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Differential effects of Mindfulness and Positive Fantasizing on Theta Power in Remitted MDD and Healthy Controls

Bachelor's Project Thesis

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Abstract: Major Depressive Disorder (MDD) is one of the leading causes of disability worldwide. Conventional medicinal treatments involve, primarily, antidepressant drugs, however their inconsistency at reducing symptoms in the long-term as well as the severity of their side effects has redirected research to new, therapeutic treatments types. Depression is a recurrent disorder, meaning that the chances of relapse increase with each subsequent episode, further justifying the need for research on treatments that have a high long-term potential. Addressing both unconventional therapeutic processes and remitted depressed individuals, this study will address the gap in scientific literature where the focus is primarily on chemical treatments for current MDD. The difference in effects of Mindfulness and Positive Fantasizing interventions on theta power will be studied in individuals with remitted-MDD (rMDD) and healthy controls (HC). A repeated measures ANOVA test found significant interaction effects between intervention type and group (HC/rMDD) across all regions being analyzed, with post hoc analyses revealing significant pairwise comparisons only in the occipital regions' models. Notably, positive fantasizing consistently increased theta power in both groups, however with a more pronounced effect in the rMDD group. This differential response suggests positive fantasizing could be targeting specific neural mechanisms associated with depression. The effects of mindfulness, however, varied significantly depending on the valence condition, group and brain region, indicating these effect may depend on individual differences between participants. This study highlights the complex relationship between theta brain activity, emotion regulation, depression and the two interventions being analyzed.

1 Introduction

Major Depressive Disorder, commonly referred to as MDD, is a mood disorder with widespread effects and is a leading cause of disability worldwide. An analysis published by the World Health Organization (2017) estimated that 4.4% of the global population suffer from depression.

Studies focusing on recently collected data tend to be localized, thereby providing a national rate of depression rather than a global one. The Lancet Journal of Regional Health found that 32.8% of the U.S. adult population experienced elevated depressive symptoms in 2021 (Ettman et al., 2022). In comparison, Ettman et al. (2022) reported the rate of depression among the adult U.S. population was estimated to be 27.8% in the early months of 2020 and a mere 8.5% prior to the onset of the global pandemic.

MDD is associated with significant and extensive behavioral symptoms that breach many, if not all elements of daily life for adults, children and adolescents. Symptoms include, but are not limited to loss of interest in pleasurable activities, social withdrawal and feelings of worthlessness. MDD also bears significant costs on macroeconomic scales. A study of the incremental economic burden of depression among the adult US population reported a 37.9% increase between the years of 2010 and 2020. Most recently, this cumulative economic cost was estimated at 326.2 billion US dollars. This further accentuates the growing demand for effective and long-lasting treatments.

Commonly classified as a recurrent disorder, MDD is characterized by episodes of remission and relapse. Studies show that the rate of post-treatment relapse for depressed individuals is 35% and with each recurrence of MDD, the risk of subsequent episodes increases by 16% (Eaton et al., 2008). This statistic further justifies the social and clinical interest to improve available treatments.

The term rMDD, namely remitted-MDD, separates the study of subsequent episodes of major depression from the initial one. This is particularly useful in understanding i) Why certain individuals relapse while others do not, ii) The pre-indicators of severity in potential relapse episodes and iii) The often hidden long term implications of said recurrence.

The cognitive biases that are initiated during episodes of MDD often result in residual symptoms that can be observed long after the episode is clinically over. By recognizing the persistence of cognitive biases beyond the acute phase of depression, the relationship between the initial episode and the long term risk of recurring episodes can be further understood.

Two common forms of residual symptoms are perseverative cognition (PC) and rumination. PC refers to the continuous and repetitive thinking of negative events, past experiences or potential fears from the future. Rumination is the repeated negative thinking about past events, and is a source of increased psychological stress. These, alongside other symptoms, serve as an indication that the recovery process is incomplete and can thereby be used to differentiate which of them are likely to materialize as relapse (Wojnarowski et al., 2019). Therefore, understanding why, how and where (physiologically) these residual symptoms persist can provide valuable insight on the healing processes and the limitations of current treatments protocols.

The increasing rates of depression reported among the general population and the associated likelihood of relapse during remission highlight the inadequacy of current treatments.

Primarily this inadequacy may persist due to modern pharmacological treatment with antidepressant medications. Antidepressants, commonly belonging to the SSRI group of medications, were first developed and introduced in the 1950s . There are many side effects of SSRI treatments, such as anxiety, restlessness, headaches and insomnia (NHS Choices, 2021). Additionally, the true effectiveness of these treatments has long been an issue of controversy among scientists and behavioral psychologists (Hengartner, 2020). Research on antidepressants and health related quality of life (HRQoL) have indicated that in a real-world environment, the effect of antidepressant medication does not continue to improve patients' HRQoL over time (Almohammed et al., 2022). This further emphasizes the need to develop approaches to treating conditions often characterized by recurrent episodes such as MDD. Although current treatment is often standardized and not preemptive, tailor-made treatments acting as preventative measures and aiming for holistic well-being are being researched heavily through advancements in neuroscience and availability of data.

Participants belonging to either the healthy control (HC) or rMDD group underwent two different types of interventions; positive fantasizing and mindfulness.

Positive fantasizing is a type of therapy in which participants take part in guided visualizations, learning to focus on future-related thinking and developing a positive sense of oneself. This intervention therefore focuses on redirecting negative thoughts into a positive context.

Mindfulness, on the other hand, involves learning to be in the present, with emphasis on interpreting present thoughts with a positive mindset, rather than becoming troubled by them. In the context of studying remitted depression, the interest in these interventions stems from their potential to create lasting positive changes in individuals who have experienced depressive episodes. By redirecting negative thought patterns through positive fantasizing, participants may develop a renewed sense of hope and self-worth, crucial factors in preventing relapses. Additionally, the emphasis on mindfulness in interpreting present thoughts positively offers a proactive approach to managing depressive tendencies, helping individuals stay resilient even after depressive symptoms have subsided. The exploration of these interventions in the upcoming methodology section 2.2.2 will shed further light on their applicability and effectiveness in promoting remission and long-term mental health.

The implicit emotion regulation task, during which participants performed the intervention they were previously taught, consisted of being subjected to a series of image stimuli having positive, neutral or negative connotations. The decision to use the implicit emotion regulation task aligns with the study's design, prioritizing ecological validity by stimulating realworld emotional responses. This approach minimizes demand characteristics, reducing the chance that participants modify their behaviour based on explicit instructions thereby allowing for the examination of the subtle, automatic effects of either intervention. Deficits in emotion regulation are a prevalent characteristic of MDD, often persisting into the remitted phase. Visted et al. (2018) found that individuals with current and remitted MDD tend to utilize maladaptive emotion regulation strategies, such as avoidance and suppression, while showing reduced use of adaptive strategies such as cognitive reappraisal and self-compassion. Additionally, Berking et al. (2014) hints at the significance of effective emotion regulation skills in predicting the severity of depressive symptoms over time, indicating a potential link to depressive relapse.

Positive fantasizing and mindfulness interventions may bolster adaptive emotion regulation strategies, addressing deficits commonly observed in individuals with rMDD. These interventions could provide crucial tools for managing distressing emotions and enhancing emotional resilience, potentially reducing the risk of depressive relapse in this vulnerable population.

Depression is an inherently subjective disorder originating from the experience of the patient. Therefore, collecting an empirical quantification of said experiences is limited to measuring the different physiological responses such as brain and heart activity. Electroencephalograms, commonly referred to as EEG devices, offer a non-invasive, real-time and high-resolution insight into the neural activity of the brain (NHS Choices, 2022). Analyzing changes in brain activity sheds light on the types and locations where neural mechanisms are affected by the emotion regulation task, thereby deeming EEG a particularly powerful tool for studying depression.

Neural oscillations are one of many measurable criteria of an EEG analysis. These oscillations reflect the synchronized activity of large neuron groups, and are categorized into different frequency bands. Each frequency band in a part of the brain reflects patterns of neural activity that are related to specific functions and states of the brain (Suurmets, 2018). For example, the beta frequency band in the motor cortex is directly correlated with voluntary motor movements and motor planning, where, in this region, the amplitudes of these oscillations increase during precise movements like reaching for an object.

Theta oscillations are of particular interest in MDD research due to their association with cognitive and emotional processes such as memory formation, creative thinking, and the integration of emotional experiences (Ertl et al., 2013; Knyazev, 2007). These processes are of particular interest as disturbances are commonly observed in depressed individuals. In this study, theta power, which essentially represents the amplitude of theta oscillations in the EEG signal, will be analyzed. The amplitude or power of these oscillations can be indicative of the level of neural activity in the brain region from which the signal is being recorded. The differential effects that each intervention has on theta power, and how these effects vary between interventions, form the basis for the comparisons performed in this study.

Studies on MDD reported effects on theta power, depending on the region of the brain and the research question being answered. The majority of these studies indicated that MDD was associated with an increase in theta power in the anterior cingulate cortex-subgenual region of the brain (Jaworska et al., 2012). Activity in this region is correlated to resolution of emotional conflicts. Therefore, an observed hyperactive theta power could represent compensatory activity, essentially acting to mitigate the impact of these emotional conflicts (Pizzagalli, 2010). This suggests that the brain may be deploying additional resources in this area to help regulate and resolve the emotional challenges being experienced, allowing for the restoration of stability and effective functionality.

Theta power will be analyzed across three different regions of interest that have been associated with emotion regulation and the two interventions. Figure 2.1 displays these regions, namely the bilateral frontal, frontalmidline and occipital. These regions were shown to experience different changes in theta oscillations between patients with rMDD and HC. A recently published review/study on the effects of Mindfulness-based cognitive therapy on theta power in recurrent MDD patients with residual symptoms, identified the bilateral frontal lobes and right occipital regions as sites in which theta power is expected to increase following MBCT intervention (Wang et al., 2022). Topographic EEG maps displaying theta power activity will aid to further narrow these identified regions into specific combinations of electrodes. These can be seen in figure: A.2 and A.1 in the Appendix. Additionally, the frontal-midline region had been identified as relevant with regards to changes in theta power. The shift in theta activity within this region is believed to reflect the modulation of cognitive and emotional control.

Theta activity in this region is said to originate from the anterior cingulate cortex, where increased activity has been observed following similar mindfulness intervention therapies (Tang et al., 2019). As prior literature also suggested an increase in frontal-midline theta following mindfulness-based cognitive therapy (Tang et al., 2019), analysis on this region will help determine if similar effects were also observed following positive fantasizing.

This research seeks to fill an evident void in the current body of literature, where the primary focus is on mindfulness interventions and their potential effects on depressed individuals while research on the efficacy of positive fantasizing is limited. More specifically, investigations on those who have remitted from MDD and are at high risk of relapse do not study these or similar interventions and thus omit an essential aspect of potential therapeutic and preventative strategies. In order to address said gap, this study aims to assess the effect of each intervention on theta power specifically comparing healthy controls to rMDD individuals. This will be achieved by recognizing differences in theta band power and determining which intervention method had a more significant effect on the rMDD group. This study intends to answer the research question: "Will mindfulness and positive fantasizing have different effects on the theta power for healthy controls and remitted MDD individuals in an emotion regulation task?"

2 Methodology

The study is designed to assess changes in theta oscillations following these interventions, enabling the exploration of potential differences in response between the HC and rMDD groups. Regional analysis will act as an additional axis through which the differences in effects can be compared. A power analysis of theta oscillations is used to assess how the effects of either intervention vary between the groups. This will provide insight as to which of the two aforementioned interventions resulted in a more significant effect on theta power compared to the baseline measurement. The data utilized in this study is part of a larger ongoing research project being administered by the University Medical Center Groningen (UMCG) in the Netherlands.

2.1 Participants

It was initially proposed (Huisman, 2021) that a sample size of 100 participants would be optimal for this research, however due to recruitment difficulties, this had not yet been achieved. of all the collected entries only 19 participants' data was eventually usable. As a result of corrupt data files and a lack of reliable participation (attendance to all four measurement sessions) on behalf of some subjects, the actual sample consists of 11 rMDD and 8 HC participants. To guarantee no actively depressed individuals were labeled as part of the rMDD group, candidates had to meet an inclusion criteria.

Specifically, these individuals were required to have endured at least two episodes of MDD in the past ten years, and importantly were not in a depressive episode at the time of investigation or two months prior to its inception. Each candidate was scored using the inventory of depressive symptomatology (IDS-SR30). Only those with IDS-SR30 scores < 21 were accepted, indicating they were essentially symptom-free. This ensures the "absence of clinically relevant depressive symptoms" (Rush et al., 2000).

The final 19 participants were between the ages of 18 and 60, had displayed regular intelligence ($IQ > 85$) and had good or corrected to good vision.

An additional screening process was performed on all participants. Dutch fluency was required to ensure the researchers' instructions were fully understood. Candidates regularly using certain medications, such as antidepressants and beta-blockers, were also excluded from this study. Candidates with prior experience in either intervention or similar techniques were omitted. This ensures an equal familiarity with the intervention techniques among all participants.

Upon completion of the aforementioned screening procedure, participants performed a questionnaire, providing researchers with relevant personal information such as their occupation and marital status. Participants received financial compensation for their contribution.

2.2 Procedure

The experiment consists of four phases of data collection. The two intervention techniques were separated by six weeks to reduce the effect of potential interference. To measure the effect of either intervention on each individual, an implicit emotion regulation task was performed. The four phases of data collection occur before and after each intervention such that the resulting changes in electrical brain activity can be accurately measured. This serves as a basis on which the effect of a specific intervention can be analyzed.

2.2.1 Stimuli

The stimuli presented were acquired from the International Affective Picture System (IAPS; Lang et al. 2008) and consisted of 96 images split evenly into three valence conditions each with 32 images. Images belonging to the positive, negative and neutral valence depicted pleasant, threatening and natural scenes respectively. All images were shown once per measurement phase in a randomized order. Stimuli was presented on a color monitor (res. 1920x1080 pixels) situated about 70 cm from the seating position. Participants were instructed to pay close attention to the images and were not given explicit instructions regarding the regulation of emotional responses. A white cross in the center of the computer screen appeared for 500 ms prior to the onset of each stimulus. Participants were requested to fixate their visual attention on said cross during those 500 ms. The stimuli was then presented for a duration of 3000 ms. A resting state measurement and a Sustained Attention to Response Task (SART; McVay & Kane 2009) were performed, however these measures exceed the scope of this analysis.

The baseline measurement, taken prior to learning and practicing the intervention, will be referred to as pre-intervention. The term post-intervention is used when referring to the second and fourth measurement phases, which follow the teaching and practice of either intervention.

2.2.2 Interventions

As mentioned in section 2.2, each participant undergoes separate training for each intervention. This training consists of a two-hour long session with a therapist, where different methods for utilizing said intervention were explained and then practiced. Participants were requested to practice applying these techniques at home to allow for consistency across all individuals.

Differences in the effects of the two forms of interventions will point towards a better and worse performing one for said individual. Likewise, a participant whose EEG data depicts minimal change between baseline activity and post-intervention activity can potentially indicate a limited acceptance of taught techniques, particularly when considering the scale of these changes in other participants.

Positive fantasizing is one of the core techniques of preventative cognitive therapy (PCT) that primarily requires participants to imagine and mentally indulge in their desired future. This is done by accentuating positive attitudes and redefining negative beliefs or expectations. Besten et al. (2017) found that positive fantasizing framed into ten-minute sessions was effective in reducing some of the negative effects being targeted by the intervention. This serves as evidence that positive fantasizing can aid in manipulating cognitive thinking patterns from which mental health disorders can arise.

The second intervention, called mindfulness, in essence focuses the attention of the participant to the present moment, while maintaining an attitude that enables for curiosity and non-judgemental thought. Mindfulness as an intervention technique can assist in emotion regulation by training to recognize difficult emotions without becoming overwhelmed by their implications. For specific details on the structure of either intervention sessions, please refer to (Huisman, 2021).

2.2.3 Pre-intervention

The pre-intervention session precedes each intervention and lasts a week, during which participants are requested to adhere to their established daily routines. This crucially ensures that the EEG measurement taken on the seventh and last day of said "session" behaves as a baseline quantification of brain activity.

On the seventh day, EEG measurements were taken. This EEG data serves as a baseline measure for each participant, to be compared with their brain activity following the intervention.

2.2.4 Post-intervention

The second phase of each intervention begins with a two-hour long session. A trained professional was introduced and the intervention was taught alongside exercises to continue practicing. Using a smartphone app to record, participants were requested to practice at home for ten minutes per day.

On the seventh and final day of this week-long phase, participants performed an EEG measure while undergoing the same implicit emotion regulation task.

Participants also performed a self-report questionnaires. The Positive and Negative Affect Scale (PANAS) (Watson et al., 1988) was used to measure changes in affect before and after the intervention. The Fantasizing subscale of the Bermond-Vorst Alexithymia Questionnaire (BVAQ) (Vorst & Bermond, 2001) measured trait fantasizing, and the Uncontrollability factor of the Leuven Adaptation of the Rumination on Sadness Scale (LARSS) (Raes et al., 2008) assessed perceived uncontrollability of ruminative thoughts. The BVAQ and LARSS were administered only during the baseline measurement to analyze individual differences. The data collected through these questionnaires will not be used in this analysis.

2.3 Design

As participants received both intervention types, their order was selected at random. This is primarily aimed to limit/minimize any cross-over effects from contaminating the data and becoming integral to the measurements.

Because each intervention consisted of two phases, each participant underwent a total of four clinical phases. The first and third phases are used to take EEG measurements prior to the first and second intervention respectively. These phases form a baseline EEG measurement of each participant's brain activity. The EEG 'post' measurements, namely the second and fourth phases, in essence show the neurological effect of said intervention in terms of brain activity. A wash-out period of six weeks was introduced to counteract the effect of the first intervention on both participants' mindset and subsequently their second interventions' EEG measurements. This time period of two months allowed brain activity to normalize following the first intervention.

2.3.1 Materials and software

A BioSemi ActiveTwo system (BioSemi B.V., Amsterdam, Netherlands) consisting of 32 AgCl electrodes was positioned following the International 10-20 application method. The Actiview program and system designed and provided by Biosemi, was used to record continuous EEG data. This EEG signal was sampled at 512 Hz and impedance was kept below 20 kΩ on all channels. No online filtering was done during recording of the data.

The EEGLAB toolbox and the ERPLAB plugin for MATLAB were utilized for offline preprocessing (Delorme & Makeig, 2004; Lopez-Calderon & Luck, 2014; The MathWorks Inc, 2020). A band-pass filter from 0.1 to 50 Hz was applied on the data. Infomax independent component analysis (ICA) was used to manually remove artifactual components, such as eye movements, blinking and other forms of noise artifacts. The data was then resampled and "single-trial EEG epochs were extracted for a period starting 200 ms before stimulus presentation and lasting for the entire duration of stimulus presentation (3000ms)" (Huisman, 2021).

2.3.2 Methodological considerations

The small sample sizes during each clinical setting and the large number of participants with discarded trials meant that a group of just nine individuals had all four phases measured. The drawbacks of conducting EEG analysis on this small of a sample is the increased influence of outliers and risk of type II error. These reduce the statistical power of the analysis, thereby decreasing the likelihood that a study will detect an effect when there is an effect to be detected.

In hopes of increasing statistical power, individuals missing just one pre-measurement (regardless of the intervention it preceded) were included and had that pre-measurement used for both interventions. Although controversial, this experimental design allowed for inclusion of additional data.

To adress potential carryover effects, a wash-out period of at least sixty days between the first and second pair of measurements was introduced. This ensured that the effects of the first intervention would not impact the pre and post measurements of the second intervention. The wash-out period played a crucial role in controlling for intervention effects in both baseline measures, justifying the inclusion of an additional ten participants.

2.4 Statistical analysis

The pre-processing and statistical analysis of the EEG data involved several key steps. Initially, the theta power was extracted from the pre-processed EEG data using an improved version of the Fast Fourier Transform (FFT) called the spectopo function of the EEGLAB toolkit. The FFT is a mathematical tool that transforms time-domain signals, such as EEG data, into frequency-domain signals, allowing for the extraction of specific frequency bands. This method is particularly relevant for EEG research as it enables the isolation of distinct frequency bands, such as theta, that are associated with different cognitive and emotional states.

In general, FFT assumes stationarity of the data, which is not the case for EEG data in its raw form. However, when EEG data is segmented into epochs of short duration, the statistical properties of the EEG signal within this time-period are unlikely to change significantly. The assumption of stationarity over short time segments acts as a practical compromise enabling for efficient spectral analysis. This approach has been widely accepted by the scientific community for EEG analysis (Yi Wen & Mohd Aris, 2020).

Welch's method for estimating power spectral density will be used. Accessed from the EEGLAB toolkit, pwelch is a revised, improved version of FFT that overcomes the assumption of stationarity by further segmenting the data and averaging the computed periodogram for each segment. This produces a power spectral density estimate, thereby reducing the variance of the estimated power spectrum and providing more reliable estimates. The theta band was isolated using a bandpass filter, in this case filtering for frequencies in the theta band of 4-8Hz range.

2.5 Regional analysis

The focus was narrowed to three specific regions of interest (ROI). These regions, as well as their composition of electrodes, can be seen in figure 2.1. The Fz and FCz electrode, located along the midline of the scalp at the top of head, were of particular interest (Ertl et al., 2013). This area is called the frontal-midline, and is involved in motivation, decision making, attention and information processing (Aftanas & Golocheikine, 2001).t plays a pivotal role in cognitive processes that influence emotional responses. This region's involvement in motivation and decision-making makes it relevant to understanding how mindfulness and positive fantasizing interventions might impact individuals with depression. Understanding how interventions affect specific brain regions provides insights into the underlying mechanisms of the observed effects. In the context of depression and emotion regulation, pinpointing the regions influenced by mindfulness and positive fantasizing helps identify where these interventions exert their therapeutic effects and how that varies between the groups and the connotation of the stimuli presented.

The 10-20 international system for EEG electrode placement does not have an FCz electrode (see figure 2.1), and although FM-theta is maximal around the Fz electrode, maximal amplitudes can occur up to 3 cm around the Fz electrode (Ishihara et al., 1981). The Cz electrode is also located directly on the midline and topographic maps show changes in frontal-midline theta occurring at both those electrode sites. The model therefore consisted of an average across the Fz and Cz electrodes.

Topographical maps were created to visualize theta power across the scalp for each group and each intervention, pre- and post-intervention.

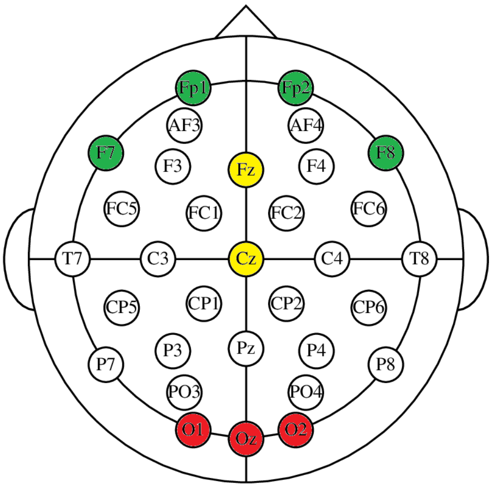

Figure 2.1: 10-20 international electrode map. Regions of interest highlighted as follows: Green- Bilateral-frontal, Yellow- Frontal-midline, Red- Occipital

These maps also revealed heightened theta activity in the occipital region for the rMDD group compared to the HC and can be seen in Appendix: A.2. This led to the decision to average theta power across the O1, OZ, and O2 electrodes, located in the occipital region. This was supported by research indicating that an increase in theta power was expected in the right occipital regions following a mindfulness-based form of cognitive therapy (Wang et al., 2022). However, as is topographically evident in Appendix: A.2, the occipital regions for both groups had a concentration of increased theta power around those three electrodes, with no emphasis on heightened activity towards the right.

Wang et al. (2022) also mentioned the bilateral frontal lobes as sites where theta power was expected to increase following mindfulness interventions. Supported by topographic representations, the bilateral frontal model consists of the average activity over electrodes F7, Fp1, Fp2 and F8.

The analysis employed a set of statistical models designed to examine the effects of the interventions on theta power within specific brain regions under different emotional valence conditions. In total, nine separate models were created, each corresponding to a unique combination of valence conditions (positive, neutral, and negative) and regions of interest (ROIs). These models were constructed as repeated measures ANOVA (RM-ANOVA) to account for the within-participant variability across the valence conditions within each ROI. The use of these models enabled a comprehensive assessment of the impact of the interventions on theta power while considering both the emotional context and the specific brain regions of interest.

The statistical software JASP (JASP Team, 2023) was used to conduct repeated measures analysis of variance (RM-ANOVA) and post-hoc analyses on the models previously described. JASP is a free and open-source software that offers a user-friendly interface for conducting a wide range of statistical analyses. In this study, JASP was particularly useful for running RM-ANOVAs, which allowed for the examination of within-subject effects of the interventions, as well as between-subject effects of group membership.

Given the research questions focus on the differential effects of the interventions between the groups, rather than the effects of the valence conditions on the groups, separate ANOVA models were made for each of the three valence conditions. This approach simplified the models and made the results easier to interpret, while still providing valuable insights into the effects of the interventions within each specific valence condition. However, it should be noted that this approach does not allow for direct statistical comparisons of effects across valence conditions.

2.5.1 Post HOC testing

Post-hoc tests are used following the detection of significant interaction effects in the RM-ANOVA. These tests identify specific group differences to help explain the significant interaction effects that were found.

To address the issue of multiple comparisons and control the overall risk of making a Type I error, post-hoc tests were employed following the initial analysis. Specifically, Bonferroni and Holm correction methods were used to adjust the significance threshold for individual pairwise comparisons. This adjustment helps maintain a more stringent standard for statistical significance when conducting multiple tests, reducing the likelihood of finding false positives. Additionally, the use of partial eta squared values can provide insights into effect sizes, further aiding in the interpretation of the results and their practical significance.

The threshold for statistical significance was set at an alpha level of 0.05, meaning results yielding a p-value less than 0.05 are deemed statistically significant. This threshold is commonly chosen to balance between minimizing the risk of false positives and false negative errors.

In summary, the pre-processing and statistical analysis of the EEG data involved a series of steps designed to isolate and examine theta activity in specific ROIs, and thereby compare the effects of different interventions between the two groups. This approach was guided by both the specific research question and the characteristics of the EEG data itself.

3 Results

This analysis primarily addressed the research question "Will mindfulness and positive fantasizing have different effects on theta power for healthy controls and remitted MDD individuals in an emotion regulation task?" The investigation focused on distinct valence conditions, specific regions of interest, the two types of interventions and the two participant groups. To determine significant effects within this complex interaction, a repeated measures ANOVA (RM-ANOVA) was utilized. This analytical approach allowed for the identification of significant differences among the various intervention conditions, participant groups, and valence conditions.

The RM-ANOVA provided a comprehensive evaluation of how the interventions impacted theta power, uncovering patterns that would be further explored through post-hoc analyses. These subsequent analyses were dedicated to understanding the origins of significant differences. Post hoc tests were conducted on models were a significant interaction effect had been observed. This targeted approach ensured a focused exploration of the specific effects of interest, providing a comprehensive understanding of the intricate relationships between the interventions, participant groups, valence conditions, and theta power within the context of the emotion regulation task.

3.1 Regional findings

3.1.1 Bilateral-frontal region

In the bilateral frontal lobes, an interaction effect between intervention and group was observed in two of the three models. When analyzing the negative and neutral valence models, interaction effects of intervention and group were deemed statistically significant ($F(1,17) = 5.890$, $p = 0.027$, $\eta_p^2 = 0.269$) and ($F(1,17) = 6.430$, $p = 0.022$,$\eta_p^2) = 0.287$). This partial ETA squared value can be interpreted as the percentage of total variability in theta power that was accounted for by the interaction between intervention and group. Figure 3.1 shows the results of the negative valence model in the bilateral frontal region. It visualizes the changes in theta power from pre to post intervention for each group. The y-axis denotes the mean theta power, and the x-axis for group 1 and group 2, namely the HC and rMDD. The white circles represent the pre-data point and the black circles the post data points. The left graph shows this for mindfulness intervention and the right one for positive fantasizing. The lines connecting the measures of both groups together allows to interpret the difference between the groups for the same measurement and intervention. The y-axis scales varied between the left and right graph. This ensured the readability of error bars and the changes from pre to post measures within each group. Although this makes any direct comparisons between the groups more difficult to discern from the graph, it emphasizes the distinct impact of each intervention on a scale that maximizes readability of that impact.

A clear difference between the interventions is evident in these two graphs. Primarily, an increase in theta power was observed following the mindfulness intervention, made evident by the fact that for both groups, theta power was higher in the post condition than in the pre condition. The rMDD group saw a smaller increase following mindfulness than the HC group, even though rMDD had a higher mean pre-measure. It is therefore difficult to discern an upward trend following mindfulness or a clear difference between these two groups as a result of the intervention.

The right graph within figure 3.1 shows the pre and post measures for positive fantasizing intervention in the negative valence model. Unlike mind-

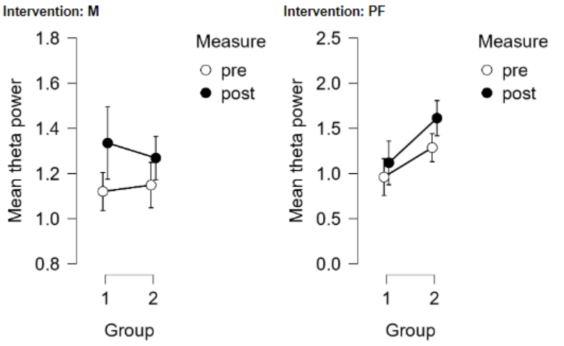

Figure 3.1: Bilateral frontal effects of mindfulness (M) and positive fantasizing (PF) on theta power in the negative valence model (Group 1: HC, Group 2: rMDD)

fulness, in positive fantasizing theta power in both groups was clearly affected similarly. The difference in mean theta power between the two groups was relatively consistent between the pre and the post condition; the difference between the groups in pre was similar to the difference between the groups in the post. That being said, a minimally larger increase in rMDD group compared to HC can suggest that positive fantasizing resulted in a larger increase in theta power for rMDD than for HC.

It is important to note the overlapping standard error bars of the pre and post condition for both groups and interventions. This suggests that in the bilateral frontal lobes under the negative stimuli condition, the difference in mean theta power following either intervention might not be statistically significant for either group. Graphs displaying the effects on the neutral and positive stimuli condition will also be made available in Appendix: A. The graphs of the other two valence conditions followed similar trends but observations were most clear in the negative valence model, hence it was selected for display.

Post HOC: Bilateral-frontal region

In the bilateral frontal region, post hoc tests were conducted on the neutral and negative models which, unlike the positive stimuli model, had significant interaction effects. In both models, however, none of the pairwise comparisons between the levels of group and intervention factors were found to be significant after adjusting for multiple comparisons using both Bonferroni and Holm methods. This suggests that although a significant interaction effect had been observed in the RM-ANOVA, this effect was not driven by a specific pairwise combination.

3.1.2 Frontal-midline region

The frontal midline region consisted of electrodes Fz and Cz. In this region, a significant interaction effect between intervention and group was also observed. This was, however, only the case in the model for the neutral stimuli condition. In this model, intervention and group had a significant interaction effect ($F(1,17) = 6.676$, $p = 0.022$, $\eta_p^2 = 0.323$) indicating that 32.3% of the variability of theta power can be accounted for by the interaction effect of intervention and group. Additionally, a marginally significant interaction effect between intervention and measure was observed in the neutral valence model, ($F(1,17) = 4.507$, $p = 0.052$, $\eta_p^2 = 0.244$). This p-value suggests that the difference in the effect of the intervention on theta power possibly depended on the measurement time point.

Although a large proportion of variability in theta power was accounted for by this interaction effect, it is important to note that p-value did not meet the conventional threshold set for significance and should therefore be interpreted with caution. In the frontal-midline region, both the negative and positive models reported neither any significant main effects nor any significant interaction effects.

Figure 3.2 again shows the change in theta power from pre to post intervention for each group, however this time the neutral model will be displayed to show the effect of the interventions in the frontal-midline region. This pair of graphs help visualize the changes in theta power when comparing groups and interventions. The pre and post measures for either groups followed different trajectories in the mindfulness intervention, seen on the left graph in figure 3.2.

In the HC group, a clear reduction in theta power is apparent following the mindfulness intervention (pre is greater than post). Standard error bars help to support the possible significance of this reduction in theta power. This is because the pre and post error bars are not overlapping, which likely suggests a significant difference between the mean

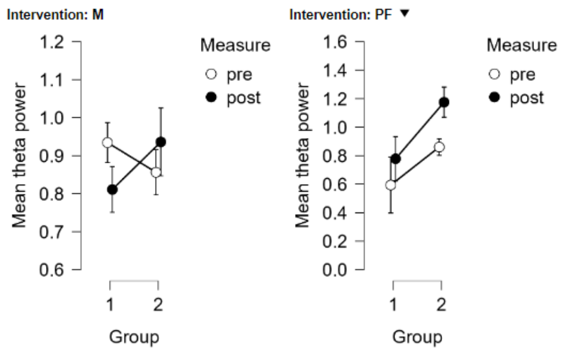

Figure 3.2: Frontal midline effects of mindfulness (M) and positive fantasizing (PF) on theta power in the neutral valence model (Group 1: HC, Group 2: rMDD)

theta power for pre and post.

In group 2, the rMDD group, and unlike the HC group, an increase in theta power was observed following the mindfulness intervention. However the overlapping error bars emphasize that there might not be a statistical difference between the measurement time points, possibly indicating that this increase is not representative of the interventions' effects.

With regards to the positive fantasizing intervention, the right graph within figure 3.2 shows that mean theta power is greater in the rMDD group than the HC, and that for both groups, an increase is observed between the pre and post values. The larger difference between pre and post in rMDD is also supported by the non-overlapping nature of the standard error bars, indicating a likely significant difference between the pre and post values in this group. While mean theta power also increased following positive fantasizing in HC, the overlapping standard error bars show that this increase following the intervention may not be statistically significant.

Similar figures for the negative and positive-valence models are presented in Appendix: A. While providing valuable insight, the trends of those two are similar to the neutral model, but had less easily discernible error bars. That being said, as neither the negative nor positive model had reported any significant main or interaction effects, the neutral models' figure was selected for display.

Post HOC: Frontal-midline region

Similarly, while the neutral model in the frontal-midline region had a significant interaction effect between intervention and group, post hoc analysis found no pairwise comparisons of group and intervention to be significant when using both Bonferroni and Holm methods. This implies that the interaction effects may not be attributed to a specific interventions' effects within a particular group.

3.1.3 Occipital region

In the occipital region, all three models produced at least one significant interaction effect. The negative valence model had a significant interaction effect between intervention and group ($F(1,17) = 5.598$, $p = 0.030$, $\eta_p^2 = 0.248$) as well as a marginally significant interaction effect between intervention and measure ($F[1,15] = 4.389$, $p = 0.051$, $\eta_p^2 = 0.205$). Partial ETA squared values show that 24.8% and 20.5% of the variability in theta power is accounted for by the interactions intervention*group and intervention*measure respectively. The significant interaction effect of intervention and group suggest that the effect of the intervention on theta power in the occipital region depends on the group.

The neutral valence model also reported a significant interaction effect between intervention and group ($F(1,17) = 7.954$, $p = 0.012$, $\eta_p^2 = 0.319$). Positive valence in the occipital region was the only model to report two significant interaction effects, namely intervention and group ($F(1,17) = 4.928$, $p = 0.040$, $\eta_p^2 = 0.225$) as well as intervention and measure ($F(1,17) = 5.177$, $p = 0.036$, $\eta_p^2 = 0.233$).

Figure 3.3 is of the positive valence model and follows the same plotting layout as the previous two figures. In the occipital region, a significant difference in response between mindfulness and positive fantasizing can be directly read from the figures. In this region, the smaller post mindfulness mean theta power compared to larger pre values depict a reduction in mean theta power following mindfulness intervention, for both the HC and the rMDD group. This however, was not the case for the positive fantasizing intervention, where an increase was observed in both groups. Similar to the effects of positive fantasizing seen on the figures corresponding to other ROIs, in the occipital region, rMDD had a higher pre and post than the

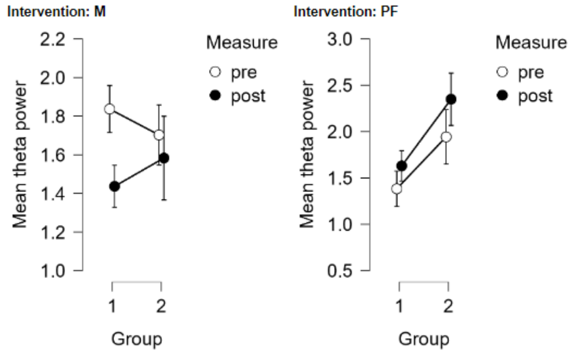

Figure 3.3: Occipital effects of mindfulness (M) and positive fantasizing (PF) on theta power in the positive valence model (Group 1: HC, Group 2: rMDD)

HC, and for both groups, the intervention resulted in an increase in theta power with regards to the baseline.

Standard error bars on figure 3.3 Intervention: M, overlapped for rMDD but not in the HC group, suggesting that the effect of mindfulness on the mean theta power of the rMDD group was less consistent compared to HC. The non-overlapping error bars in the HC group indicate a more reliable effect of mindfulness on theta power, whereas the overlapping error bars in rMDD suggest a greater variability in the response to mindfulness among rMDD individuals.

The descriptive plots of the negative and positive models will be made available in Appendix: A.

Post HOC: Occipital region

Post hoc testing in the occipital region was conducted on all three valence models, as they all reported significant interaction effects.

The positive model in this region, although exclusively reporting two significant interaction effects (intervention and group as well as intervention and measure), had no pairwise comparisons between the levels of group, intervention and measure factors that were found to be significant with either Bonferroni or Holm methods.

The negative and neutral models, on the other hand, had both reported significant pairwise comparisons in their respective post hoc tests. In both the negative and neutral valence models, a significant difference was found between mindfulness and positive fantasizing interventions in the rMDD group. In the negative stimuli model, the rMDD group demonstrated significantly lower theta power associated with the mindfulness intervention compared to the positive fantasizing intervention ($t(18) = -3.098$, $p = 0.039$). Similarly, in the neutral model mindfulness intervention was associated with a significantly lower theta power than positive fantasizing intervention in the rMDD group, ($t(18) = -3.692$, $p = 0.011$).

Post hoc analysis on the interaction of Intervention and Measure revealed that, in the post condition, the mindfulness intervention was associated with a significantly lower theta power compared to the positive fantasizing intervention ($t(18) = -2.817$, $p = 0.048$). This finding justified further post hoc analysis of the three-way interaction between intervention, measure and group. This analysis showed that, specifically for the rMDD group under the post condition, mindfulness was associated with a significantly lower theta power compared to positive fantasizing ($t(18) = -3.685$, $p = 0.022$).

The lack of other significant post hoc findings in this model suggest that the effects of the interventions on theta power may not be driven by simple pairwise differences between the levels of factors.

4 Discussion

The present study aimed to explore differences in theta power between groups with rMDD and healthy controls (HC) following two distinct interventions. The investigation involved a detailed analysis of interactions between interventions, groups, and measurement time points in various brain regions.

The research employed a repeated measures analysis of variance (RM-ANOVA) to study each valence condition and brain region separately. This approach yielded significant interaction effects between intervention and group in numerous models. This indicates that the impact of the interventions differed based on participant groups. Specifically, the mindfulness intervention led to a reduction in theta power in both HC and rMDD groups in the occipital and frontal-midline regions. However, the response was divergent in the frontal-midline region, where the effect of mindfulness was group-dependent, resulting in increased theta power for the rMDD group.

Post-hoc analyses further highlighted the distinctive effects of interventions and groups, providing a deeper understanding of the significant interaction effects identified by the RM-ANOVA. While some post-hoc results aligned with the RM-ANOVA findings, not all significant interactions were corroborated. This suggests that additional combinations of factors might contribute to the observed theta power effects.

Comparing these results with existing literature, the study revealed parallels with previous research that explored theta power alterations in patients with rMDD following mindfulness-based cognitive therapy. However, discrepancies were evident, possibly due to variations in intervention types, duration of sessions and amount of practice, and the nature of this implicit emotion regulation task employed. Notably, the positive fantasizing intervention showcased a consistent increase in theta power across both groups, presenting therapeutic potential for enhancing cognitive engagement among individuals with MDD.

These findings accentuate the need for further research on the efficacy of positive fantasizing interventions, particularly considering the scarcity of prior literature. The increase in theta power and its cognitive implications suggest possibilities for therapeutic applications in the context of major depressive disorder.

4.1 Limitations

The most significant limitation in the present study was the small sample size, which was largely due to a substantial amount of missing data. While a sample size of 100 subjects was intended, the number of subjects with data for all four measurement phases was significantly lower. To increase the sample size, subjects with just one of the two pre-measures were also included. However, this decision introduced its own set of limitations. For instance, the fact that some subjects had only one pre-measure while others had both could have influenced the comparability of the pre- and post-intervention measures. Specifically, for those with only one pre-measure, the same data points were used as a baseline for both interventions. This implies that those reused pre-measures would not directly correspond to a post-measure, potentially introducing biases and reducing the reliability of any conclusions drawn on the effect of an intervention. The small sample size, consisting of just 19 subjects even after including those with three measures, could have limited the statistical power of the study and increased the risk of type II errors, where true effects are missed. As a result of the small sample size, caution is necessary when generalizing these findings to larger populations.

Another possible limitation of this study stems from the design of the implicit emotion regulation task. The same set of 96 images were shown across all four phases of data collection. This repetition might have led to habituation or anticipation effects, where subjects' emotional responses to the images changes over time due to familiarity or expectations. For example, subjects might have anticipated the emotional context of upcoming images based on the context of previous images they had seen in this or previous sessions. The observed responses, therefore, might not fully reflect the true emotional reaction to that stimulus. The absence of a control group that underwent neither intervention also raises concern. Due to this, some of the effects that had been attributed to an intervention could be related to any of many external factors that were not controlled for.

It is also likely that the full effects of either intervention had not been attained within just one week of practice, as the benefits of Mindfulness based cognitive therapy (MBCT) and Preventive cognitive therapy (PCT) are often sustained over several weeks or months. The interventions in this study, however, were only implemented for a single week, deviating from existing literature that tested the effects after 8 weeks of therapy (Tovote et al., 2015). Therefore, this study may not have allowed sufficient time for the interventions to maximize their effect, making it hard to discern between the cause being not enough time practicing an intervention and that intervention not having a significant effect.

4.2 Future research directions

These limitations provide points for improvements in the current study, however they can also guide future research in other, relevant directions. The present study has illuminated the differences between mindfulness and positive fantasizing interventions on theta power in rMDD individuals and HC. However, the complexity of these interactions invites specific refinements and interesting new directions for exploration in future research.

Refinement of EEG analysis: Subsequent investigations could benefit from modeling each electrode independently. This would enable an examination of theta asymmetry across diverse brain regions as well as comparison across all electrodes. This could potentially reveal patterns of theta activity that remained obscured due to the current regional analysis structure.

Additionally, transitioning from an emphasis on theta power to an exploration of theta oscillatory activity could uncover information on the frequency and timing of theta rhythms, such as peak frequencies. These are not captured by power measures, meaning this shift in focus could provide a more detailed understanding of the neural dynamics associated with these interventions .

Other frequency bands: Although the current study focused on theta power, other frequency bands may also hold relevance in the context of depression and its remission.

Examining other frequency bands alongside theta power analysis could yield a more comprehensive perspective on the effects of mindfulness and positive fantasizing interventions. This approach would provide a broader understanding of how these interventions influence neural oscillations. By incorporating multiple frequency bands, the analysis could potentially reveal distinct patterns of neural modulation induced by the interventions. This direction for future analysis aligns with the current aim of uncovering the specific impacts of these interventions on brain activity, thereby contributing to a more complete representation and understanding of their internal mechanisms and the brains of individuals suffering from depression.

Intervention design and duration: The relatively short duration during which the interventions were taught, and the low number of sessions completed in this study could have had an influence on the intensity of the effects observed.

Future research could explore the effects of increasing the duration of intervention sessions or the number of sessions, as existing literature suggests that the impacts of mindfulness may become more pronounced over time (Tovote et al., 2015).

Furthermore, the temporal progression of an interventions' effects could be examined by extending the duration of the interventions and assessing the changes in theta power at multiple time points along the intervention process. Highlighting the time point at which the interventions' impact on theta power is the most pronounced, this direction for future research might deduce the optimal duration of either intervention.

5 Conclusions

In conclusion, this study has expressed the complex dynamics of theta power in remitted depressed individuals and healthy controls, highlighting how this neural activity is influenced by mindfulness and positive fantasizing interventions.

The effects of positive fantasizing on theta power were more consistent across both groups and across all brain ROIs, suggesting a more uniform response to this intervention than mindfulness. In contrast, the effects of mindfulness were more variable than positive fantasizing, depending on the group, brain region and emotional valence, thereby producing a less homogenous effect on theta power. This variability highlights the complex nature of these effects and the multitude of factors and combinations that can influence them.

Interestingly, the positive valence models exhibited the fewest significant interaction effects compared to the other valence models. Significant interaction effects in the positive valence model were only observed in the occipital region. This suggests that the impact of the interventions on theta power may be more pronounced in response to neutral and negative stimuli, a finding that invites further research.

In summary, this study analyzed the difference in effects of mindfulness and positive fantasizing on theta power, and conveyed the need for further research to fully discern the implications of these findings on current and future treatments for depression.

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A Appendix

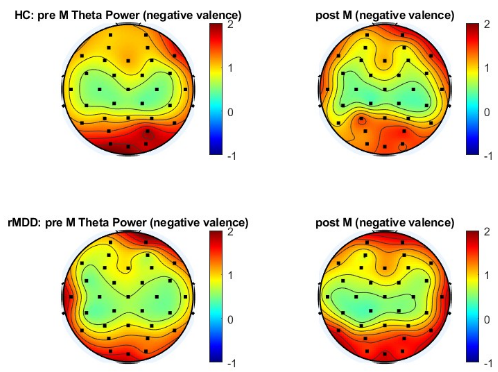


Figure A.1: Topographic maps pre/post Mindfulness intervention under negative valence condition. See figure 2.1 for ROIs. Black spots represents electrode. Darker colors represent more theta power at electrode site.

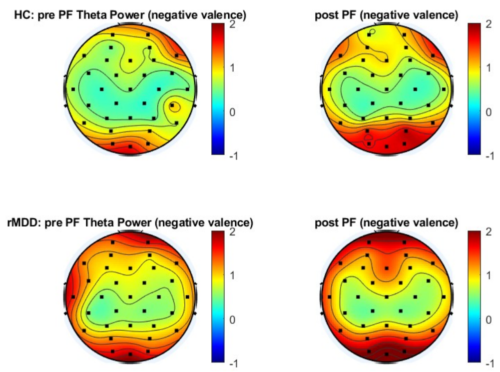
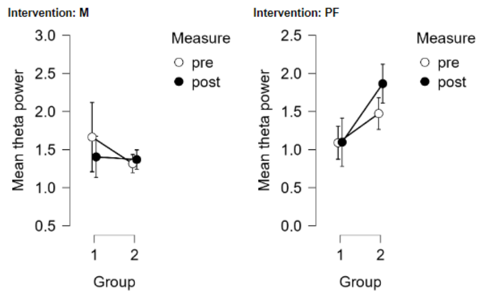
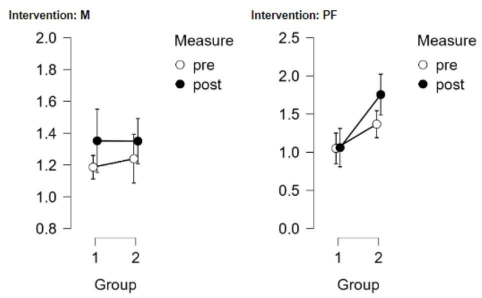


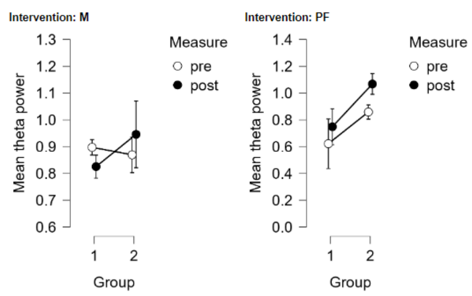
Figure A.2: Topographic maps pre/post Positive fantasizing intervention under negative valence condition.



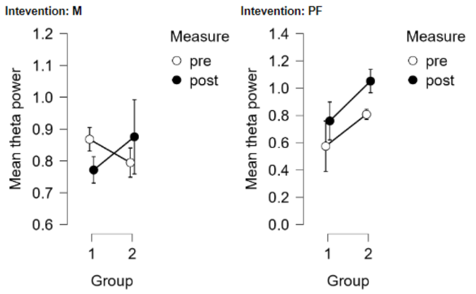
Bilateral frontal: Effects of Mindfulness (M) and Positive Fantasizing (PF) under neutral valence condition (Group 1: HC, Group 2: rMDD).



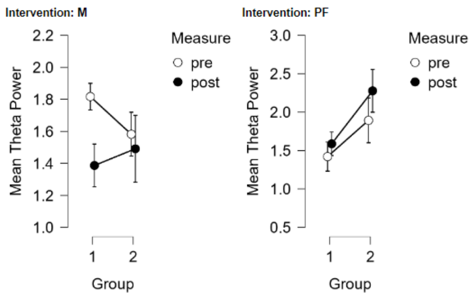
Bilateral frontal: Effects of Mindfulness (M) and Positive Fantasizing (PF) under positive valence condition (Group 1: HC, Group 2: rMDD).



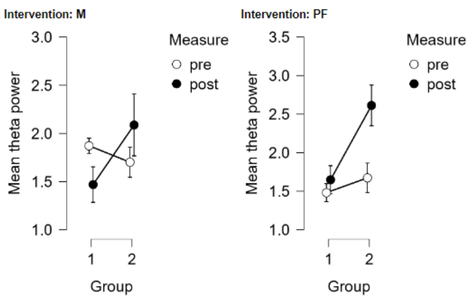
Frontal midline: Effects of Mindfulness (M) and Positive Fantasizing (PF) under positive valence condition (Group 1: HC, Group 2: rMDD).



Frontal midline: Effects of Mindfulness (M) and Positive Fantasizing (PF) under negative valence condition (Group 1: HC, Group 2: rMDD).



Occipital: Effects of Mindfulness (M) and Positive Fantasizing (PF) under negative valence condition (Group 1: HC, Group 2: rMDD).



Occipital: Effects of Mindfulness (M) and Positive Fantasizing (PF) under neutral valence condition (Group 1: HC, Group 2: rMDD).