Effects of meditation on frontal α-asymmetry in previously suicidal individuals

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This study investigated the effects of a meditation-based treatment for preventing relapse to depression, mindfulness-based cognitive therapy (MBCT), on prefrontal α-asymmetry in resting electroencephalogram (EEG), a biological indicator of affective style. Twenty-two individuals with a previous history of suicidal depression were randomly assigned to either MBCT (N=10) or treatment-as-usual (TAU, N=12). Resting electroencephalogram was measured before and after an 8-week course of treatment. The TAU group showed a significant deterioration toward decreased relative left-frontal activation, indexing decreases in positive affective style, while there was no significant change in the MBCT group. The findings suggest that MBCT can help individuals at high risk for suicidal depression to retain a balanced pattern of baseline emotion-related brain activation. *NeuroReport* 18:709–712 © 2007 Lippincott Williams & Wilkins.

Keywords: depression, prefrontal asymmetry, resting electroencephalogram, suicidality

Introduction

Suicide is the most serious complication of depressive disorders. About 25% of community samples who meet criteria for major depressive disorder (MDD) and 50% of inpatients with MDD report suffering from suicidal ideation during episodes, with rates of suicidal ideation being particularly pronounced in patients who suffer from chronic depression or frequent recurrence [1]. In those who have been suicidal in the past, suicidality is likely to consistently resurface as part of the symptom constellation during further episodes of depression and overall risk for relapse to depression is known to increase significantly with number of previous episodes [2,3].

Mindfulness-based cognitive therapy (MBCT) is a meditation-based skills training that has been shown to reduce significantly risk for relapse in previously depressed patients with three or more episodes [4,5]. MBCT trains concentrative and attentional capacities through daily meditation practice and utilizes these skills to help individuals become more aware of and respond differently to thoughts, feelings and bodily sensations that might fuel reactivation of depressogenic thinking patterns. An overarching goal of the meditation training is the enhancement of emotion regulation. Previous research comparing long-term meditation practitioners and nonmeditators suggests lasting effects on brain structure and functioning, including increased cortical thickness in areas associated with attention, interoception, and sensory processing such as the prefrontal cortex and right anterior insula [6] and increased electroencephalogram (EEG) γ-band activity and synchronicity [7]. This study investigated the effects of short-term meditation training for previously suicidal individuals on a neurophysiological indicator of global affective style, prefrontal α-asymmetry in resting EEG.

Research on prefrontal α-asymmetry is based on the idea that EEG α-activity provides an inverse indicator of brain activation. Asymmetry measures are computed as the difference in α-power density at homologous left and right hemispheric regions. A large body of studies on this parameter has demonstrated that relative left prefrontal activation, that is higher right than left α-power density, is related to an affective style characterized by stronger tendencies toward positive emotional responses and behavior that is approach- and reward-oriented, whereas relative right prefrontal activation, that is higher left than right α-power density, is associated with stronger tendencies toward negative emotional responses and behavior that is avoidant and withdrawal-oriented (for recent overviews see Refs. [8,9]). Prefrontal α-asymmetry under resting conditions has been shown to predict emotional responses to elicitors such as emotional film clips, emotional pictures, words and maternal separation in young infants and studies using repeated assessments have found resting asymmetry to be relatively stable in both nonclinical and clinical groups with trait components estimated to account for about 40–60% of variance [10,11]. Acute depression is characterized by relative left-frontal hypoactivation in resting EEG [12,13] and studies showing this same pattern in previously depressed individuals [14,15] suggest that such hypoactivation may remain as a latent risk factor even after recovery. Despite its trait-like nature, evidence from a recent study by Davidson *et al.* [16] suggests that prefrontal asymmetry can

be changed through meditation-based treatments. Davidson *et al.* investigated the effects of an 8-week course in mindfulness-based stress reduction in healthy volunteers and found significant group differences in resting asymmetry both immediately after the training and at 6-month follow-up, due in both cases to increases in left-sided activation in the treatment group and a reversed trend in the control group.

This study investigated whether MBCT can change the pattern of functional prefrontal asymmetry in a clinical group at high risk of relapse to depression. Functional prefrontal asymmetry was assessed in groups of previously suicidal individuals randomly assigned to either MBCT or TAU before and after the treatment period. We expected changes toward higher relative left prefrontal activation, that is stronger approach predisposition, following treatment in the MBCT group and no change or deteriorations toward higher relative right prefrontal activation, that is stronger withdrawal predisposition, over the waiting period in the TAU group.

Method

Participants

Participants were recruited via posters and advertisements asking for people who had been suicidal in the past but were feeling well at the moment. They were screened in a telephone interview and those indicating a history of suicidal depression and no core symptoms of depression or suicidality during the last 2 months were then invited for an assessment session. This session included the Mini International Neuropsychiatric Interview [17] with the addition of a SCID-II assessment for borderline personality disorder [18], conducted by trained research psychologists. To qualify for the trial, participants had to (a) fulfil criteria for a previous episode of major depression with suicidal ideation, (b) be in recovery for at least 8 weeks with no more than one core symptom and one other symptom of depression for any longer than 1 week at a time and (c) be between 18 and 65 years of age. Exclusion criteria were current alcohol or substance misuse, eating disorders, obsessive–compulsive disorder, schizophrenia or current mania and presence of habitual self-harming (e.g. self-cutting). Participants had to be right-handed.

A total of 34 individuals volunteered to take part in the EEG assessment. Sixteen of these participants had been randomly assigned to the MBCT group and 18 to the TAU group. In the MBCT group, six of the participants were lost for the post-treatment assessment, four of them had withdrawn before the start of the treatment and two had dropped out of treatment. In the TAU group, six participants were lost for the post-treatment assessment. The final samples consisted of 10 participants in the MBCT group and 12 participants in the TAU group. Participants in the MBCT group were significantly older [MBCT: M=48.0, SD=10.2; TAU: M=38.6, SD=9.6, $t(20)$=2.2, P=0.04] and tended to have a higher number of previous episodes than participants in the TAU group (MBCT: median=5.0, range=1–30; TAU: median=3.5, range=1–7, U=28, P=0.06). Levels of current depressive symptoms as assessed by BDI (MBCT: M=10.2, SD=8.9; TAU: M=6.1, SD=3.9; $t(20)$=1.4, P=0.16), age of onset of first episode of MDD (MBCT: M=22.8, SD=15.9; TAU; M=19.6, SD=9.7, $t(20)$=0.5, P=0.57), gender distribution (MBCT: 5m/5f, TAU: 6m/6f) and proportions of participants currently using antidepressants [MBCT: 7 yes/3 no; TAU: 6 yes/6 no, $\chi^2(1,22)$=0.90, P=0.34] were comparable in both groups.

Questionnaires

Beck Depression Inventory-II

The BDI-II [19] is a widely used self-description questionnaire for assessing the presence and severity of depressive symptoms during the last 2 weeks.

Positive and negative affect schedule: state version

The positive and negative affect schedule (PANAS) state version [20] was used to measure state positive and negative affect at the time of testing. It consists of two scales, one for positive and one for negative affect, each consisting of 10 adjectives, with regard to which respondents rate their current mood on a Likert-type scale.

Procedure

Resting EEG and EOG (for artefact screening) were measured before and after the 8-week treatment period. Upon arrival participants were informed about the laboratory tasks and asked for their written consent. Before the EEG recording was prepared and electrodes affixed to their face and scalp, participants filled in the BDI-II and the PANAS. Resting EEG was measured while participants sat in the dimly lit chamber over eight 1-min intervals, four with eyes open and four with eyes closed, in counterbalanced order (COOCCOOC and OCCOOCCO).

EEG recording and quantification

EEG was recorded from sites Fp1, Fp2, AF3, AF4, Fz, F3, F4, F7, F8, FC1, FC2, FC5, FC6, Cz, C3, C4, T7, T8, CP1, CP2, CP5, CP6, TP9, TP10, Pz, P3, P4, P7, P8, O1, O2, A1 and A2 using an EasyCap system with sintered Ag/AgCl electrodes. All sites were referenced to the average during recording, and re-referenced off-line to derive an averaged ears (A1/A2) reference, which was used as the reference of choice for all analyses.

Impedances were reduced to less than 3 kΩ and differences between homologous sites were less than 1 kΩ in all cases. Signals were amplified with a BrainVision Quickamp with 22-bit A/D conversion and a resolution of 71.5 nV (range ± 150 mV) and digitized at a rate of 500 Hz. The recorded data were re-sampled to 512 Hz by use of spline interpolation and filtered with a time constant of 0.3 s and an upper cutoff frequency of 40 Hz (−24 dB/October). Each segment was divided into 1 s epochs that overlapped by 50% to compensate the differential weighting of data points due to the imposition of a Hamming window before spectral analysis, resulting in 119 epochs for each of the 1-min baseline segments. To control for ocular artefacts, data were subjected to an algorithm that automatically rejected epochs when ocular signals exceeded ± 100 μV.

Artefact-free epochs were extracted through a Hamming window that tapered data at the distal 10% of each epoch and subjected to a fast Fourier transform (FFT) to derive measures of spectral power density (μV^2/Hz) in 0.5 Hz bins. The resulting spectra were averaged over all artefact-free episodes of a given segment and power density within the α band (8–13 Hz) was extracted. To derive a single measure

for the eight baseline recordings, α power density values were averaged over all 1-min segments, weighted by the number of artefact-free epochs in each segment. The aggregated power density values were transformed using the natural log to normalize data. EEG hemispheric asymmetry metrics were computed by subtracting left hemisphere values from right hemisphere values [ln(α power density right)−ln(α power density left)] for midfrontal (F4/F3) and lateral frontal sites (F8/F7). As α power density is inversely related to cortical activity, lower scores of this metric indicate relatively lower left-sided cortical activity. Previous research has most consistently linked approach- and avoidance-related psychological parameters with asymmetry in anterior sites F4/F3, however, positive findings have sometimes also been reported for sites F8/F7. Analyses, therefore, included asymmetry in both of these homologous pairs as dependent variables. Internal consistency of asymmetry scores over the eight 1-min intervals was Cronbach's α=0.90 and 0.86 for F4/F3 and 0.87 and 0.89 for F8/F7 at pre-assessment and post-assessment, respectively.

Treatment

MBCT

The treatment program followed the manual of Segal *et al.* [21] with several adaptations to focus on suicidal depression including an elaborated development of relapse prevention plans and a discussion of thoughts and feelings characteristic of suicidality. Participants in the MBCT group met for 8 weekly sessions of 2-h duration and a whole day of meditation practice between weeks 5 and 6 of the program. Participants were provided with CDs or tapes for daily guided meditation and yoga exercises.

TAU

Participants in the TAU group continued treatments under the care of their physician.

Results

Mean asymmetry scores in both groups at pre-testing and post-testing are shown in Fig. 1. A repeated measures MANOVA of F4/F3 and F8/F7 asymmetry scores with time (pre vs. post) as within- and group (MBCT-S vs. TAU) as between-subjects factor yielded a marginally significant main effect of time, F(2,19)=3.32, P=0.058, partial η^2=0.259, which was qualified by a significant group by time interaction, F(2,19)=3.70, P=0.044, partial η^2=0.281. Separate univariate tests for asymmetry at sites F4/F3 and F8/F7 showed that both effects, the main effect for time [F4/F3: F(1,20)=4.89, P=0.039, partial η^2=0.196; F8/F7: F(1,20)=6.61, P=0.018, η^2=0.248] and the time by group interaction [F4/F3: F(1,20)=5.29, P=0.032, partial η^2=0.209; F8/F7: F(1,20)=7.42, P=0.013, η^2=0.271], were present at both sites. To investigate the nature of the interaction effect, we computed Bonferroni-corrected simple comparisons. These showed significant pre to post-decreases in asymmetry scores in the TAU group (F4/F3: M_{I-J}=0.046, SE=0.014, P=0.003; F8/F7: M_{I-J}=0.084, SE=0.021, P=0.001), whereas there were no significant pre to post changes in the MBCT group (F4/F3: M_{I-J}=−0.001, SE=0.015, P=952; F8/F7: M_{I-J}=−0.002, SE=0.024, P=0.918). Results remained unchanged when PANAS-positive and PANAS-negative affect scores, both at pre-testing and post-testing, were entered as covariates. Exploratory data analyses using boxplots ensured that data did not include any outliers. Analyses of pre- to post-differences in both groups using nonparametric Wilcoxon signed rank tests yielded substantially the same findings.

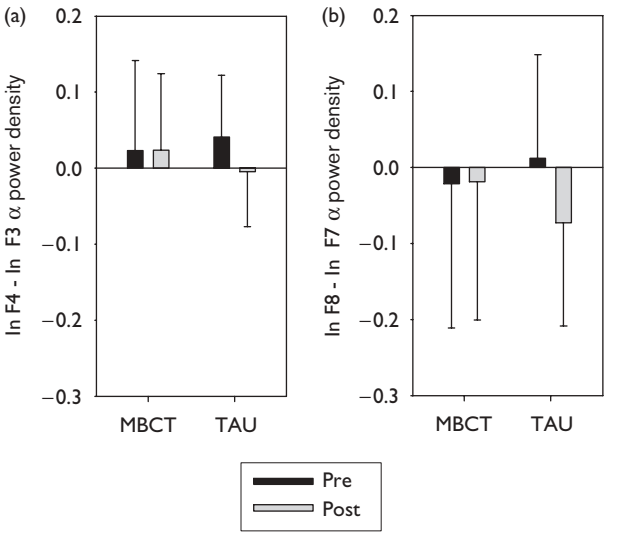

Fig. 1 Mean prefrontal asymmetry scores (ln α-power density right; – ln α-power density left) at F4/F3 (a) and F8/F7 (b) in MBCT (N=10) and TAU (N=12) participants. Error bars represent standard deviations. MBCT, mindfulness-based cognitive therapy.

To investigate the relationship between prefrontal asymmetry and state affect at time of testing, we computed correlations between PANAS positive and negative affect scores and asymmetry scores at electrode sites F4/F3 and F8/F7. This yielded no significant correlations (all $P>0.30$).

Discussion

The aim of this study was to investigate the effects of MBCT on functional prefrontal asymmetry in previously suicidal individuals. While the TAU participants showed significant deterioration toward relatively stronger right-sided activiation, that is a more avoidance-related affective style, MBCT participants retained a balanced pattern of prefrontal activation, suggesting a protective effect of the meditation-based treatment.

The fact that the TAU group deteriorated in their pattern of prefrontal activation must be viewed in light of the extremely high risk of relapse in this group. Risk for relapse in individuals with more than three episodes of depression has been estimated to be at 90% [22]. The observed change in asymmetry is consistent with an increase in vulnerability that may precede such relapse. This trend is likely to be particularly pronounced because of the relatively strict inclusion criteria in our study. For many of the participants, minimal symptoms over a period of at least 8 weeks represent a hyper-normal state from which negative change is more likely to occur.

A limitation of our study is that it assessed prefrontal asymmetry only during resting state and not following mood-challenge, which would have provided information on potential state effects. In line with previous research, however, that has found resting state assessments of

prefrontal α-asymmetry to be related to dispositional measures but not state measures of affective style [8], we did not find any relation with current mood and high internal consistency of the assessments both before and after the treatment interval, which indicates that these were not influenced by fluctuations during the time of testing. The study by Davidson *et al*. [16] found changes in prefrontal asymmetry following mindfulness meditation training in normal volunteers both for resting state and mood challenge assessments, which suggests that they might produce equivalent results.

The current data add to the existing body of research demonstrating effects of mindfulness meditation on vulnerability for depression. Retaining a balanced pattern of prefrontal asymmetry, and thereby a balanced affective style, may play an important protective role through decreasing the likelihood and frequency of negative affective responses and, consequently, reducing the probability of downward spirals of negative mood and cognition that have been shown to play such a prominent role in relapse to depression.

The exact mechanisms by which meditation-based interventions impact on prefrontal asymmetry remain speculative. Although there is ample evidence for the psychological validity of the parameter and research has demonstrated systematic relationships with other physiological variables such as cortisol levels [23] and immune functioning [24], knowledge about the neuroanatomical bases of prefrontal asymmetry is relatively restricted. In a recent overview, Craig [25] has pointed out parallels between asymmetries in the peripheral autonomous nervous system and forebrain asymmetries and described how structures of the left and right forebrain implicated in the circuitry underlying prefrontal asymmetry [9], particularly the left and right insula and the left and right anterior cingulate cortex, are differentially involved in parasympathetic and sympathetic regulation. On the basis of these observations he suggests that forebrain asymmetry is related to homeostatic function with the left forebrain being involved more strongly in energy-conserving, parasympathetic activity and the right forebrain being involved more strongly in energy-expending, sympathetic activity. From this perspective, part of the observed effect of meditation on prefrontal asymmetry may be due to general effects of meditation on sympathetic/parasympathetic balance, for example through reduction of prolonged states of arousal and a general fostering of relaxation.

Conclusion

The current findings suggest that intensive short-term meditation practice during times of recovery can help individuals at high risk of relapse retain a pattern of emotion-related brain activation that has been associated with decreased vulnerability.

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