. PubMed offers in-depth access to medical and health-related literature. PsycINFO focuses on psychological research, ensuring good coverage of the literature.

Three groups of search terms were used for the initial collection of articles as follows: "Mindfulness Brain Network Review", "Mindfulness Network Review", and "Mindfulness Brain Network" going from more specific to less specific respectively in order to gather as many appropriate articles as possible. All articles that met these criteria (2,755 articles) were then screened. Six hundred and five articles were eliminated due to duplicates, 683 articles were eliminated due to not being from peer-reviewed journals, and 1,036 articles were eliminated due to not being reviews or metanalyses. This left 431 articles left for further evaluation. Due to other exclusion factors (the bulk being not being classified as reviews or metanalyses) the remaining review or metanalysis article for this umbrella review consisted of 11 articles (see figure 3.1).

Data extraction included a systematic and standardized approach employed to gather critical information from each included systematic review and meta-analysis. This process involved detailing the number of studies, sample sizes, effect estimates, and confidence intervals reported in each review. A pre-defined data extraction form was utilized to ensure consistency and minimize bias across the review team. Two independent reviewers extracted data, and any discrepancies were resolved through discussion or consultation with a third reviewer. This method aimed to consolidate and compare data accurately and provided a foundation for synthesizing the evidence on the effectiveness of mindfulness interventions.

Quality assessment of the included systematic reviews and meta-analyses were also conducted using the AMSTAR 2 tool, a validated instrument designed to evaluate the methodological rigor of systematic reviews and metanalyses. This tool assesses various dimensions of quality, including the adequacy of literature searches, the justification of excluded studies, the risk of bias in included studies, and the appropriateness of meta-analytical methods, among others. Each review was independently appraised by two reviewers to ensure an unbiased evaluation process. This assessment identified potential biases and determined the reliability of the findings reported in the systematic reviews and meta-analyses under consideration.

For synthesizing the data, both qualitative and quantitative approaches will be utilized. Heterogeneity will be quantitatively assessed using the I^2 statistic, which quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. Substantial heterogeneity ($I^2 > 50\%$) will prompt further exploration through subgroup analyses and sensitivity testing. Qualitatively, a synthesis will be provided discussing trends and patterns in the context of study quality and methodological differences. Potential biases in the studies will be assessed through funnel plots to visually inspect for publication bias to ensure an understanding of the evidence, taking into account the variability and potential biases of the included reviews and metanalyses.

Strength of the evidence will be evaluated using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach for intervention studies. This method provides a systematic framework for rating the quality of evidence and the strength of recommendations. The GRADE criteria assess several factors, including the risk of bias, inconsistency, indirectness, imprecision, and publication bias. Each factor is carefully considered to downgrade or upgrade the quality level of the evidence from high, moderate, low, to very low.

3.3 Results

Included Article Aims

Among the data points extracted from each article was the general aim of each study (See Table 1). The reviews included in this analysis collectively aim to elucidate the effects of mindfulness-based interventions (MBIs) on various aspects of brain connectivity. Common themes across these reviews include examining the neural mechanisms underlying mindfulness practices and determining the efficacy of these interventions in enhancing cognitive and emotional regulation. For instance, Felsch and Kuypers (2022) investigate whether the combination of mindfulness meditation (MM) and psychedelics can produce unique connectivity effects, while Gotink et al. (2016) explore the neuronal expression of mindfulness through various methodologies such as Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT).

Despite the shared interest in mindfulness and brain connectivity, the specific aims of each review demonstrate notable diversity. Lodha and Gupta (2022) re-examine the effects of mindfulness on attention and executive function, focusing on how these cognitive processes are influenced by different types of meditation practices. Melis et al. (2022) seek to summarize the effects of MBIs on functional connectivity within specific brain networks, providing a more detailed analysis of how these interventions impact neural communication pathways. Each review, while contributing to a common goal, approaches the subject from unique angles, thus giving us multifaceted perspective on the impact of mindfulness on the brain.

Included Articles Main Takeaways

The overall conclusions from the systematic reviews reveal a consistent recognition of the diverse methodologies and experimental designs employed in studying mindfulness-based interventions (MBIs; See Table 1). A recurring theme is the broad spectrum of assessment methods and experimental manipulations, including various lengths and types of mindfulness training, differences in mindfulness experience, and a mix of observational and randomized controlled trials (RCTs). These studies often involve diverse participant samples, ranging from clinical patients to healthy individuals, but many suffer from small sample sizes and a lack of active control groups. Additionally, one study incorporated psilocybin alongside mindfulness practices, so only the portions of this review that were specifically related to mindfulness were considered here.

Eight of the eleven reviews underscore the heterogeneity in outcome measures and participant characteristics, noting the inclusion of individuals with brain pathology and the presence of social confounds during training. There is also notable variation in neuroimaging analysis techniques and the categorization of brain networks. This variability extends to the selection of seeds for neuroimaging studies and the use of different imaging modalities. The lack of standardization in classifying functional networks and the differences in preprocessing and analysis procedures further complicate the synthesis of findings across studies.

The challenges identified across these reviews include the definitional difficulties of mindfulness and its various training types, the absence of proper control groups, and the inconsistency in combining observational and experimental designs. There are also significant limitations in correlational and cross-sectional studies of trait mindfulness, as well as variability in expertise among participants. The authors collectively call for future research to employ more homogeneous populations, control groups, and randomized longitudinal studies. They emphasize the need for well-defined MRI data analysis protocols to ensure more reliable and comparable results across studies. Overall, the findings suggest that mindfulness changes relationships within the triple network model as well as other functional connectivity.

Default Mode Network

In one of the selected reviews and meta-analyses, mindfulness practices were found to influence the DMN by decreasing its activity during rest and mindfulness meditation. This modulation is accompanied by an increase in functional connectivity between the DMN and the SN, which indicates a dynamic interaction between these networks during mindfulness activities was reported in five of the articles. Additionally, there is a notable decrease in within-network functional connectivity within the DMN in three of the reviews, but that was countered by a noted increase in within-network functional connectivity in the DMN in two of the articles. These changes when paired with reduced connectivity between the DMN and the amygdala, which suggests a potential mechanism for the reduction of emotional reactivity often observed in mindfulness practitioners, however the conflict in results is notable.

Some evidence from MBSR training indicates that an 8-week program results in overall increased connectivity between the prefrontal cortex, hippocampus, and amygdala without significantly altering the DMN. This result conflicts with other reviews highlighting how MBIs alter the DMN and functional connectivity with other networks. While another review highlights long-term mindfulness is associated with increased functional connectivity between the DMN and the Central Executive Network (CEN), but decreased connectivity between the DMN and motor/pain pathways.

One review pointed out how mindfulness meditation practices lead to increased within-network connectivity within the DMN and heightened functional connectivity between the DMN and the ventromedial prefrontal cortex (vmPFC), and special case of within-network connectivity. This emphasizes the importance of the vmPFC in the integration of self-referential processing and emotional regulation within the DMN framework. Moreover, mindfulness meditation increases functional connectivity between the DMN and SN, with notable connectivity changes such as increased dACC-PCC connectivity, indicating enhanced communication between these networks.

Meditation practices broadly affect the DMN by increasing its connectivity with the prefrontal cortex regions, including the dorsolateral prefrontal cortex (dlPFC), dorsomedial prefrontal cortex (dmPFC), ventromedial prefrontal cortex (vmPFC), and orbitofrontal cortex (OFC). Mindfulness also leads to increased functional connectivity with other networks such as the Frontoparietal Network (FPN) and the Ventral Attention Network (VAN). This decreased activity and altered connectivity during meditation suggest a reorganization of the DMN that supports enhanced attention processing and reduced self-referential thinking. Increased coupling between the posterior cingulate cortex (PCC) node of the DMN and the dlPFC node of the FPN has been observed. This enhanced coupling may underlie improved attention control and self-awareness, which are key benefits of mindfulness practices.

Finally, two reviews found that mindfulness and meditation impact the DMN by enhancing the regulation of the DMN by the CEN. This interplay between the DMN and CEN underscores the potential of mindfulness to promote cognitive flexibility and emotional stability through improved network regulation. Overall, the influence of mindfulness on the DMN highlights its significant role in brain network interactions, contributing to the wide-ranging cognitive and emotional benefits associated with these practices. However, conflicting findings are important to note and may be related to heterogeneity in methods and reporting.

Central Executive Network

One review points out that mindfulness practices improve connectivity within the CEN, particularly in executive control and inhibition. While three other studies indicate that mindfulness has either no significant effect on the CEN or at best has mixed modulation of the network. Two of the articles point out increased task-based functional connectivity within the CEN during task-based scans. More detail was highlighted in one review showing that the prefrontal cortex regions such as the dlPFC, dmPFC, vmPFC, and OFC are more interconnected. Two of the articles show increased functional connectivity between the CEN and the amygdala. However, three studies show somewhat conflicting findings support mindfulness meditation not showing significant differences in functional connectivity within the CEN at least compared to other interventions, emphasizing the need for precise and consistent operational definitions and methodologies in mindfulness research.

Mindfulness practices also increase connectivity between the CEN and the SN, particularly involving the right insula. This increased connectivity suggests more integrated network functioning, where the CEN effectively coordinates with the SN to prioritize and manage salient stimuli. The right insula's involvement underscores the importance of interoceptive awareness and emotional regulation in this process.

Salience Network

Mindfulness practices significantly increase activity in the SN in two of the articles. This network plays a crucial role in detecting and filtering salient stimuli, and its heightened activity during mindfulness practices indicates improved sensitivity to relevant environmental cues. Additionally, two reviews concluded that mindfulness increases FC between the SN and the DMN, suggesting enhanced integration between networks responsible for self-referential thought and those involved in processing salient external stimuli. One review highlighted increased connectivity between the SN and the dorsal attention network (DAN), highlighting the SN's role in facilitating attentional shifts and maintaining focus on relevant tasks.

One of the reviews pointed out mindfulness practices leading to increased connectivity between the SN and the CEN, particularly involving the right insula. This increased connectivity suggests a more integrated network functioning, where the SN effectively coordinates with the CEN to prioritize and manage salient stimuli. The right insula's involvement underscores the importance of interoceptive awareness and emotional regulation in this process. Moreover, mindfulness is associated with increased connectivity between the SN and the vmPFC (part of the DMN), highlighting the integration of self-referential processing and emotional regulation within the SN framework.

Related changes in functional connectivity within and between large-scale brain networks include significant alterations involving the cingulate cortex. Increased coupling between the cuneus and SN has been observed, which may underlie enhanced attention control and self-awareness. Improved pain processing is also associated with increased within-network coupling within the SN, suggesting that mindfulness practices can enhance the brain's ability to manage and process pain effectively. The specific increase in connectivity between the SN and DMN during mindfulness practices emphasizes the role of the SN in integrating these networks and reducing mind wandering and self-referential thoughts.

The salience network findings are also not without conflict. Two of the review concluded that there was no different in connectivity between the SN and CEN, and two others reported either mixed results in SN modulations and / or connectivity.

Other Function Connectivity

Though not related to the triple-network model, some other functional connectivity is worth noting from these reviews as they pertain to possible different effect of mindfulness training. Mindfulness practices are associated with increased overall functional connectivity efficiency, particularly in the integration of large-scale brain networks. This general enhancement suggests that mindfulness can improve the brain's ability to communicate across different regions, promoting more cohesive and efficient network functioning. Notably, the benefits of increased functional connectivity do not always correlate with the duration of mindfulness practice, indicating that even shorter periods of mindfulness can lead to significant neural changes.

Mindfulness and meditation practices lead to significant changes in functional connectivity involving the cingulate cortex. Improved pain processing is linked to increased within-network coupling within the SN, suggesting that mindfulness can enhance the brain's ability to manage and process pain effectively.

Lastly, these reviews show mindfulness and meditation practices show shared and divergent effects on large-scale brain networks. These differences suggest that mindfulness and meditation can facilitate better integration of cognitive and emotional processing, but also may have negligible effects depending on the study. Clearly, methodological and reporting heterogeneity must be addressed.

Quality Assessment – AMSTAR2

The application of the AMSTAR 2 tool to our systematic reviews revealed several critical insights into their methodological quality (See Figure 3.2). Most of the reviews performed well on basic methodological criteria, such as the comprehensiveness of the literature search (AMSTAR 4) and the inclusion of detailed study characteristics (AMSTAR 8). However, fewer reviews adequately addressed more advanced requirements, such as providing a satisfactory explanation for observed heterogeneity (AMSTAR 14) or accounting for risk of bias in the interpretation of results (AMSTAR 13).

In terms of critical versus non-critical weaknesses, the AMSTAR 2 analysis highlighted significant gaps. Reviews with critical flaws, such as failure to account for the risk of bias or improper meta-analytical techniques, were markedly downgraded in confidence. This distinction is crucial as it ensures that only systematic reviews with robust methodological rigor are deemed highly reliable, thereby improving the credibility of their conclusions. This rigorous evaluation underscores the importance of addressing both fundamental and advanced methodological practices in systematic reviews.

The findings from the AMSTAR 2 analysis underscore the need for improvements in handling biases and ensuring comprehensive and transparent reporting in systematic reviews. While many reviews met basic methodological standards, the more nuanced aspects of systematic review methodology, such as heterogeneity explanation and bias risk accounting, require further attention. This comprehensive appraisal ensures that healthcare decisions are grounded in the highest quality evidence available, ultimately leading to better outcomes in healthcare interventions.

GRADE – Strength of Evidence

The systematic reviews and meta-analyses generally provided moderate-quality evidence for the effects of mindfulness and meditation on brain connectivity (see Figure 3.3). For instance, Gotink (2016) and Melis et al. (2022) were initially rated as high-quality studies due to their systematic methodologies. However, the final quality of evidence was downgraded to moderate due to concerns about risk of bias, inconsistency in results, imprecision of the effect estimates, and potential publication bias. These studies highlighted consistent findings showing that mindfulness-based interventions (MBIs) can alter brain connectivity, particularly in the prefrontal cortex and DMN, although the exact degree of these changes varied.

Narrative reviews, such as those by Felsch and Kuypers (2022), Lodha and Gupta (2022), Mooneyham et al. (2016), Rathore et al. (2022), Sezer et al. (2022), and Sim et al. (2024), were assessed as low quality. These reviews lacked the methodological rigor and comprehensive risk of bias assessments seen in systematic reviews, leading to significant concerns about bias, inconsistency, and imprecision. For example, the narrative review by Felsch and Kuypers (2022) suggested potential benefits of meditation on cognitive functions and emotional regulation but failed to provide robust quantitative analyses to support these claims. Similar limitations were observed in other narrative reviews, which often did not systematically address heterogeneity among the included studies or potential publication bias.

Zagkas et al. (2022), specifically focusing on how meditation affects the DMN, was evaluated with moderate confidence. This review systematically examined 16 controlled trials involving both experienced and novice meditators, revealing consistent findings that meditation practices can reduce within-network connectivity in the DMN. The studies reviewed showed reduced connectivity within the DMN and altered connectivity patterns with other brain networks, such as the somatomotor and FPN. While the review provided strong evidence supporting the role of meditation in modulating DMN activity, concerns about the risk of bias in the included studies and the precision of the effect estimates led to a moderate quality rating.

While systematic reviews and meta-analyses provide moderate-quality evidence supporting the positive impact of mindfulness and meditation on brain connectivity, narrative reviews offer limited and lower-quality evidence due to methodological shortcomings. Future research should focus on addressing these limitations by conducting high-quality randomized controlled trials and systematic reviews with robust methodologies to further elucidate the mechanisms through which meditation influences brain function and connectivity.

3.4 Discussion

The primary objective of this umbrella review was to systematically evaluate and synthesize the existing evidence from systematic reviews and meta-analyses concerning the effects of mindfulness practices on various aspects of brain connectivity. Specifically, this review aimed to explore how mindfulness influences structural, functional, and effective connectivity within the brain. The overarching goal was to clarify the extent to which mindfulness practices alter brain networks involved in processes such as attention, emotion regulation, cognitive task-related functioning, and self-referential thinking. However, many methodological and reporting concerns also came to light.

The systematic reviews included in this analysis collectively sought to elucidate the effects of mindfulness-based interventions (MBIs) on brain function and connectivity. Common themes across these reviews included examining the neural mechanisms underlying mindfulness practices and determining the efficacy of these interventions in enhancing cognitive and emotional regulation. For instance, Felsch and Kuypers (2022) investigated whether the combination of mindfulness meditation (MM) and psychedelics could produce unique neurobiological effects, while Gotink et al. (2016) explored the neuronal expression of mindfulness through methodologies such as MBSR and MBCT. These studies provided crucial insights into how different forms of mindfulness training impact brain connectivity.

The synthesis revealed inconsistent findings indicating significant changes in key brain networks due to mindfulness practices. For example, the DMN, associated with self-referential thinking and mind-wandering, showed increased functional connectivity (within between?) and altered activity patterns, but some review also reported decreased within-network connectivity. These thought positive changes suggest that mindfulness may enhance the coherence and integration of the DMN, leading to a more present-centered and less self-referential mode of thinking, the contradictory findings suggest that maybe mindfulness has a negligible effect on the DMN. Similarly, the CEN, crucial for cognitive control and executive functions, exhibited increased connectivity and heightened activity during tasks requiring executive function, but some evidence suggests no significant differences.

In addition, the SN, which plays a vital role in detecting and filtering salient stimuli, demonstrated increased connectivity and activity. This enhancement indicates that mindfulness practices may improve the brain's ability to process and respond to important environmental and internal cues effectively, but again, conflicting results suggest either mixed results or mixed modulation of the SN. Moreover, increased connectivity with the amygdala and other brain regions responsible for emotional processing was observed, suggesting enhanced emotional regulation capabilities. These results collectively support the aim of exploring how mindfulness practices influence various brain networks involved in critical cognitive and emotional functions, but once again highlight the need for better methods and reporting.

The results from this umbrella review effectively answer the questions posed in the aims by demonstrating that mindfulness practices significantly alter key brain networks involved in attention, emotion regulation, cognitive task-related functioning, and self-referential thinking. The systematic reviews provided a broad spectrum of assessment methods, varying lengths and types of mindfulness training, and diverse participant samples, offering a comprehensive view of how different aspects of mindfulness practices can impact brain connectivity. This synthesis highlights the robust effects of mindfulness on structural, functional, and effective connectivity within the brain, thereby contributing to a deeper understanding of the neurobiological foundations of mindfulness practices and their potential benefits for mental health outcomes.

Positive implications

The findings from this umbrella review have several larger implications for both clinical practice and public health policy. One of the most significant implications is the potential for mindfulness-based interventions (MBIs) to be integrated into standard therapeutic practices for mental health. The demonstrated effects of mindfulness on enhancing brain connectivity and improving cognitive and emotional regulation suggest that MBIs can be effective in treating a range of mental health conditions, including anxiety, depression, and ADHD. This is particularly relevant given the increasing prevalence of these conditions and the limitations of current treatment options, such as the side effects of medication and the need for long-term therapy.

The improved connectivity within the DMN and the CEN highlights mindfulness's role in fostering cognitive resilience. By promoting a more present-centered and less self-referential mode of thinking, mindfulness practices can help individuals better manage stress and reduce the risk of mental health issues. This has broader implications for workplace wellness programs and educational settings, where mindfulness can be incorporated to enhance focus, reduce burnout, and improve overall mental well-being. Schools and employers could implement mindfulness training programs to support the cognitive and emotional health of students and employees, leading to better academic and professional outcomes.

The enhanced connectivity in the SN and between the amygdala and prefrontal cortex also suggests that mindfulness can play a crucial role in improving emotional regulation. This can be particularly beneficial in high-stress professions, such as healthcare and emergency services, where emotional resilience is critical. Training programs that include mindfulness practices could help professionals in these fields manage stress more effectively, reducing the incidence of burnout and improving job performance. Moreover, these findings support the use of mindfulness in community and clinical settings to help individuals develop healthier coping mechanisms and improve their quality of life.

From a public health perspective, the evidence supporting the neurobiological benefits of mindfulness practices can inform policy decisions related to mental health promotion and disease prevention. Public health campaigns could advocate for the inclusion of mindfulness training in community wellness programs, highlighting its benefits for brain health and emotional well-being. Additionally, policymakers could allocate funding for research and implementation of mindfulness-based programs in various settings, further integrating these practices into the fabric of healthcare and education systems.

The implications of these findings are far-reaching, suggesting that mindfulness practices can significantly contribute to mental health and cognitive well-being across different populations and settings. By incorporating mindfulness into therapeutic, educational, and professional environments, we can enhance the overall mental health of individuals and communities, ultimately leading to a healthier, more resilient society. The integration of mindfulness-based interventions into mainstream practices represents a promising avenue for improving mental health outcomes and fostering cognitive and emotional resilience on a broader scale. However, more research is also needed to determine if there are groups that do not benefit from mindfulness or in which complications might arise.

Methodological Concerns

The current state of research in mindfulness and brain networks reveals a landscape characterized by considerable methodological variability and a lack of standardization. This variability spans across multiple dimensions, including study lengths, training types, participant experience, and sample diversity. These inconsistencies hinder the ability to draw robust conclusions and underscore the necessity for better methodological approaches and more refined operational definitions within this field.

One significant issue is the wide range of training types and experience levels among participants. Studies often include both clinical and non-clinical samples, each with varying baseline characteristics and mindfulness expertise. This diversity, while enriching, also introduces confounding variables that complicate the interpretation of findings. For instance, the comparison of outcomes from short-term interventions with those from long-term practitioners without accounting for baseline differences can lead to misleading conclusions. Therefore, establishing standardized protocols for participant selection and intervention administration is crucial.

Another major concern is the lack of control groups and randomization in many studies. The absence of these methodological rigor elements limits the ability to attribute observed effects directly to mindfulness interventions. Randomized controlled trials (RCTs) are essential for distinguishing genuine intervention effects from placebo or other non-specific effects. Additionally, the use of small sample sizes in numerous studies reduces the statistical power and generalizability of findings. Larger, well-controlled studies are necessary to validate preliminary findings and establish more robust evidence bases.

Neuroimaging studies within mindfulness research also exhibit considerable heterogeneity. Differences in neuroimaging modalities, analysis techniques, and seed selection (choice of specific brain regions of interest from which the temporal correlation with other brain areas is calculated to assess functional connectivity) contribute to inconsistent results across studies. For example, variations in task-based versus resting-state MRI protocols, along with different neuroimaging analysis methods, can lead to divergent conclusions about the same brain regions or networks. The lack of a standardized framework for neuroimaging analysis exacerbates this issue, making it difficult to compare results across studies and build a cohesive understanding of mindfulness-related brain changes.

Moreover, the categorization of brain networks and the selection of seeds for connectivity analysis vary widely, further complicating cross-study comparisons. A standardized approach to defining and categorizing brain networks, as well as selecting seeds, would enhance the reliability and comparability of findings. This standardization would also facilitate meta-analyses and systematic reviews, which are critical for synthesizing evidence and guiding future research directions.

The inconsistencies across studies are not limited to intervention research but extend to trait mindfulness studies as well. The lack of clear operational definitions and standardized measures of trait mindfulness results in varying interpretations and findings. This issue highlights the need for consensus on definitions and measurement tools, which would allow for more accurate comparisons and interpretations of trait mindfulness research.

The field of mindfulness and brain-network research stands to benefit significantly from improved methodological rigor and standardization. Addressing issues related to varied study lengths, training types, participant diversity, and neuroimaging protocols will enhance the reliability and validity of findings. By adopting standardized operational definitions and intervention protocols, researchers can produce more comparable and generalizable results. This, in turn, will advance our understanding of the neural mechanisms underlying mindfulness and its potential therapeutic benefits, ultimately contributing to the development of more effective mindfulness-based interventions.

3.5 Limitations

Despite the promising findings, this umbrella review has several limitations that must be considered when interpreting the results. One significant limitation is the heterogeneity among the included reviews. The systematic reviews and meta-analyses analyzed in this review encompass a wide range of methodologies, participant populations, and mindfulness practices. This diversity, while providing a broad perspective, also introduces variability that can complicate the synthesis of results. Different studies used various lengths and types of mindfulness training, and participants ranged from healthy individuals to those with specific mental health conditions, making it challenging to draw generalized conclusions.

Another limitation is the quality of the included studies. Although the AMSTAR 2 analysis provided insights into the methodological quality of the systematic reviews, several studies exhibited critical weaknesses. These weaknesses include inadequate handling of biases, insufficient explanation of observed heterogeneity, and improper meta-analytical techniques. Such methodological flaws can affect the reliability and validity of the findings. Reviews with critical flaws were markedly downgraded in confidence, highlighting the need for more rigorous research designs and comprehensive reporting standards in future studies.

The sample sizes of the individual studies within the systematic reviews also pose a limitation for the umbrella review overall. Many studies had relatively small sample sizes, which can limit the statistical power and generalizability of the findings. Small sample sizes increase the risk of type I and type II errors, making it difficult to detect true effects or to generalize the results to larger populations. Additionally, the field of mindfulness research is still evolving, and many findings have yet to be replicated in larger, more diverse cohorts. This lack of replication further complicates the interpretation and application of the results.

Moreover, the reliance on self-reported measures in some studies introduces the potential for bias. Self-reported data on mindfulness practice and its effects can be influenced by participants' subjective perceptions and social desirability, leading to overestimation or underestimation of the true effects. Objective measures, such as neuroimaging data, provide more reliable insights but are not always available or feasible in all studies. The combination of subjective and objective measures is necessary to gain a comprehensive understanding of the impacts of mindfulness practices.

Finally, the cross-sectional nature of many studies limits the ability to draw causal inferences. While longitudinal studies provide more robust evidence of the long-term effects of mindfulness practices, they are less common and often face challenges such as participant dropout and adherence to the intervention. Future research should prioritize longitudinal designs to better understand the causal relationships and long-term impacts of mindfulness on brain connectivity and mental health.

Addressing these limitations will enhance the reliability and applicability of future research in this field. More rigorous and standardized research is needed to validate and expand upon the current findings.

In conclusion, this umbrella review highlights the significant impact of mindfulness-based interventions on brain connectivity, demonstrating enhanced functional and structural integration within key neural networks such as the DMN, CEN, and SN. These findings underscore the potential of mindfulness practices to improve cognitive control, emotional regulation, and overall mental health. However, the review also identifies critical methodological limitations, including heterogeneity among studies, small sample sizes, and issues with bias and study quality. Future research should address these limitations with more rigorous, standardized methodologies to validate and expand upon these promising findings. Overall, the integration of mindfulness into clinical, educational, and public health practices holds great promise for enhancing mental well-being and resilience.

CHAPTER 4

COMPASSION MINDFULNESS COMPARED WITH VISUALIZATION DURING FMRI

4.1 Introduction

Mindfulness, a practice deeply rooted in Buddhist meditation, has transcended its spiritual origins to become a key focus of contemporary psychological and neuroscientific research (Weder, 2022). It encompasses the intentional and non-judgmental focus of one's attention on the emotions, thoughts, and sensations occurring in the present moment (Kabat-Zinn, 2003). This tradition has been adapted in modern therapeutic practices to help reduce stress, promote emotional regulation, and enhance overall cognitive capabilities (King et al., 2013; Vibe et al., 2017). As mindfulness gains prominence in psychological research, it continues to be shaped by its historical context and evolving interpretation, reflecting its integration into therapeutic frameworks. This background forms the foundation of ongoing studies aimed at exploring its benefits and mechanisms, highlighting its significance.

Mindfulness has increasingly become a subject of modern neuroscience, particularly through the use of functional magnetic resonance imaging (fMRI). This technique allows researchers to observe brain activity in real time, providing insights into the neural underpinnings of mindfulness practices (Ogawa et al., 1990). By examining changes in brain regions associated with attention, self-awareness, and emotion regulation during mindfulness exercises, fMRI studies have begun to map out how these practices influence the brain's structure and function over time. This growing body of research not only enriches our understanding of mindfulness but also enhances its applicability in therapeutic contexts, where it can be used to address various psychological and neurological disorders.

In the context of mindfulness, two primary types are often studied: focused-attention (FA) and open-monitoring (OM) mindfulness. FA mindfulness involves concentrating one's attention on a particular object, thought, or sensation, in order to promote the enhancement of attentional stability and control (Lutz et al., 2008). On the other hand, OM mindfulness does not focus on a specific object but rather involves non-reactive monitoring of the content of experience from moment to moment. Both types of mindfulness aim to cultivate a state of alert, focused relaxation by directing attention in different ways, each engaging distinct but sometimes overlapping brain systems.

Recent studies using fMRI have demonstrated how FA and OM mindfulness affect brain activity. FA mindfulness typically activates brain regions involved in attentional control, such as the dorsolateral prefrontal cortex and posterior parietal cortex (M. D. Fox et al., 2005; Tallon-Baudry, 2004). OM mindfulness entails broadened awareness and is associated with increased activation in brain regions related to monitoring and awareness, such as the somatosensory cortex, insula, and posterior cingulate cortex (K. Fox et al., 2014; M. D. Fox et al., 2005; Ursu et al., 2009). By examining the specific brain regions activated during different types of mindfulness practices, researchers can better understand the mechanisms through which these practices exert their effects.

The relevance of mindfulness in neuroscience extends beyond its therapeutic potential. Studies using fMRI to observe brain patterns during mindfulness practices have revealed significant changes in areas related to attention (Dickenson et al., 2013), emotion regulation (Guendelman et al., 2017), and self-awareness (Farb et al., 2007). These findings suggest that mindfulness can induce tangible changes in brain function and connectivity (Kilpatrick et al., 2011; Melis et al., 2022).

Despite the growing body of research, significant gaps remain in our understanding of how compassion mindfulness, influences brain activity. Compassion mindfulness involves cultivating feelings of loving-kindness and compassion towards oneself and others. This practice differs from other forms of mindfulness, such as focused attention (FA) and open monitoring (OM), by emphasizing emotional connectivity and empathetic responses.

Current research primarily focuses on FA and OM meditation practices. These studies often overlook the unique emotional and cognitive processes involved in compassion mindfulness. The gap lies in the limited understanding of how this distinct practice impacts brain regions associated with empathy, emotional regulation, and social cognition. By investigating these specific impacts, this study aims to enrich our understanding of how compassion mindfulness could enhance emotional resilience, social connectedness, and overall well-being. While compassion mindfulness shares some characteristics with FA (concentrating on themselves or groups of people) and OM (extending awareness to the world), compassion mindfulness has been demonstrated to have additional effect on empathy and pro-social behavior (Lippelt et al., 2014).

Additionally, there is a need to examine these effects using rigorous, controlled experimental designs to rule out confounding variables and ensure the reliability of findings. This study addresses these gaps by comparing brain activation patterns between audio visualization (control) and compassion-guided mindfulness (experimental) exercises. The comparative approach will not only highlight specific brain regions involved in each exercise, but also point to new therapeutic applications such as compassion-focused therapy (Gilbert, 2009). Little is known about how this practice affects the brain during practice.

The primary aim of this study is to compare the neural correlates of two distinct exercises—audio visualization and audio guided compassion mindfulness—using fMRI technology. To our knowledge there is no existing study with such a comparison from data collected while participants engage in these exercises in the scanner.

Our goal is to explore how this form of mindfulness practice influences brain activity over time and to identify specific changes in areas associated with emotional regulation and pro-social behavior. We aim to examine differential brain activity in response to compassion mindfulness compared to baseline measurements. We expect to see significant changes in a linear response (versus baseline) in whole-brain activity during compassion mindfulness practice relative to baseline as well as differential activity in key regions of interest (ROIs) that have been implicated in emotional regulation and pro-social behavior, including the amygdala, anterior cingulate cortex (ACC), ventromedial prefrontal cortex (vmPFC), and insula.

We seek to contribute to the broader field of neuroscience by providing empirical data on how an audio guided compassion mindfulness practice modulates brain activity. This research will not only fill existing knowledge gaps but also pave the way for future studies to explore how these practices can be integrated into mental health treatments.

4.2 Methods

Participants

Participants were 42 adults between the ages of 21-77 (M = 46.3 yrs., SD = 19.9 yrs) and consisted of 20 male participants (37%) and 34 female participants (63%) in terms of sex assigned at birth. Participants tended to be highly educated, on average. Eight were high school graduates (15%), 18 had bachelor's degrees (33%), 16 had master's degrees (30%), and 5 had doctoratal degrees (9%). The sample was largely White (n = ???; 83%) with 2 black participants (4%), 2 Asian or pacific islander participants (4%), and 5 multiracial participants (9%). Participants were recruited from the Fort Collins, CO area through flyers posted around the community and community recruitment (see Table 1). Inclusion criteria included being right-handed, aged 18 to 85 years old, fluent in English, good (or correctable) vision and hearing, and able to perform the cognitive and imaging tasks required. Exclusion criteria included inability to give consent (i.e., under conservatorship or otherwise unable to make financial and/or health decisions), contraindications for MRI, significant head injury (head injury that resulted in a concussion, scalp laceration, or skull fracture or penetration), physical or psychological disability, prescription for medications that affect the neurovascular system, alcohol or substance dependence, neurological illness, left handedness as this can cause problem when examining potential lateralized effects in the brain, that is left-handed individuals tend to show less lateralization overall (Johnstone et al., 2021). We also specifically recruited participants without major neurological or psychiatric disorders and without major physical or psychological disabilities.

The study was approved by and carried out in accordance with the recommendations of the Institutional Review Board (IRB) at Colorado State University (IRB# 3517) with written. informed consent from all participants.

Procedure

After establishing contact, participants underwent a phone screening procedure for inclusion and exclusion criteria which included a short questionnaire and MRI contraindications screening. Mindfulness experience was assessed in the pre-screen. Qualifying individuals were scheduled for appointments at the Colorado State University Translation Medicine Institute (TMI) MRI Center.

Informed written consent was obtained in person from the research staff. A second, in-person screen was then conducted by trained research staff. A brief physical examination was conducted to assess height, weight, blood pressure, and eyesight to confirm participants' ability to complete the study requirements. A brief cognitive assessment, the Montreal Cognitive Assessment (MoCA), was used to screen for dementia.

Participants were randomly assigned to either the guided visualization or compassion mindfulness paradigm using a between subjects design. A randomization table was created using the blockrand R package based on our target of 60 participants. Both tasks are matched on time of the guided protocol and time of audio versus non-audio portions. The task design followed a progression that started with relaxation and instruction (40s), then self-focused compassion or visualization (50s * 2), then rest and instruction (50s), then other focused compassion or visualization (50s * 2), then rest and instruction (30s), then world focused compassion or visualization (50s * 2). Please see Figure 4.1 for task design and supplementary materials for scripts.

MRI Acquisition

We acquired images on a Siemens 3.0T Magnetom XQ Numaris/X VA30A-03GR system with XQ gradient strength of 45 mT/m gradients and 200 T/m/sec slew rates and XT gradient strength of 60 mT/m gradients and 200 T/m/sec slew rates. After brief scout and field map scans were completed, T1-weighted images were acquired using a 3D MPRAGE (TR = 2300 ms; TE = 2.32 ms; TI: 900 ms; matrix = 256 × 256; FOV = 240 mm; 192 slices; 0.9 × 0.9 × 0.9 mm3 voxels size; GRAPPA acceleration factor 2). Blood oxygen level dependent (BOLD) fMRI scans for the visualization or compassion mindfulness portion of the scan lasting 8:02 min were acquired while the participant listened to and participated in the guided protocols (TR 800 ms; TE = 38 ms; FOV 210mm; 54 slices; 593 measurements).

MRI Preprocessing

Results included in this manuscript come from preprocessing performed using fMRIPrep 20.2.7 (Esteban, Markiewicz, et al. (2018); Esteban, Blair, et al. (2018); RRID:SCR_016216), which is based on Nipype 1.7.0 (Gorgolewski et al. (2011); Gorgolewski et al. (2018); RRID:SCR_002502). The below statement is copied directly from output of the pipeline and is required to be included in manuscripts verbatim as part of the agreement for using this software.

Anatomical data preprocessing

The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al. 2010), distributed with ANTs 2.3.3 (Avants et al. 2008, RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 5.0.9, RRID:SCR_002823, Zhang, Brady, and Smith 2001). Brain surfaces were reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847, Dale, Fischl, and Sereno 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (RRID:SCR_002438, Klein et al. 2017). Volume-based spatial normalization to two standard spaces (MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al. (2009), RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym], FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model [Evans et al. (2012), RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym].

Functional data preprocessing

For each of the 4 BOLD runs found per subject (across all tasks and sessions), the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. A B0-nonuniformity map (or fieldmap) was estimated based on a phase-difference map calculated with a dual-echo GRE (gradient-recall echo) sequence, processed with a custom workflow of SDCFlows inspired by the epidewarp.fsl script and further improvements in HCP Pipelines (Glasser et al. 2013). The fieldmap was then co-registered to the target EPI (echo-planar imaging) reference run and converted to a displacements field map (amenable to registration tools such as ANTs) with FSL's fugue and other SDCflows tools. Based on the estimated susceptibility distortion, a corrected EPI (echo-planar imaging) reference was calculated for a more accurate co-registration with the anatomical reference. The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve and Fischl 2009). Co-registration was configured with six degrees of freedom. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 5.0.9, Jenkinson et al. 2002). The BOLD time-series (including slice-timing correction when applied) were resampled onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility distortions. These resampled BOLD time-series will be referred to as preprocessed BOLD in original space, or just preprocessed BOLD. The BOLD time-series were resampled into several standard spaces, correspondingly generating the following spatially-normalized, preprocessed BOLD runs: MNI152NLin2009cAsym, MNI152NLin6Asym. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Corresponding "non-aggresively" denoised runs were produced after such smoothing. Additionally, the "aggressive" noise-regressors were collected and placed in the corresponding confounds file. Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions, Power et al. (2014)) and Jenkinson (relative root mean square displacement between affines, Jenkinson et al. (2002)). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al. 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor, Behzadi et al. 2007). Principal components are estimated after high-pass filtering the preprocessed BOLD time-series (using a discrete cosine filter with 128s cut-off) for the two CompCor variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 2% variable voxels within the brain mask. For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space. The implementation differs from that of Behzadi et al. in that instead of eroding the masks by 2 pixels on BOLD space, the aCompCor masks are subtracted a mask of pixels that likely contain a volume fraction of GM. This mask is obtained by dilating a

GM mask extracted from the FreeSurfer's aseg segmentation, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al. 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardised DVARS were annotated as motion outliers. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos 1964). Non-gridded (surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Many internal operations of fMRIPrep use Nilearn 0.6.2 (Abraham et al. 2014, RRID:SCR_001362), mostly within the functional processing workflow. For more details of the pipeline, see the section corresponding to workflows in fMRIPrep's documentation.

Post-Processing

For the functional MRI data, a key step in the processing pipeline is the application of smoothing which is applied to the pre-processed BOLD images using Gaussian kernels, which helps in improving the signal-to-noise ratio and ensures that the data conforms to the assumptions of random field theory. The AROMA technique operates by decomposing the fMRI data into independent components and then classifying these components as either signal or noise based on their spatial and temporal characteristics. The noise components, primarily related to motion, are subsequently removed, enhancing the overall quality of the fMRI data. This dual approach of smoothing and artifact removal ensures that the resulting images are both clearer and more representative of the true neural activity, facilitating more accurate downstream analyses.

Analysis

General Linear Model (GLM)

The GLM analysis was conducted using a custom Python script designed to automate parameter estimation of general linear models (GLMs) on fMRI data from a BIDS-formatted dataset. Initially, the script configured to set paths for the BIDS dataset and output directory, along with the task name to be analyzed. A BIDS layout object was then initialized to navigate the dataset structure.

For each subject, the script ran a function to format the subject and session IDs and created a subject-specific output directory. It retrieved functional MRI files and event files for the specified task using the BIDS layout object, manually filtering functional files to include only those with appropriate preprocessing and smoothing.

The event files were read to create timing files for each condition (e.g., ‘linear’, 'self', 'other', 'world') by extracting onset times and durations. These conditions and their corresponding onset times were used to prepare the AFNI GLM, specifying stimulus times and labels. Motion parameters we retrieved from the fMRIPrep pipeline’s confounds tab separated values output files. These were later included in the design matrix and following regression.

We then defined the AFNI GLM parameters, including input functional MRI files, parallel processing jobs, overwriting existing files, local times for stimulus timing, polynomial trend removal, paths to save the design matrix and JPEG images, various statistical outputs (F-statistics, R^2 statistics, T-statistics, variance estimates, beta coefficients), the number of stimulus time series, stimulus times and labels, general linear test contrasts, motion parameters for nuisance regression, and paths to save GLM results and residual time series. The AFNI 3dDeconvolve command (which estimates the parameters of a GLM for fMRI data, providing statistical maps and design matrices for brain activation analysis) was executed to estimate the GLM parameters for each subject (baseline (calculated from a combination of initial relaxation, rest periods, and instruction periods), linear, quadratic, quartic, and task phase parameters (self, other, world).

Calculate percent signal change & extraction for ROI analysis

Next we used a Python script to calculate percent signal change and extract region-of-interest (ROI) statistics from fMRI data (see figure 4.2 for ROIs). The script defined indices corresponding to various conditions (e.g., linear, baseline, self, other, world, and contrasts between these conditions) and specified the calculations to be performed (linear vs. baseline). A function `run_3dcalc` was created to run the AFNI `3dcalc` command, which calculates the percent signal change between specified conditions for a given subject.

To binarize the ROI masks, a function `binarize_mask` was defined. This function took the path to a mask file, created a binarized version of the mask using the `3dcalc` command with a step function, and returned the path to the binarized mask. If the binarized mask already existed, it was reused.

The script iterated through all subjects, constructing the path to each subject's directory. If a subject's directory did not exist, the script skipped to the next subject. For each subject, it performed the specified calculations using the `run_3dcalc` function and extracted data for each mask using the `run_3dROIstats` function (calculates statistical summaries (e.g., mean, standard deviation) within specified regions of interest (ROIs) in fMRI datasets, facilitating region-specific analysis).

Combine data

The analysis involved using a Python script to combine data from multiple text files into a single CSV file. This process ensured that the relevant percent signal change data from the ROI stats files was aggregated into a single, clean CSV file for further analysis.

ROI analysis in R

An R script was then used to perform an analysis of fMRI data using various t-tests to compare groups and linear versus baseline conditions for each ROI. We used single-sample t-tests to compare the percent change in fMRI signal within each condition and ROI against baseline for each group separately, calculating effect sizes (Cohen's d) and storing the results in a tidy format. Independent-sample t-tests compare the percent change between the compassion and visualization groups for each condition and mask combination, again calculating Cohen's d for effect size. The results of all t-tests are compiled into data frames and output to CSV files for further analysis and visualization.

Finally, A whole brain voxel wise analysis was conducted to identify significant changes in brain activity. This analysis employs a voxel-based approach, which examines the brain at a fine-grained level, allowing for detailed mapping of functional and structural changes without a priori assumptions about specific regions of interest. This method is particularly advantageous for detecting widespread or diffuse changes in brain activity and connectivity. Specifically, we used the AFNI 3dttest++ command (which performs voxel-wise t-tests on fMRI datasets, allowing for single-sample, paired-sample, and independent-sample statistical comparisons across brain images) on grey matter masked post-GLM images to perform group single-samples ttest for within group comparisons as well as independent-samples to compare between group effect. Enhancement of Thresholded Adaptive Clustering (ETAC) was used during the 3dttest to control for false positives in neuroimaging data by adjusting thresholds based on spatial clustering. We then thresholded the results at $p = 0.05$ and used the AFNI clustering tool (identifies and visualizes clusters of significant voxels in statistical maps, enhancing the interpretation of brain imaging results by highlighting spatial patterns of activation) set to NN of 2 (meaning it considers voxels to be significant clusters if faces or edges are touching) to identify significant results.

4.3 Results

Whole Brain Results

Before motion correction and ETAC, significantly less relative activity was detected in the medial superior prefrontal cortex (msPFC) for the compassion mindfulness group versus the visualization group for a 204 voxel cluster ($p < 0.05$). Significantly less relative activity was also detected in the primary motor cortex (BA 4) for the compassion mindfulness group versus the visualization group for a 90 voxel cluster ($p < 0.05$). The right cerebellum showed significantly less relative activity for the compassion mindfulness group versus the visualization group within

72 voxels ($p < 0.05$). Significantly less relative activity was also seen in the left ACC (Broadman Area 32) for a 38 voxel cluster ($p < 0.05$).

After motion correction and ETAC, significantly different relative activity was detected in several brain regions for the compassion meditation group versus the visualization group (See Figure 4.3). In the left posterior cingulate cortex, significantly greater relative activity was found in the compassion meditation group for a 40 voxel cluster ($p < 0.05$). The right precuneus showed significantly greater relative activity for the compassion meditation group within a 33 voxel cluster ($p < 0.05$). The left frontal pole exhibited significantly greater relative activity for the compassion meditation group for a 29 voxel cluster ($p < 0.05$). In the right inferior parietal lobule, significantly greater relative activity was detected for the compassion meditation group within a 28 voxel cluster ($p < 0.05$). The left cerebellum showed significantly greater relative activity for the compassion meditation group within a 27 voxel cluster ($p < 0.05$). The right cerebellum also exhibited significantly greater relative activity for the compassion meditation group within a 25 voxel cluster ($p < 0.05$). Another significant cluster was observed in the right precuneus with greater relative activity for the compassion meditation group within a 22 voxel cluster ($p < 0.05$). Finally, the left supramarginal gyrus showed significantly greater relative activity for the compassion meditation group within a 21 voxel cluster ($p < 0.05$).

Region of Interest Results

When examining the linear versus baseline effects of different conditions in single sample t-tests, we observe notable patterns in specific brain regions (See Tables 4.2 and 4.3). The compassion condition consistently shows positive effect sizes across all masks. For instance, in the amygdala, the compassion condition shows a small effect size. In the anterior cingulate cortex (ACC) and the insula, the compassion condition exhibits larger effect sizes, particularly in the insula, where the effect size is 0.416 and the p-value trends towards significance, indicating a possible meaningful engagement of this region during compassion practices.

In contrast, the visualization condition presents a more varied picture. In the amygdala, the visual condition shows a moderate negative effect size, with a p-value that is trending, implying a potential reduction in engagement of this region. The ACC and the ventromedial prefrontal cortex (vmPFC) under the visual condition display minimal effect sizes, indicating that these regions are not substantially affected by the visualization task compared to the baseline. Overall, the compassion condition appears to engage the amygdala, ACC, and insula more robustly than the visual condition. This suggests that compassion practices might stimulate these regions associated with emotional processing and interoception more effectively.

The results of the independent-samples t-test comparing the effects of compassion mindfulness and visualization on various regions of interest (ROIs) are summarized in Table 4.3. In the amygdala, anterior cingulate cortex (ACC), ventromedial prefrontal cortex (vmPFC), and insula, there were no statistically significant differences between the compassion mindfulness and visualization groups. Although there were variations in the mean differences and effect sizes across these ROIs, none reached statistical significance.

4.4 Discussion

This study explored the impact of compassion mindfulness practice on brain activity, focusing on areas associated with emotional regulation and pro-social behavior. We hypothesized that there would be significant changes in whole-brain activity and specific regions of interest (ROIs), such as the amygdala, anterior cingulate cortex (ACC), ventromedial prefrontal cortex (vmPFC), and insula, when comparing compassion mindfulness practice to baseline measurements. The results provide partial support for our hypotheses. While there were observable trends indicating increased engagement in the amygdala, ACC, and insula during compassion mindfulness practice, only the insula showed a near-significant effect size. The relative reduction in whole-brain activity for compassion mindfulness compared to visualization suggests a interplay of neural dynamics that may not align with a simple increase or decrease in activity. Future studies should further investigate these patterns to better understand the nuanced effects of compassion mindfulness on brain function.

Whole Brain Analysis

The results from the whole-brain voxel-wise analysis highlight significant neural modulation in several key brain regions during compassion mindfulness practice. Understanding why these regions are important can provide deeper insights into the neural mechanisms underlying this practice. The msPFC plays a crucial role in self-referential thinking, decision-making, and social cognition, including understanding others' emotions and intentions. The mPFC is also involved in regulating emotional responses and integrating information about oneself with external social information. Its functions are essential for introspection, empathy, and maintaining a coherent sense of self. Decreased activity in the msPFC during compassion mindfulness were unexpected and may suggest reduced self-referential processing and enhanced emotional regulation (Beadle et al., 2018).

The primary motor cortex's relative decrease might reflect the embodiment of compassion, where imagining compassionate actions may activate motor representations. This aligns with the concept of embodied cognition, suggesting that mental practices can engage physical systems in the brain. The anterior cingulate cortex (ACC) is known for its role in emotional regulation, attention, and error detection (Eisenberger, 2015). A relative decrease in activity in the ACC during compassion mindfulness might indicate relaxed emotional processing and open monitoring between compassionate intentions and negative responses.

Finally, the right cerebellum, traditionally associated with motor control, is increasingly recognized for its role in cognitive and emotional processing (Adamaszek et al., 2017). Involvement of the cerebellum during compassion mindfulness might relate to the relaxation of fine-tuned emotional responses and cognitive processes, contributing to the overall effectiveness of the practice. Together, these findings provide a comprehensive map of brain activity differences during compassion mindfulness, illustrating significant neural modulation in regions associated with motor, attentional, emotional, and cognitive functions.

Post-motion-correction and ETAC, the identified significant clusters of activation differences between participants engaging in compassion meditation and those performing visualization tasks during fMRI suggest differential engagement of cognitive and emotional processes in these groups. The left posterior cingulate cortex, a region associated with self-referential thinking and emotional regulation, showed significant relative increased activation in the compassion meditation group. The right precuneus, involved in visuo-spatial imagery and episodic memory retrieval, also showed significant relative increased activation for the compassion group, which was unexpected give its likely role in the visualization task. This could indicate changes in the default mode network, but that is outside of the scope of this paper. The left frontal pole, associated with complex cognitive functions such as planning and decision-making, exhibited a significant relative decrease in activation for the compassion group, perhaps reflecting a lower cognitive demand for compassion meditation. The right inferior parietal lobule, related to attention and spatial awareness, showed a significant relative increase in activation for the compassion group, suggesting increased attention and awareness. Both the left and right cerebellum, which are crucial for motor control and coordination, showed relatively significant increases in three clusters for the compassion group, which would be more expected from the visualization group. However, as mentioned earlier, the cerebellum has been increasingly recognized for its role in cognitive and emotional processing (Adamaszek et al., 2017). Additionally, the left supramarginal gyrus, associated with language processing and perception, exhibited a significant relative increase in activation for the compassion group, possibility indicating involvement of greater cognitive resources dedicated to perception during the meditation task. All of these findings point to distinct neural mechanisms underlying compassion meditation, setting this type of meditation apart from FA and OM mindfulness. This also highlights the importance of treating different types of mindfulness differently and a simultaneous call for more research on these types.

ROI Analysis

First, and perhaps most importantly, the independent samples t-tests revealed no significant differences between conditions across the various masks, indicating that the comparisons between different types of stimuli did not yield substantial neural activity changes. However, some conditions showed trending effects, suggesting potential areas for further investigation.

The compassion condition consistently showed positive engagement across all ROIs, with notable effect sizes in the amygdala, anterior cingulate cortex (ACC), and insula. The insula, in particular, exhibited a larger effect size, suggesting a significant engagement during compassion practices. This aligns with previous research indicating the insula's role in interoception and emotional processing, which are key components of compassion practices.

In contrast, the visualization condition presented a more varied pattern. While the amygdala showed a moderate negative effect size, implying a potential reduction in engagement, the ACC and ventromedial prefrontal cortex (vmPFC) displayed minimal effect sizes, indicating that these regions were not substantially affected by the visualization task compared to the baseline. This suggests that visualization may not engage the neural circuits associated with emotional processing and interoception to the same extent as compassion practices.

These results underscore the potential of compassion mindfulness practices to more effectively stimulate brain regions involved in emotional regulation and self-awareness. The engagement of the amygdala, ACC, and insula highlights the unique neural activation patterns elicited by compassion practices, which could be leveraged in therapeutic settings to enhance emotional and cognitive functioning.

Across these analyses, several conditions showed trending effects rather than significant results. These trends, coupled with the small sample size, suggest that while some effects may be present, they might not reach statistical significance due to limited statistical power. The small sample size could lead to Type 2 errors in the results, indicating that larger studies are needed to confirm these findings. The observed trends provide valuable insights and directions for future research, highlighting areas where significant effects may be found with increased sample sizes and more robust experimental designs.

4.5 Limitations

This study, while providing insights into the neural mechanisms of compassion mindfulness, has several limitations that should be considered when interpreting the results. Firstly, the small sample size of 42 participants may affect the statistical power of the findings. With such a limited number of participants, the ability to detect subtle effects is reduced, and the results may not be generalizable to a larger population. The small sample size increases the risk of Type II errors, where true effects are not detected, and may also inflate the effect sizes observed. There was also no specific evaluation of the extent to which participants actually engaged in the audio compassion meditation task outside of overall comments about their experience during the study. Also, the use of traditional compassion mindfulness practices in the study could lead to potential collinearity with the linear regressor (the traditional linear progression of the practice and subsequent ‘task’ timing could be correlated to scanner drift) and a lack of proper randomization of self, other, and world conditions. The baseline condition in this study included audio instruction time, which may not provide a proper baseline for comparison. This could introduce variability and confounding factors that obscure the true effects of the conditions being studied. We did not collect data on the participant’s mindfulness experience, which could be a potential moderator of the brain activity we saw in the results. Additionally, the lack of randomization could result in order effects, where the sequence of conditions influences the outcomes. Thirdly, some effects observed in the study could potentially be a linear trend confounded with scanner drift. Scanner drift is a gradual change in the scanner's sensitivity over time, which can introduce systematic bias into the results. If the observed main effect is partially due to scanner drift, it may not accurately reflect the neural activity associated with the experimental conditions. Lastly, the lack of diversity in the sample based on the area in which the participants were recruited is a significant limitation. The sample may not represent the broader population, limiting the generalizability of the findings. A homogenous sample can introduce biases related to demographic factors such as ethnicity, socioeconomic status, and cultural background, which may influence neural processing and the effects of mindfulness practices.

Future directions

Based on the discussion and limitations of the current study, several avenues for future research emerge to advance the understanding of mindfulness and its neural mechanisms.

Increasing the sample size in future studies is essential. Larger, more diverse samples will enhance statistical power and generalizability, aiding in detecting subtle neural effects and reducing the risk of Type II errors. This approach will support more robust conclusions and broader applicability to diverse populations.

Improving the design and randomization of mindfulness interventions is another critical area. Ensuring proper randomization of conditions, establishing a more accurate baseline condition that excludes audio instruction time, and accounting for participant mindfulness experience will help in isolating the true effects of mindfulness practices. Such improvements will minimize potential confounding factors, providing clearer insights into the specific neural mechanisms involved.

Addressing technical factors such as scanner drift is crucial for future research. Implementing strategies to control for scanner drift and other technical variations will aid in accurately interpreting observed neural changes as genuine effects of mindfulness practice, rather than artifacts of the scanning process.

Recruiting more diverse samples is necessary to ensure findings are representative and applicable across various demographic groups. Including participants from different ethnic, socioeconomic, and cultural backgrounds will provide a more comprehensive understanding of how mindfulness practices impact diverse populations.

Beyond these methodological enhancements, several promising research areas warrant exploration. Examining the long-term effects of compassion mindfulness practice on brain function and structure through longitudinal studies can offer valuable insights into how sustained mindfulness practice influences neural plasticity and cognitive functions over time.

Investigating mindfulness in specific populations, such as children and adolescents, holds significant potential. Research focusing on how mindfulness interventions can support emotional regulation, attention, and academic performance in younger populations can inform educational practices and mental health interventions.

Additionally, exploring the phenomenological aspects of mindfulness practice can provide a deeper understanding of the full spectrum of mindfulness-related outcomes. Investigating the subjective experiences of individuals during mindfulness meditation, including non-ordinary states of consciousness and spiritual experiences, can enrich our knowledge of mindfulness practice's diverse effects.

Overall, future research should aim for rigorous fMRI studies using different types of mindfulness practices to understand their unique neural mechanisms. By addressing these areas, we can better appreciate the complexities and benefits of mindfulness, ultimately enhancing its application in both clinical and non-clinical settings..

This study underscores the nuanced role of various brain regions in compassion mindfulness, particularly highlighting significant neural changes in the ACC, Amygdala, Insula, and vmPFC. While the findings provide valuable insights into the neural mechanisms of mindfulness, several limitations, including a small sample size, potential collinearity, lack of proper randomization, and limited diversity, necessitate cautious interpretation. Future research should address these limitations by increasing sample sizes, improving experimental design, and exploring long-term effects and diverse populations. Advancing mindfulness research in these directions will enhance our understanding of its neural underpinnings and broaden its applicability and effectiveness across various contexts. Specifically, compassion mindfulness has the potential to help increase empathy and compassion, improve self-talk and lower self-criticism, improve prosocial behavior and emotional regulation. Knowing how these practices alter brain function can also help us apply different mindfulness techniques in perhaps unexpected ways. For instance, knowing that compassion mindfulness produces a relative increase in posterior cingulate activity, could help counteract decreases in activity noted in that region in Alzheimer's disease (and a range of others; (Leech & Sharp, 2014)

Overall, these findings contribute to our understanding of the neural underpinnings of self-referential and other-related processing during compassion mindfulness, emphasizing the roles of the ACC, Amygdala, Insula, and vmPFC, posterior cingulate, precuneus, and cerebellum in these cognitive and emotional processes. The nuanced patterns of neural activity underscore the complexity of brain functions and the importance of considering both significant and trending results in neuroimaging research.

CHAPTER 5

OVERALL DISCUSSION

This dissertation aimed to enhance our understanding of mindfulness through psychometric analysis, neurobiological synthesis, and experimental neuroimaging. It evaluates the validity and reliability of the MAAS and FFMQ in PTSD populations, conducts an umbrella review of literature on brain networks related to mindfulness, and uses fMRI to compare brain activity during a visualization task and a guided compassion mindfulness task. This comprehensive approach aims to reveal how mindfulness practices influence brain function and connectivity, contributing to both methodological advancements and deeper insights into the neural mechanisms underlying mindfulness.

The preceding chapters of this dissertation have provided a comprehensive examination of the multifaceted concept of mindfulness, incorporating psychometric evaluations, brain network research, and experimental fMRI studies. The primary objective has been to elucidate the psychological constructs, neurobiological mechanisms, and experiential activation dimensions of mindfulness.

Chapter 2 focused on the psychometric evaluation of the Mindful Attention Awareness Scale (MAAS) and the Five Facet Mindfulness Questionnaire (FFMQ) within populations diagnosed with PTSD. This chapter aimed to validate these tools in a specific clinical context, providing insights into their reliability and applicability. The findings indicated that both MAAS and FFMQ are robust measures of mindfulness, capable of capturing distinct facets of mindfulness experiences in individuals with PTSD. The psychometric properties confirmed their utility in both clinical and research settings, supporting the integration of these tools into broader studies on mindfulness and mental health. However, we also observed that higher order constructs do not seem to align with a simple single latent construct of ‘mindfulness’.

From Chapter 2, we learned that mindfulness is a complex, multifaceted construct that can be reliably measured using psychometric tools like MAAS and FFMQ. These tools have demonstrated validity in diverse populations, including those with PTSD, suggesting that mindfulness encompasses various dimensions such as attention regulation, present-moment awareness, and non-judgmental acceptance. The evaluation also highlighted the importance of using psychometrically sound instruments to capture the nuanced experiences of mindfulness, which is critical for both clinical assessment and research purposes. Moreover, it points to the possibility that mindfulness is not a single construct, but instead could be more than the single construct we are attempting to measure. More refined tools are needed to delineate the complex nature of mindfulness. Importantly, we also found that these mindfulness measures, while reliable and valid, do not all assess the same individual difference dimension / higher order construct. Therefore, researcher might be measuring things that they refer to as mindfulness, which could represent different aspects of mindfulness and different human traits.

Chapter 3 presented an umbrella review of the existing literature on brain networks and connectivity related to mindfulness. This chapter synthesized findings from multiple systematic reviews and meta-analyses, providing a comprehensive overview of how mindfulness practices influence structural, functional, and effective connectivity within the brain. The review highlighted the impact of mindfulness on large-scale brain networks, particularly the DMN, CEN, and SN. Findings consistently showed that mindfulness practices can modulate these networks, enhancing cognitive and emotional regulation. However, the review also pointed out significant methodological heterogeneity and the need for standardized approaches in future research.

In Chapter 3, we expanded our understanding of mindfulness by examining its network relationships. The review demonstrated that mindfulness practice is associated with significant changes in brain connectivity, particularly in networks involved in self-referential thinking, cognitive control, and emotional regulation. These findings support the notion that mindfulness is not merely a psychological state but also a practice that can induce substantial neuroplasticity. However, and perhaps more importantly, the chapter also highlighted issues with variability in research methodologies that have led to conflicting results even between reviews and metanalyses, including differences in study design, participant characteristics, and neuroimaging techniques. This variability underscores the need for more rigorous and standardized research methodologies to ensure the reliability and generalizability of findings.

The methodological heterogeneity identified in Chapter 3 is particularly notable. Studies varied widely in their definitions of mindfulness, the specific practices examined, the duration and intensity of interventions, and the neuroimaging methods employed. For example, some studies focused on brief mindfulness inductions, while others examined long-term meditation practice. Additionally, differences in participant characteristics, such as age, gender, and baseline mental health status, further complicate the comparison of results across studies. This lack of standardization leads to inconsistencies in findings and poses significant challenges for synthesizing and interpreting the evidence on mindfulness and brain connectivity. Future research must address these methodological issues by adopting standardized protocols and ensuring greater consistency in study designs and participant characteristics.

Chapter 4 explored the neural correlates of compassion mindfulness compared to a visualization task using fMRI. The study revealed significant differences in brain activation patterns between the two conditions. Compassion mindfulness was associated with decreased activity in the medial superior prefrontal cortex (msPFC), primary motor cortex, right cerebellum, and anterior cingulate cortex (ACC) compared to the visualization task. These findings suggest that compassion mindfulness engages brain regions involved in emotional regulation, motor control, and cognitive functions. The region of interest (ROI) analyses further supported these results, showing significant changes in neural activity in areas such as the ACC, amygdala, insula, and ventromedial prefrontal cortex (vmPFC) during self-referential processing.

Integrating these chapters, the discussion addresses the central questions and concerns raised in Chapter 1. The psychometric validation of mindfulness scales confirms their relevance and accuracy in assessing mindfulness in both clinical and non-clinical populations. The synthesis of brain network research underscores the transformative impact of mindfulness on neural connectivity, highlighting its potential to enhance cognitive and emotional functioning through the modulation of key brain networks. The experimental fMRI study provides empirical evidence of the distinct neural mechanisms underlying compassion mindfulness, suggesting its unique benefits for emotional and cognitive health.

The findings from Chapter 2 affirm that mindfulness, as a construct, is multidimensional and can be effectively quantified using validated psychometric tools. This chapter emphasized the necessity of rigorous psychometric evaluations to ensure that mindfulness measures accurately reflect the construct's various dimensions. The reliability and validity of these tools in clinical populations, such as those with PTSD, highlight their utility in both research and therapeutic contexts. These insights are crucial for developing targeted mindfulness-based interventions and for advancing our understanding of mindfulness as a therapeutic tool.

Chapter 3's umbrella review provided a broader perspective on how mindfulness affects brain connectivity. It highlighted the consistent impact of mindfulness on large-scale brain networks such as the DMN, CEN, and SN, which are involved in self-referential thinking, cognitive control, and emotional regulation, respectively. However, it also brought to light the significant methodological heterogeneity across studies. The review identified substantial variability in how mindfulness interventions were implemented, the types of participants included, and the neuroimaging techniques used. This heterogeneity complicates the synthesis of findings and highlights the need for more standardized research methodologies. Ensuring consistency in study designs, participant characteristics, and neuroimaging protocols is essential for advancing our understanding of how mindfulness practices affect brain connectivity and for developing more effective mindfulness-based interventions.

Chapter 4 expanded our knowledge of the neural mechanisms underlying specific mindfulness practices, such as compassion mindfulness. The fMRI study revealed significant neural differences between compassion mindfulness and visualization tasks, suggesting that compassion mindfulness uniquely engages brain regions involved in emotional and cognitive regulation. The ROI analysis further highlighted the specific brain areas affected by compassion mindfulness, providing deeper insights into its potential therapeutic mechanisms. These findings are particularly relevant for developing mindfulness-based interventions tailored to enhance emotional regulation and cognitive functioning.

The overall findings align with the dissertation's aim to advance the understanding of mindfulness through a multidimensional approach. By combining psychometric analysis, neurobiological synthesis, and experimental neuroimaging, this research contributes to a deeper comprehension of mindfulness and its varied effects on the brain. It also underscores the importance of methodological rigor and the need for standardized research practices to ensure the reliability and comparability of findings across studies.

Future research should focus on addressing the limitations identified in the current studies, such as small sample sizes, methodological inconsistencies, and the need for more diverse populations. Longitudinal studies are essential to explore the long-term effects of mindfulness practices on brain function and structure. Additionally, research should investigate the impact of mindfulness in specific populations, such as children, adolescents, and individuals with different cultural backgrounds, to enhance the generalizability and applicability of findings.

Moreover, there is a pressing need for improved research methodologies in the field of mindfulness. Chapter 2 highlighted the necessity of using validated psychometric tools to accurately measure mindfulness, while Chapter 3 emphasized the importance of standardized neuroimaging techniques and consistent study designs. Future studies should adopt rigorous methodological standards, including larger sample sizes, randomized controlled trials, and standardized neuroimaging protocols. These measures will help mitigate the variability and inconsistencies observed in current research, leading to more robust and generalizable findings.

In conclusion, this dissertation provides a comprehensive examination of mindfulness, integrating psychometric validation, brain network synthesis, and experimental fMRI studies. The findings underscore the profound impact of mindfulness on psychological well-being and neural connectivity, highlighting its potential as a powerful therapeutic tool. This research paves the way for future studies to further explore the neurobiological mechanisms of mindfulness and its applications in diverse clinical and non-clinical contexts. By addressing the methodological challenges and expanding our understanding of mindfulness, we can develop more effective mindfulness-based interventions and enhance their integration into therapeutic practices.

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Table 2.1

Demographics and descriptive statistics measured at baseline.

	Study 1 (N=173)	Study 2 (N=168)	Study 3 (N=146)	Overall (N=487)
Age (y)				
Mean (SD)	48.9 (14.5)	54.0 (12.0)	57.1 (10.1)	53.1 (12.9)
Median [Min, Max]	51.0 [22.0, 74.0]	57.0 [23.0, 73.0]	58.6 [23.4, 83.6]	57.0 [22.0, 83.6]
Missing	0 (0%)	1 (0.6%)	0 (0%)	1 (0.2%)
Gender				
Male	147 (85.0%)	154 (91.7%)	142 (97.3%)	443 (91.0%)
Female	26 (15.0%)	14 (8.3%)	4 (2.7%)	44 (9.0%)
Education				
8th grade or less	1 (0.6%)	0 (0%)	1 (0.7%)	2 (0.4%)
Some high school	2 (1.2%)	3 (1.8%)	7 (4.8%)	12 (2.5%)
High school equivalency (GED)	9 (5.2%)	9 (5.4%)	0 (0%)	18 (3.7%)

High school graduate	31 (17.9%)	23 (13.7%)	36 (24.7%)	90 (18.5%)
Some college	92 (53.2%)	93 (55.4%)	64 (43.8%)	249 (51.1%)
Bachelor's degree	22 (12.7%)	22 (13.1%)	27 (18.5%)	71 (14.6%)
Post-graduate degree	16 (9.2%)	17 (10.1%)	11 (7.5%)	44 (9.0%)
Missing	0 (0%)	1 (0.6%)	0 (0%)	1 (0.2%)
Ethnicity				
American Indian or Alaska Native	13 (7.5%)	6 (3.6%)	4 (2.7%)	23 (4.7%)
Asian	7 (4.0%)	5 (3.0%)	2 (1.4%)	14 (2.9%)
Black or African American	27 (15.6%)	35 (20.8%)	36 (24.7%)	98 (20.1%)
Native Hawaiian or other Pacific Islander	7 (4.0%)	5 (3.0%)	7 (4.8%)	19 (3.9%)
White	111 (64.2%)	110 (65.5%)	85 (58.2%)	306 (62.8%)
Hispanic or Latino	8 (4.6%)	6 (3.6%)	11 (7.5%)	25 (5.1%)
Missing	0 (0%)	1 (0.6%)	1 (0.7%)	2 (0.4%)
MAAS				
Mean (SD)	--	3.34 (0.955)	3.16 (0.854)	3.26 (0.912)
Median [Min, Max]	--	3.27 [1.13, 5.60]	3.07 [1.13, 5.93]	3.20 [1.13, 5.93]

Missing	173 (100%)	8 (4.8%)	4 (2.7%)	185 (38.0%)
FFMQ Observe				
Mean (SD)	27.2 (6.61)	25.8 (6.50)	--	26.5 (6.58)
Median [Min, Max]	27.0 [8.00, 40.0]	26.0 [10.0, 40.0]	--	27.0 [8.00, 40.0]
Missing	4 (2.3%)	6 (3.6%)	146 (100%)	156 (32.0%)
FFMQ Describe				
Mean (SD)	24.9 (7.16)	22.8 (6.86)	--	23.8 (7.09)
Median [Min, Max]	25.0 [8.00, 40.0]	23.0 [8.00, 40.0]	--	24.0 [8.00, 40.0]
Missing	4 (2.3%)	6 (3.6%)	146 (100%)	156 (32.0%)
FFMQ Act with Awareness				
Mean (SD)	23.6 (6.27)	22.3 (6.79)	--	23.0 (6.55)
Median [Min, Max]	23.0 [9.00, 40.0]	22.0 [8.00, 39.0]	--	22.0 [8.00, 40.0]
Missing	4 (2.3%)	6 (3.6%)	146 (100%)	156 (32.0%)
FFMQ Nonjudgement of Experience				
Mean (SD)	22.5 (7.16)	21.2 (6.38)	--	21.9 (6.81)
Median [Min, Max]	23.0 [8.00, 40.0]	21.0 [8.00, 38.0]	--	22.0 [8.00, 40.0]

Missing	4 (2.3%)	6 (3.6%)	146 (100%)	156 (32.0%)
FFMQ Nonreactivity to Experience				
Mean (SD)	19.3 (4.71)	18.6 (4.63)	--	19.0 (4.68)
Median [Min, Max]	20.0 [7.00, 32.0]	19.0 [7.00, 31.0]	--	19.0 [7.00, 32.0]
Missing	4 (2.3%)	6 (3.6%)	146 (100%)	156 (32.0%)
PCL-4M Total				
Mean (SD)	58.4 (11.8)	--	--	58.4 (11.8)
Median [Min, Max]	59.0 [23.0, 85.0]	--	--	59.0 [23.0, 85.0]
Missing	9 (5.2%)	168 (100%)	146 (100%)	323 (66.3%)
WHOQOL Sum				
Mean (SD)	75.6 (12.9)	72.3 (16.8)	--	74.0 (15.0)
Median [Min, Max]	74.0 [45.0, 115]	72.0 [26.0, 124]	--	73.0 [26.0, 124]
Missing	7 (4.0%)	5 (3.0%)	146 (100%)	158 (32.4%)
Treatment				
Control	84 (48.6%)	48 (28.6%)	75 (51.4%)	207 (42.5%)
Treatment	89 (51.4%)	120 (71.4%)	71 (48.6%)	280 (57.5%)

Table 2.2

Correlation and Reliability Estimates for the Mindful Attention Awareness Scale (MAAS) and Five Facet Mindfulness Questionnaire (FFMQ)

	MAAS Total	FFMQ Observing	FFMQ Describing	FFMQ Acting Awareness	FFMQ Nonjudgmental Inner Experience	FFMQ Nonreactivity
MAAS Total	**0.89** **(n = 306)**	0.11 (n = 158)	0.28** (n = 158)	0.68** (n = 158)	0.45** (n = 158)	0.15 (n = 158)
FFMQ Observing	0.11 (n = 158)	**0.81** **(n = 333)**	0.34** (n = 331)	0.03 (n = 331)	-0.15* (n = 331)	0.39** (n = 331)
FFMQ Describing	0.28** (n = 158)	0.34** (n = 331)	**0.9** **(n = 333)**	0.34** (n = 331)	0.21** (n = 331)	0.26** (n = 331)
FFMQ Acting with Awareness	0.68** (n = 158)	0.03 (n = 331)	0.34** (n = 331)	**0.87** **(n = 333)**	0.44** (n = 331)	0.08 (n = 331)

FFMQ Nonjudgmental Inner Experience	0.45** (n = 158)	-0.15* (n = 331)	0.21** (n = 331)	0.44** (n = 331)	**0.86** **(n = 333)**	0.05 (n = 331)
FFMQ Nonreactivity	0.15 (n = 158)	0.39** (n = 331)	0.26** (n = 331)	0.08 (n = 331)	0.05 (n = 331)	**0.77** **(n = 333)**

NOTE: Reliability (alpha) values are bolded in the diagonal. Correlations between scales are in the off-diagonal. Statistical significance (asterisks) are not reported for reliability estimates as is common. * = $p < 0.05$. ** $p < 0.01$.

Table 2.3

Standardized Parameter Estimates for the Regression of Demographic and Clinical Variables onto Baseline and Change Scores for the Mindful Attention Awareness Scale (MAAS) and Five Facet Mindfulness Questionnaire (FFMQ)

	MAAS		FFMQ Observing		FFMQ Describing		FFMQ Acting with Awareness		FFMQ Nonjudging		FFMQ Nonreactivity	
	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change
Age	0.07 (n = 298)	-0.09 (n = 261)	0.10 (n = 327)	-0.05 (n = 262)	0.04 (n = 327)	-0.04 (n = 262)	0.09 (n = 327)	-0.07 (n = 262)	0.05 (n = 327)	-0.04 (n = 262)	0.20* (n = 327)	-0.11 (n = 262)
Sex	0.07 (n = 298)	0.16 (n = 261)	0.08 (n = 327)	0.01 (n = 262)	0.03 (n = 327)	0.04 (n = 262)	-0.04 (n = 327)	0.13* (n = 262)	-0.06 (n = 327)	0.12* (n = 262)	-0.07 (n = 327)	0.11 (n = 262)

Education	0.02 (n = 298)	0.06 (n = 261)	0.17* (n = 327)	-0.16* (n = 262)	0.14* (n = 327)	0.06 (n = 262)	0.05 (n = 327)	0.04 (n = 262)	0.02 (n = 327)	-0.03 (n = 262)	0.02 (n = 327)	0.00 (n = 262)
Treatment	-0.04 (n = 298)	0.24* (n = 261)	-0.09 (n = 327)	-0.02 (n = 262)	-0.03 (n = 327)	0.05 (n = 262)	0.00 (n = 327)	0.11 (n = 262)	-0.03 (n = 327)	0.10 (n = 262)	-0.14* (n = 327)	0.20* (n = 262)
PCL-4M (Change)	-0.13 (n = 183)	-0.32* (n = 180)	0.10 (n = 257)	-0.06 (n = 253)	0.06 (n = 257)	-0.19* (n = 253)	0.04 (n = 257)	-0.31* (n = 253)	0.04 (n = 257)	-0.23* (n = 253)	0.07 (n = 257)	-0.30* (n = 253)
WHOQOL (Change)	-0.14 (n = 126)	0.33* (n = 124)	-0.12 (n = 261)	0.23* (n = 258)	-0.10 (n = 261)	0.28* (n = 258)	-0.02 (n = 261)	0.29* (n = 258)	-0.12* (n = 261)	0.27* (n = 258)	-0.27* (n = 261)	0.42* (n = 258)

NOTE: * $p < .05$
These are linear mixed-effects model standardized coefficients (see Results, page 12)
Sex coded – 1 = Male, 2 = Female
Treatment coded – 0 = Control, 1 = Treatment
PCL-4M = Posttraumatic Stress Disorder Checklist for DSM-4
WHOQOL = World Health Organization Quality of Life scale
Change = Posttreatment minus initial assessment

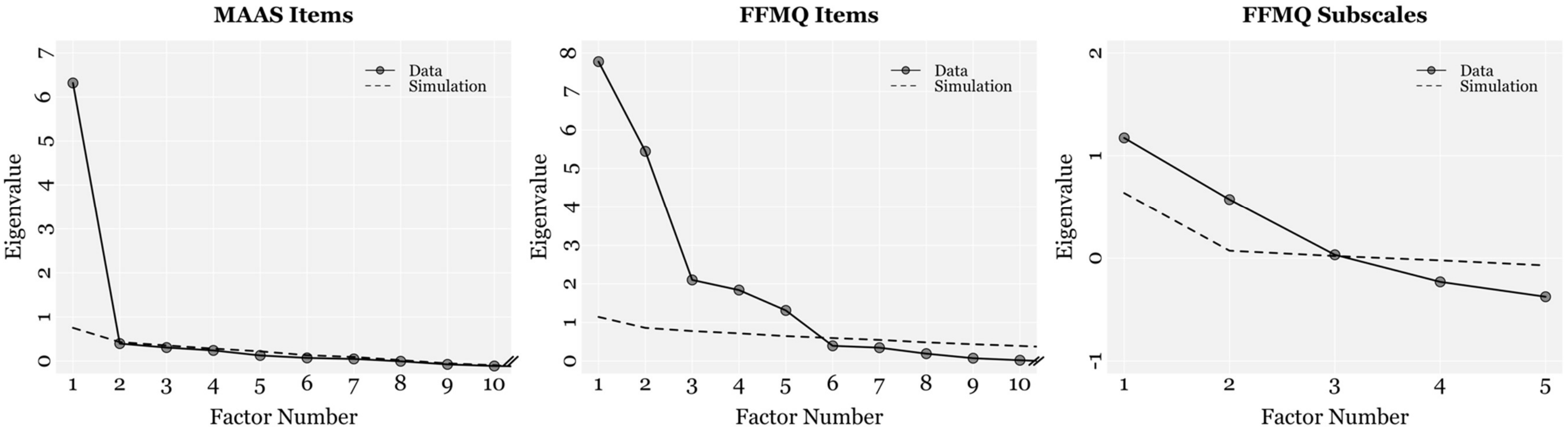


Figure 2.1. Scree plots and parallel analysis for Mindful Attention Awareness Scale (MAAS) scores, Five Facet Mindfulness Questionnaire (FFMQ) item scores, and Five Facet Mindfulness Questionnaire (FFMQ) subscale scores.

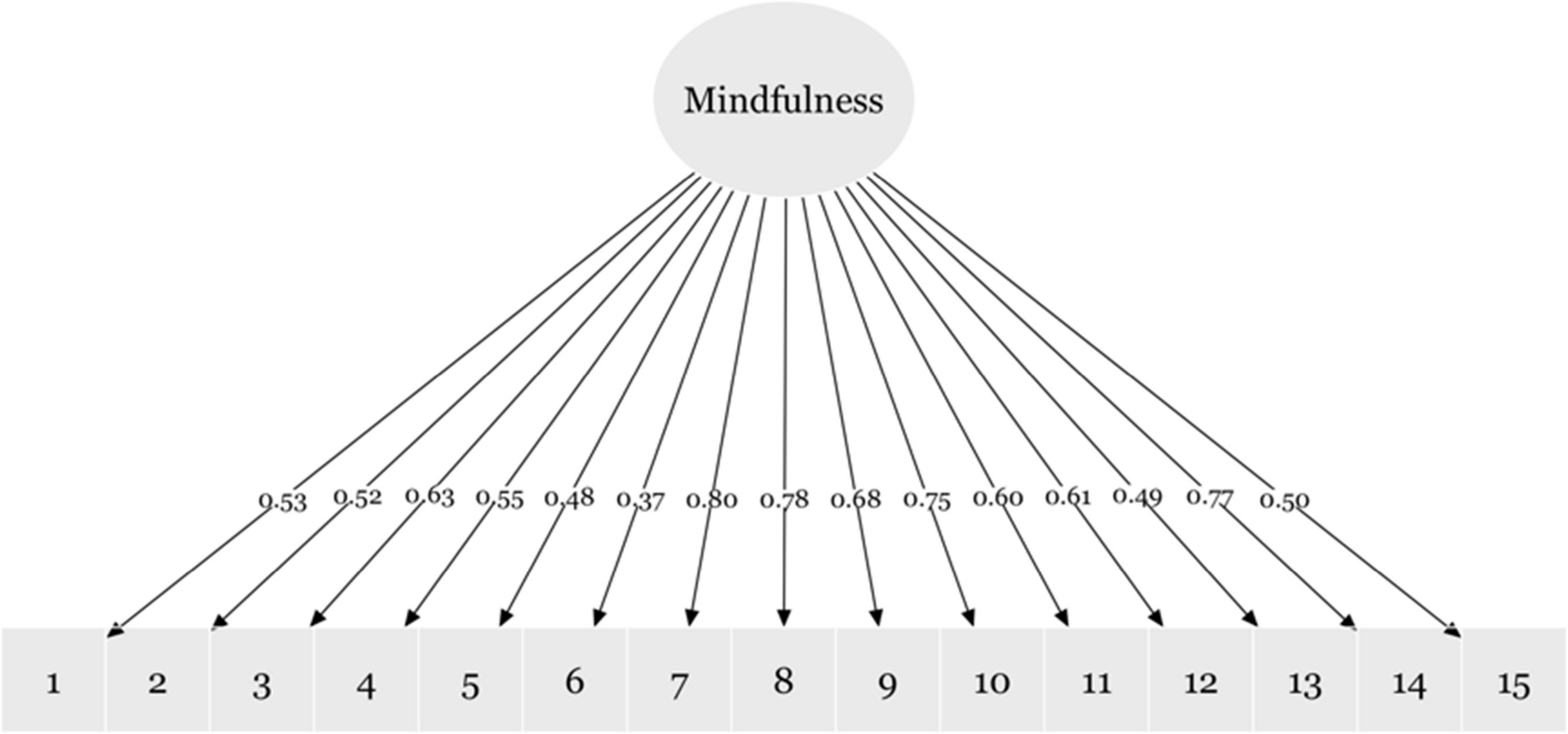


Figure 2.2. Confirmatory factor analysis standardized parameter estimates for the Mindful Attention Awareness Scale (MAAS).

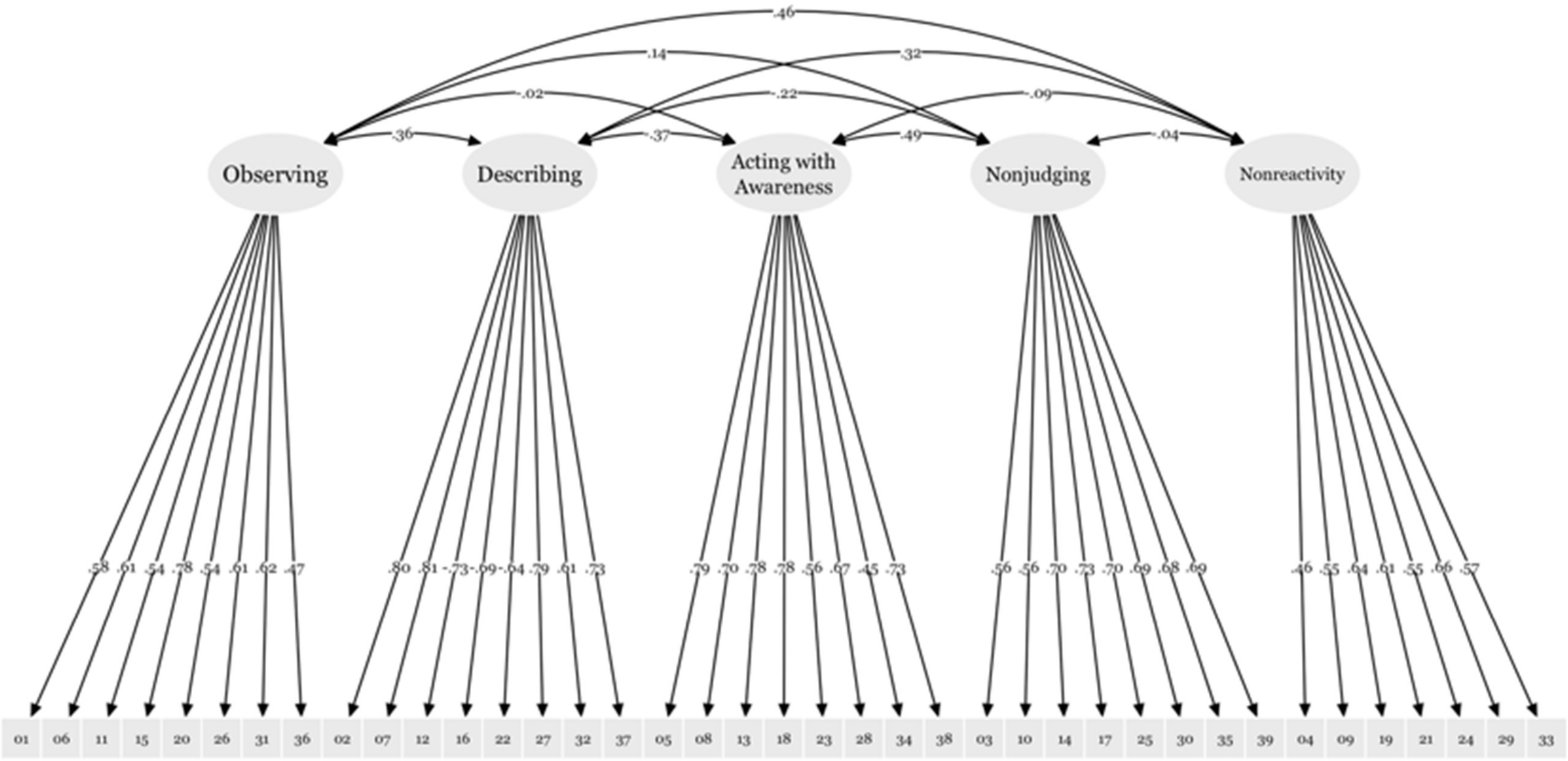


Figure 2.3. Confirmatory factor analysis standardized parameter estimates for the Five Facet Mindfulness Questionnaire (FFMQ).

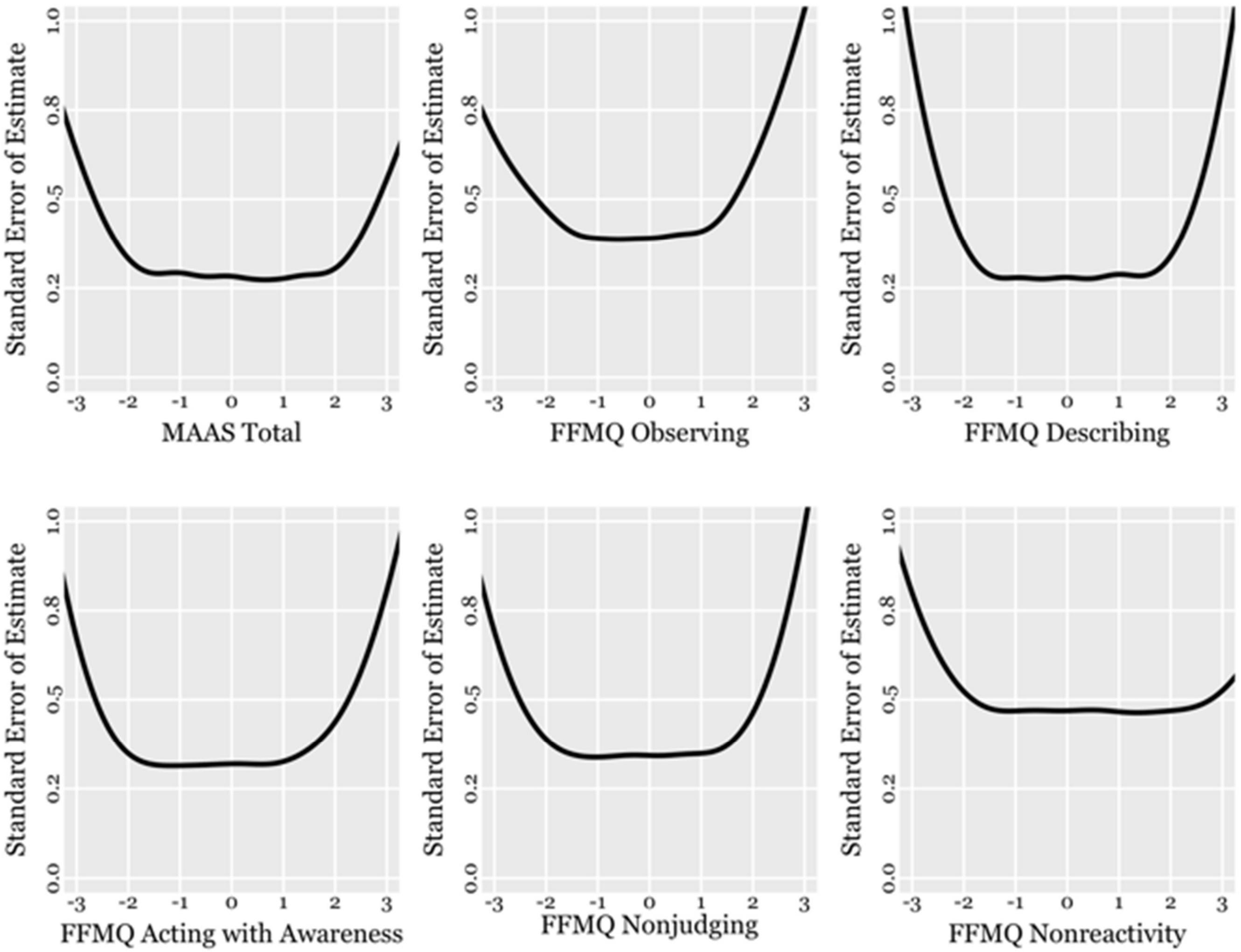


Figure 2.4. Item response theory standard error of estimate for the Five Facet Mindfulness Questionnaire (FFMQ) and Mindful Attention Awareness Scale (MAA

Table 3.1

Author	Aim of review	n	Ratio / MA	RCT vs Obs	Connectivity	Interventions	Metanalysis	Methodological heterogeneity	Reporting heterogeneity	Take-Away
Felsch & Kuypers (2022)	Combination of MM and psilocybin as a successful neurobiological treatment for SAD	30	0.47	0.87	CEN, DMN, SN, DN, Amygdala Conn	MT, Long term vs. Naive, MAAS, FA, MBSR, HEM, Pain Reduction, 5-day retreat.	No	Varied Lengths, Training Types, Experience Differences, Diverse Samples, Clinical and Non-Clinical Samples, Small Samples, Subjective Symptoms, Mixed observational and RCT, Lack of Controls, Task-based vs. resting-state MRI, some studies focusing heavily on psilocybin	Not explicitly mentioned.	↑ SN, ↓DMN during rest and meditation, ↑FC (SN - DMN), ↓ FC within DMN, ↓ within FC Amygd Conn, mixed modulations to CEN, DN, and VAN

Gotink et al. (2016)	Neuronal and stress-reducing effects of 8-week secular MT (MBSR & MBCT)	30	1	0.43	SN, DMN, Amygdala FC,	MBSR, MBCT, 4-day MT, MAAS & FFMQ Scores.	No	Diverse Samples, Clinical vs. Non-Clinical Samples, Variable / Small Samples,Outcome Variables, Lack of Controls, Social confounds during training	Possible overestimation in correlational studies, Some deductions might be overstated due to confounding factors	↑ FC (PFC, hippocampus, amygdala) from 8-week MBSR, similar to traditional long-term meditation styles, no change in DMN, disparate results for insula connectivity.
Lodha & Gupta (2022)	Effects of mindfulness on attentional networks and executive	55	1	0.62	CEN, attentional networks (alerting & orienting)	FA, OM, combinded FA & OM, MBSR, MBCT, MBAT,	No	Varied Lengths, Training Types, Small Samples, Outcome Variables,	Lack of critical intervention-related details and inconsistencies in the	↑ CEN, particularly in executive control and inhibitio

	functioning in healthy individuals.					retreat, BA, IBMT		Lack of Controls, Lack of Randomization	reporting of meditation experience between studies.	n, mixed results for SN in attentional flexibility, less consistent effects on DMN. Long-term mindfulness is associated with increased efficiency in overall functional connectivity, though benefits do not always correlate

										with the duration of practice.
Melis et al. (2022)	Summarize the effects of MBI on FC	14	1	0.86	DMN, SN, CEN, DAN, Amygdala conn.	6 or 8-week MBSR, MT, PM, MBCT.	No	Varied Lengths, Training Types, Lack of Controls, Diverse Samples, Blinding Differences, Neuroimaging Analysis Differences, Network Categorization Differences, Seed selection Differences, Lack of a common tool for validity assessment.	Lack of standardization in reporting, (control groups, variability in measuring outcomes, & reporting of drop-out rates.	↑ FC (DMN - CEN), ↓ FC (DMN and motor/pain pathways), ↑ FC within SN, ↑ FC (SN - DAN), ↑ task-based within FC CEN, ↑ FC (amygdala - CEN)
Mooneyham et al. (2016)	Discuss methodological challenges in MM neuroimagi	???	???	???	DMN, SN, CEN	???	No	Varied operational definitions of mindfulness, selection of control groups,	Not explicitly mentioned.	↑ FC (DMN - vmPFC), ↑ FC (SN - CEN

	ng studies, review connectivity in the triple-network model as it pertains to mindfulness							specificity of intervention, intervention fidelity. Better characterization of fMRI tasks, accounting for confounds, and assessing consistency across datasets.		[right insula])
Rahrig et al. (2022)	Meta-analysis to determine if MT modifies IFC observed during resting states	12	1	0.92	DMN, SN, CEN	MBSR, retreat, MBET (MBCT and PTSD psychoeducation), RDMT, CB, PM	Yes	Varied Lengths, Training Types, Intensity Differences, Small Samples, Neuroimaging Analysis Differences, Seed Selection Differences, Network Categorization Differences.	Not explicitly mentioned.	↑ within FC DMN, ↑ FC (SN-DMN), no significant differences in CEN FC, ↑ FC (dACC-PCC) as a result of intervention: indicatin

										g ↑ (DMN-SN) internetwork connectivity,
Rathore et al. (2023)	Examines FC in the PFC through various mindfulness practices, comparing meditators to non-meditators.	23	1	0.87	PFC, DMN, SN, CEN	MT, CB, TM, FA, LK, Sahaj yoga	No	Not explicitly mentioned.	Not explicitly mentioned.	↑FC within DMN, SN, and CEN, particularly in the PFC
Sezer et al. (2022)	Review of MM rsFC studies involving both trait mindfulness and MBI to synthesize relations between mindfulness and rsFC in both clinical and non-clinical	14	1	0.71	DMN, SN, FPN, and other related networks	MBSR, HEP, retreat, MBCT, MBET	No	Definitional Differences of Mindfulness and Training Types, Experience Differences, Lack of Controls, Neuroimaging Analysis Differences, Seed and Target Selection	Not explicitly mentioned.	↑ FC (DMN[PCC] DMN - FPM[dlPFC], ↑ cuneus-SN coupling, ↑ FC within SN, and better emotion regulatio

	contexts and suggesting implications for resultant psychology							Differences, Network Categorization Differences, Mixed observational and RCT, inconsistency across trait versus intervention studies, limitations of correlational and cross-sectional studies of trait mindfulness		n via corticolimbic circuitry.
Shen et al. (2020)	Meta-analysis on the effects of MM on changing brain internetwork connectivity using seed-based FC	13	1	???	DMN, somatomotor network, FPN, VAN, DAN	FA, OM, LK, MBSR, Theravada, buddhist traditon / BA, Sahaja Yoga, brain wave vibration meditation, zen meditation, attention-based CB	Yes	Diverse Samples, Small Samples, Training Types, Neuromaging Analysis Differences, Seed Selection Differences, Network and Localization Categorization Differences,	Estimated durations of meditation practice time from each paper, Lack of Specificity in RCT Designation.	↓ FC (DMN-DMN and DMN-SN), ↑ FC (DMN-FPN-VAN).

								Differences in Imaging Modalities		
Sim et al. (2024)	Scoping review on MM and hypnosis MRI studies, synthesizing the functional, morphometric, and metabolic changes associated with both practices, and comparing the two	97	0.86	0.83	DMN, SN, CEN	MBSR, MT, MAT, CBCT, MMFT, BMMRI, ABT, MPEAK, HEM, ATB, MBCT, MOM, IBMT, WBMT, MBI, CBMA, BATA, PMI, MTPC, EcoMeditation, MM and hypnosis	No	Not explicitly mentioned	Not explicitly mentioned.	↓ within FC (DMN), ↑FC (CEN - SN)
Zagkas et al (2023)	Review the effects of MM on the DMN	16	1	1	DMN	FA, OM, CB, vairocana, IM, TM, concentration, Vipassana, MSA, LK, CA, MED	No	Generalized Design Differences, Training Types, Small Samples	Not explicitly mentioned.	↓ within FC (DMN), ↑ FC (DMN - CEN)

NOTE**:** This table is a summary of extracted data from the reviews and metanalyses selected for this umbrella review. Acronyms are defined as follows: MM - mindfulness meditation, SAD - social anxiety disorder, MBI - Mindfulness Based Interventions, FC - functional connectivity, PFC - pre-frontal cortex, rsFC - resting state functional connectivity, DMN – Default Mode Network, CEN, Central Executive Network, SN – Salience Network.

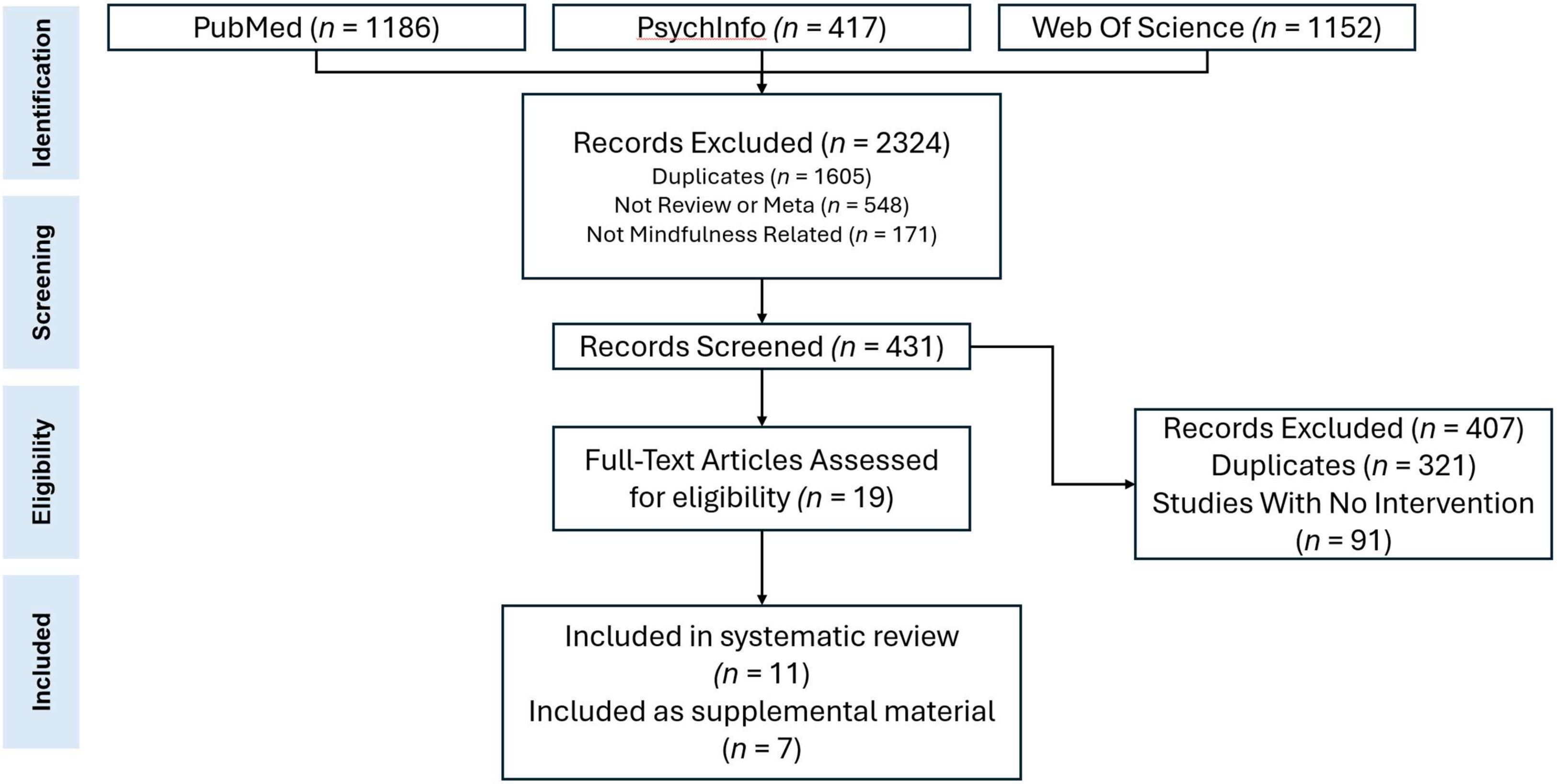
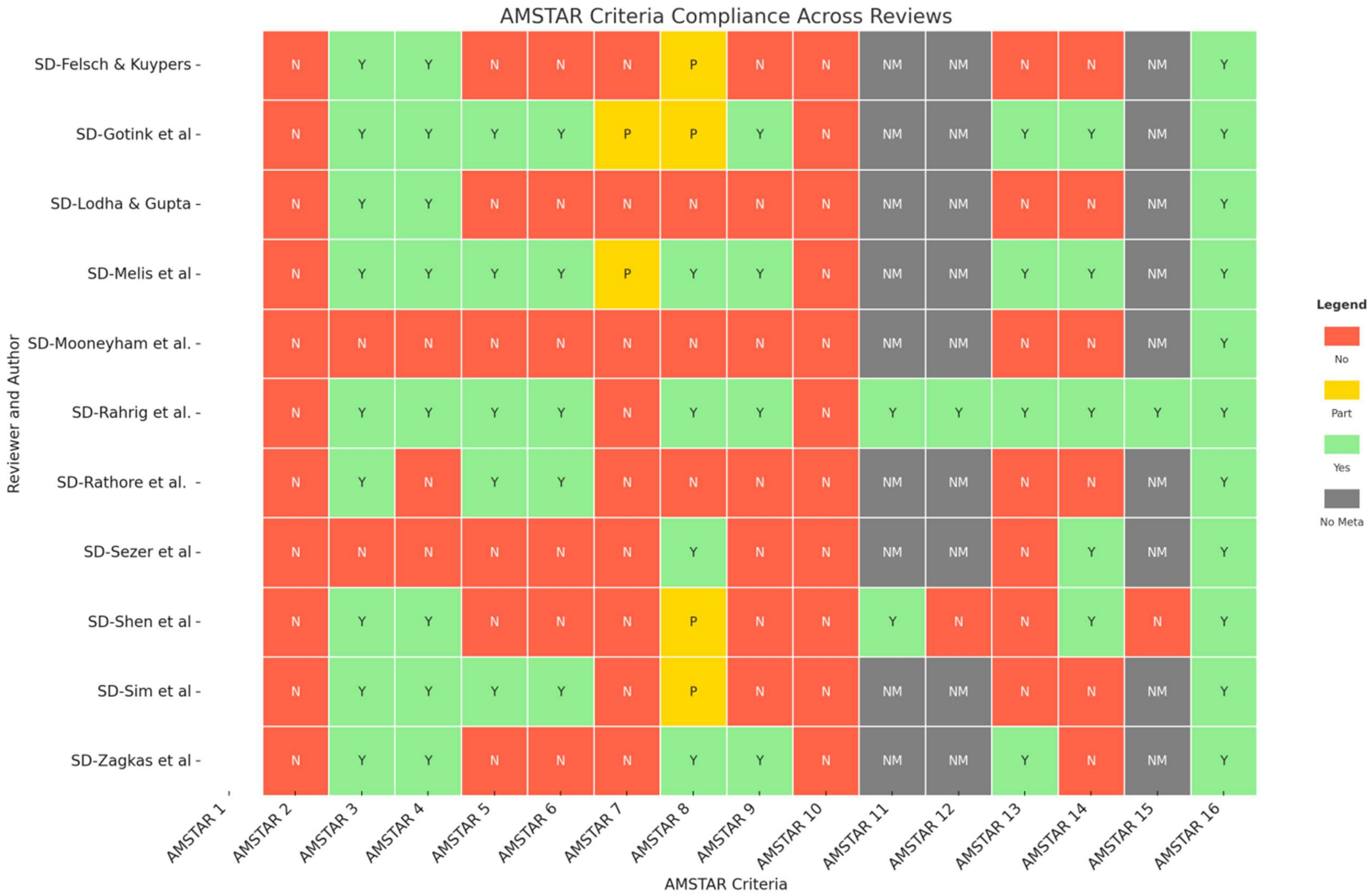


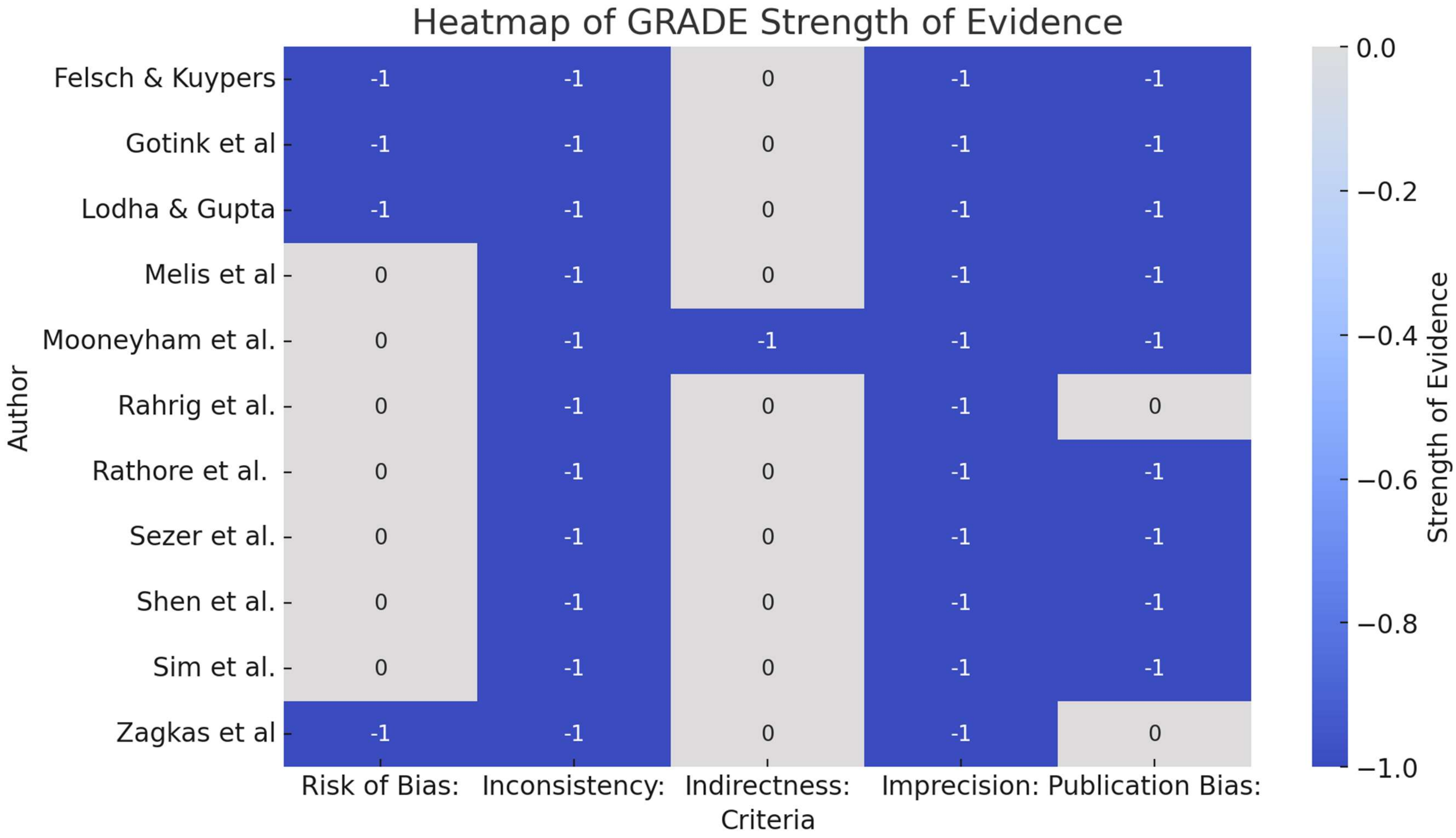
Figure 3.1: PRIMA Flow Diagram for filtering articles.



Reviewer and Author	AMSTAR 1	AMSTAR 2	AMSTAR 3	AMSTAR 4	AMSTAR 5	AMSTAR 6	AMSTAR 7	AMSTAR 8	AMSTAR 9	AMSTAR 10	AMSTAR 11	AMSTAR 12	AMSTAR 13	AMSTAR 14	AMSTAR 15	AMSTAR 16
SD-Felsch & Kuypers		N	Y	Y	N	N	N	P	N	N	NM	NM	N	N	NM	Y
SD-Gotink et al		N	Y	Y	Y	Y	P	P	Y	N	NM	NM	Y	Y	NM	Y
SD-Lodha & Gupta		N	Y	Y	N	N	N	N	N	N	NM	NM	N	N	NM	Y
SD-Melis et al		N	Y	Y	Y	Y	P	Y	Y	N	NM	NM	Y	Y	NM	Y
SD-Mooneyham et al.		N	N	N	N	N	N	N	N	N	NM	NM	N	N	NM	Y
SD-Rahrig et al.		N	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y
SD-Rathore et al.		N	Y	N	Y	Y	N	N	N	N	NM	NM	N	N	NM	Y
SD-Sezer et al		N	N	N	N	N	N	Y	N	N	NM	NM	N	Y	NM	Y
SD-Shen et al		N	Y	Y	N	N	N	P	N	N	Y	N	N	Y	N	Y
SD-Sim et al		N	Y	Y	Y	Y	N	P	N	N	NM	NM	N	N	NM	Y
SD-Zagkas et al		N	Y	Y	N	N	N	Y	Y	N	NM	NM	Y	N	NM	Y

Figure 3.1: This figure is a summary of AMSTAR 2 scores from rating all studies involved in this umbrella review. Red indicates 'No'. Yellow indicates a partial 'Yes'. Green indicates a 'Yes'. Grey indicates that this was not a metanalysis. AMSTAR 2 assesses the quality of systematic reviews by examining: (1) Did the research questions and inclusion criteria for the review include the

components of PICO?, (2) Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?, (3) Did the review authors explain their selection of the study designs for inclusion in the review?, (4) Did the review authors use a comprehensive literature search strategy?, (5) Did the review authors perform study selection in duplicate?, (6) Did the review authors perform data extraction in duplicate?, (7) Did the review authors provide a list of excluded studies and justify the exclusions?, (8) Did the review authors describe the included studies in adequate detail?, (9) Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?, (10) Did the review authors report on the sources of funding for the studies included in the review?, (11) If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?, (12) If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?, (13) Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?, (14) Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?, (15) If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?, (16) Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?



Author	Risk of Bias:	Inconsistency:	Indirectness:	Imprecision:	Publication Bias:
Felsch & Kuypers	-1	-1	0	-1	-1
Gotink et al	-1	-1	0	-1	-1
Lodha & Gupta	-1	-1	0	-1	-1
Melis et al	0	-1	0	-1	-1
Mooneyham et al.	0	-1	-1	-1	-1
Rahrig et al.	0	-1	0	-1	0
Rathore et al.	0	-1	0	-1	-1
Sezer et al.	0	-1	0	-1	-1
Shen et al.	0	-1	0	-1	-1
Sim et al.	0	-1	0	-1	-1
Zagkas et al	-1	-1	0	-1	0

Figure 3.3: The GRADE framework evaluates the quality of evidence based on criteria such as risk of bias, inconsistency, imprecision, and publication bias. A score of 0 indicates no serious concern, while a score of -1 indicates serious concern in the respective category.

Table 4.1 – Participant

Sample characteristics

Table 1 - Demographics		Compassion	Visual	Total N	Total %	*p*-Val
Total		21	21	42	100.00%	1.00
Age						
	18-39	10	10	20	47.62%	1.00
	40-64	6	4	10	23.81%	0.72
	65+	5	7	12	28.57%	0.73
				42		
Sex @ Birth						
	Male	10	6	16	38.10%	0.34
	Female	11	15	26	61.90%	0.34
				42		
Education						
	No Degree	0	0	0	0.00%	1.00
	GED	1	1	2	4.76%	1.00
	High School	0	0	0	0.00%	1.00
	Associate	0	0	0	0.00%	1.00
	Bachelor's	5	7	12	28.57%	0.72
	Master's	8	5	15	35.71%	0.47
	Doctorate	2	3	5	11.90%	1.00
				42		
Race /Ethnicity						
	White	18	18	36	85.71%	1.00

	Black or African American	2	0	2	2.38%	0.49
	Asian or Pacific Islander	1	0	1	4.76%	1.00
	Multiracial	0	3	3	7.14%	0.23

NOTE: Sample characteristics by age, sex assigned at birth, education levels (GED = General Education Development, HS = High School, Assoc = Associates Degree, Bach = Bachelor’s Degree, Masters = Master’s Degree, Doc = Doctorate Degree), and race / ethnicity.

Table 4.2

Single-sample ttest result

group	mask	estimate	statistic	p.value	conf.low	conf.high	effect_size	condition
Compassion	Amygdala	8.735	0.253	0.803	-63.262	80.733	0.055	linear_vs_baseline
Visual	Amygdala	-42.210	-1.851	† 0.079	-89.773	5.352	† -0.404	linear_vs_baseline
Compassion	ACC	66.977	1.620	0.121	-19.252	153.205	0.354	linear_vs_baseline
Visual	ACC	5.515	0.240	0.813	-42.423	53.454	0.052	linear_vs_baseline
Compassion	vmPFC	45.938	1.297	0.209	-27.938	119.815	0.283	linear_vs_baseline
Visual	vmPFC	24.596	1.416	0.172	-11.637	60.829	0.309	linear_vs_baseline
Compassion	Insula	68.905	1.907	† 0.071	-6.476	144.287	† 0.416	linear_vs_baseline
Visual	Insula	15.917	0.771	0.449	-27.119	58.952	0.168	linear_vs_baseline

NOTE: Single sample ttest results for ROI analysis. † indicates a trending effect size / result.

Table 4.3

Independent-Sample Ttest Results

mask	estimate	estimate1	estimate2	statistic	p.value	conf.low	conf.high	effect_size
Amygdala	50.946	8.735	-42.210	1.232	0.226	-33.062	134.954	0.380
ACC	61.461	66.977	5.515	1.299	0.203	-34.964	157.886	0.401
vmPFC	21.342	45.938	24.596	0.541	0.593	-59.323	102.007	0.167
Insula	52.989	68.905	15.917	1.273	0.212	-31.794	137.772	0.393

NOTE: Independent sample ttest for ROI analysis.

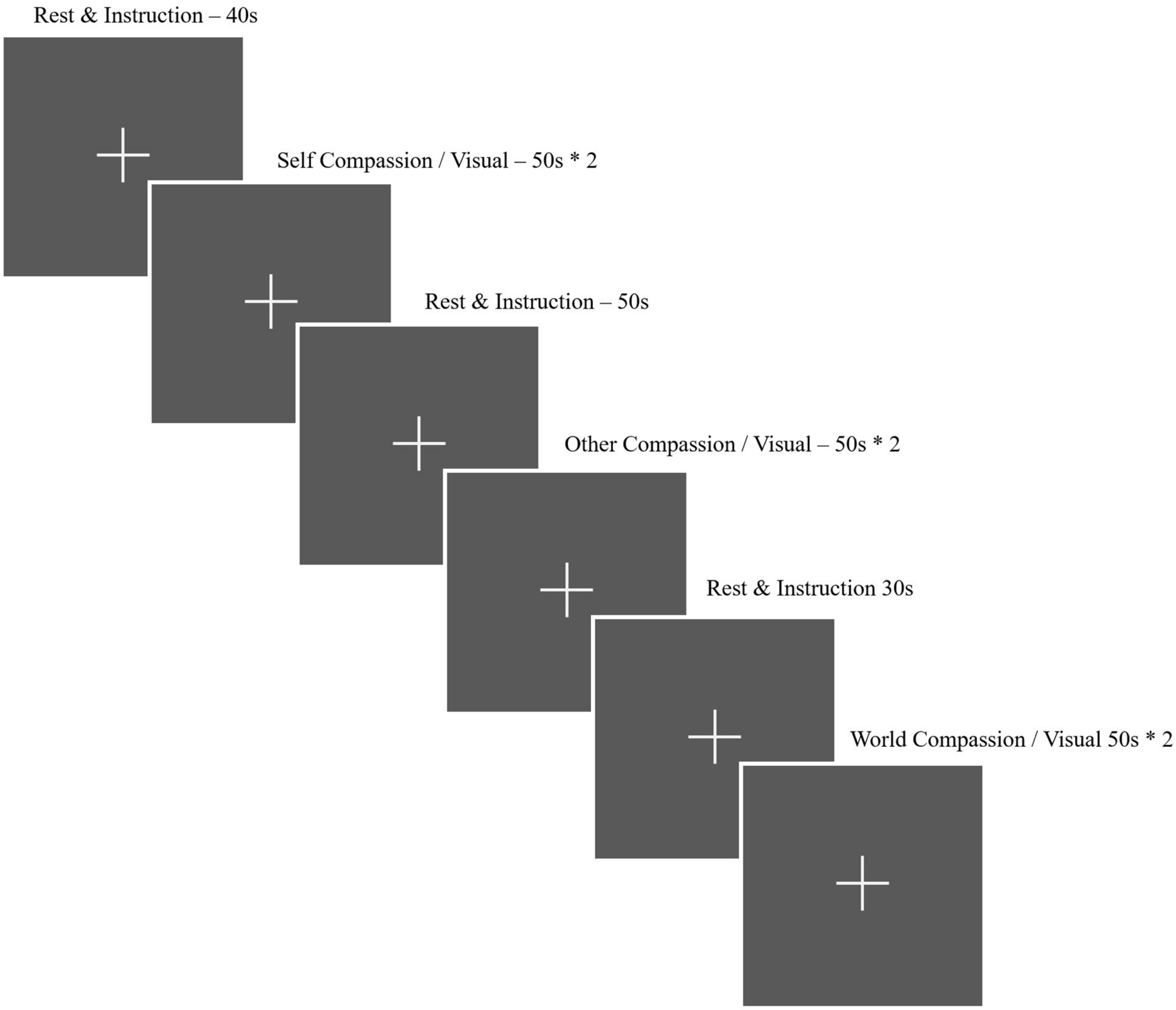


Figure 4.1: Task timing diagram. Task timing noted in seconds.

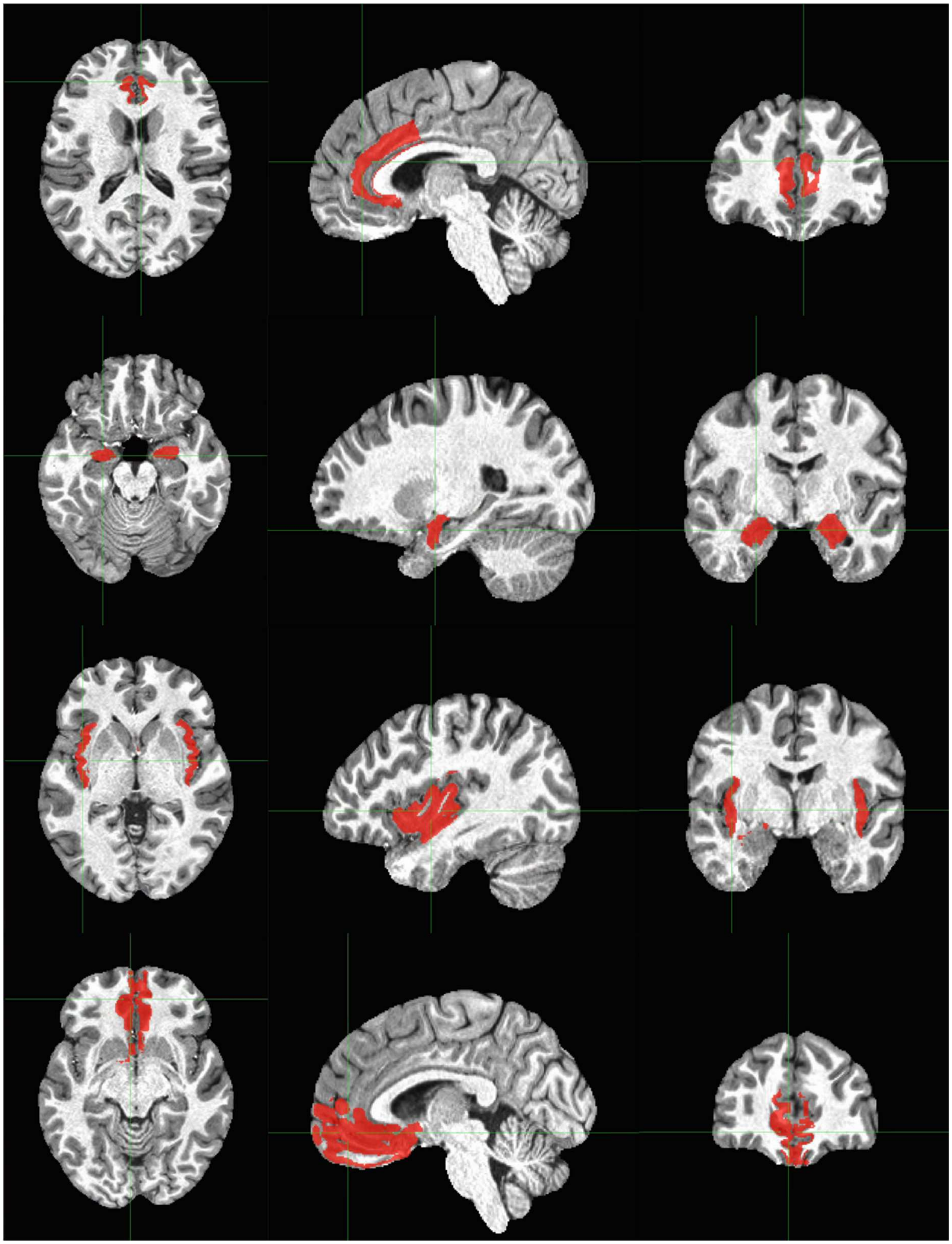


Figure 4.2: Top Anterior Cingulate Mask. 2nd Amygdala Mask. 3rd Insula Mask. Last Ventromedial Prefrontal Cortex Mask.

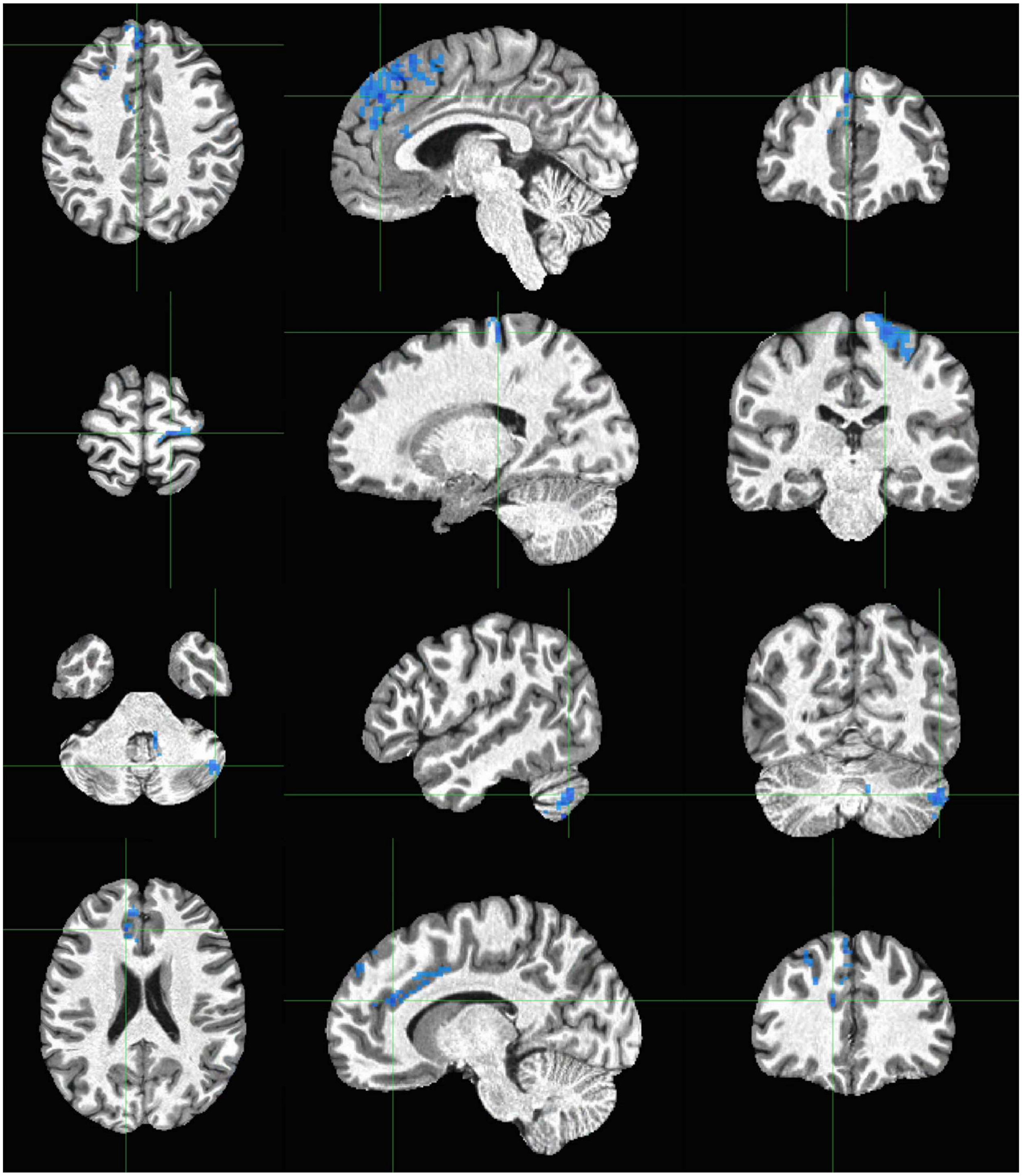


Figure 4.3: Pre-Motion correction and ETAC Independent Samples T-test results. Top to bottom. Left Superior Medial Frontal. Right Primary Motor Cortex. Right Cerebellum. Left Anterior Cingulate Cortex.

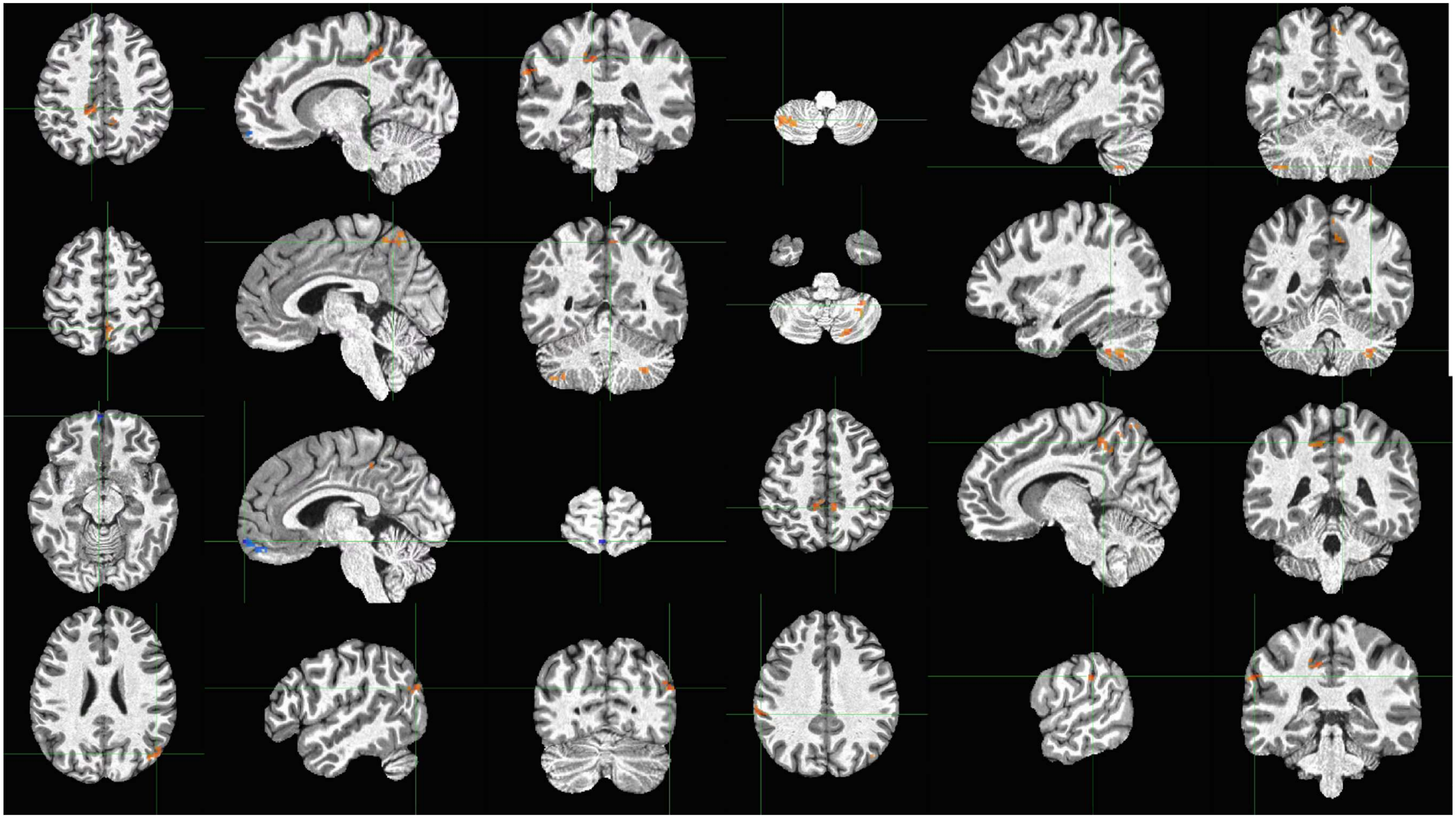


Figure 4.3: Post-Motion correction and ETAC Independent Samples T-test results. Top to bottom. Posterior Cingulate. Precuneus. Frontal Pole. Inferior Parietal. Cerebellum (x2). Precuneus. Supramarginal.