

Brief Digital Mindfulness and Compassion Training drives Behavioral and Neural Plasticity in Healthcare Professionals

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Statistical Analysis Plan

Behavioral Data Analyses. For behavioral subjective scales, scores on self-compassion and mindfulness were calculated at T1, T2 and T3; and for MBI at T1 and T2. T2 vs. T1 and T3 vs. T1 scores were compared within each group using paired t-tests or its non-parametric equivalent Wilcoxon signed-rank test depending on the distribution of the behavioral scores; normality of distributions was checked using the Levene's test. For mindfulness, we compared state mindfulness across the three time points, which is a component of the dispositional trait mindfulness scale [1] as we expected state but not trait mindfulness to be malleable with training.

Cohen's d effect sizes were calculated for both within and between-group differences. Repeated measures analyses of variance comparing between-group behavioral differences were not conducted in this first study given the large effect sizes ($d > 0.8$) needed to observe significant group differences with adequate power.

To investigate the relationship between outcome gains and training engagement, behavioral changes in the *WellMind* training group were correlated with the number of training sessions completed by participants using Spearman's correlations.

Neurocognitive Data Analyses. We applied a uniform processing pipeline to all EEG data published in several of our studies [2-10]. This included: 1) EEG channel data processing, and 2) cortical source localization of the EEG data to estimate source-level neural activity. This included: 1) EEG channel data processing, and 2) cortical source localization of the EEG data to estimate source-level neural activity.

1) EEG channel data processing was conducted using the EEGLAB toolbox v2020 in MATLAB v2020 [11]. EEG data was resampled at 250 Hz and filtered in the 1-45 Hz range to exclude ultraslow DC drifts at < 1 Hz and high-frequency noise produced by muscle movements and external electrical sources at > 45 Hz.

Within the interoceptive attention task, EEG data were average-referenced and epoched to the LSL time-stamps of the response taps made by participants after every two breaths. Trials were epoched in the -4.0 sec to +4.0 sec window around response and categorized as either high

consistency, i.e. attentive trials (trials with $RT \leq 1$ median absolute deviation of median RT) or low consistency, i.e. distracted trials (trials with $RT > 1$ median absolute deviation of median RT). This epoch was chosen because it was not contaminated by motor artifacts given that median response times for two-breath monitoring across subjects were ~ 8 sec in the interoceptive task.

There were no missing channels in the EEG data across subjects. Epoched data were cleaned using the `autorej` function in EEGLAB to remove noisy trials, i.e. $>5SD$ outliers rejected over max 8 iterations, followed by further cleaning of electrooculographic, electromyographic or non-brain source artifacts using the Sparse Bayesian learning (SBL) algorithm (<https://github.com/aojeda/PEB>) [10,12]. The cleaned data were then band filtered in the physiologically relevant theta (4-7 Hz), alpha (8-12 Hz), and beta (13-30 Hz) frequency bands. Given that alpha band oscillations are dominant during eyes closed [13–16], as was also evidenced in our data (see Results), we exclusively source localized alpha band neural processing.

2) We used the block-Sparse Bayesian learning (BSBL-2S) algorithm to localize the alpha frequency band filtered EEG data and partitioned the signals into cortical regions of interest (ROIs) and artifact sources [10,12]. BSBL-2S is a two-step algorithm in which the first-step is equivalent to low-resolution electromagnetic tomography (LORETA [17]). LORETA estimates sources subject to smoothness constraints, i.e. nearby sources tend to be co-activated, which may produce source estimates with a high number of false positives that are not biologically plausible. To guard against this, BSBL-2S applies sparsity constraints in the second step wherein blocks of irrelevant sources are pruned. Notably, this data-driven sparsity constraint reduces the effective number of sources considered at any given time as a solution, thereby reducing the uncertainty of the inverse solution. Thus, it is not that only higher channel density data can yield source solutions, the ill-posed inverse problem can also be solved by imposing more aggressive constraints on the solution to converge on the source model at lower channel densities, as also supported by prior research [18,19]. Of note, the BSBL-2S two-stage algorithm has been benchmarked to produce evidence-optimized inverse source models at 0.95AUC relative to the ground truth [10,12].

For the source space activations, ROIs were based on the standard 68 brain region Desikan-Killiany atlas [28] using the Colin-27 head model [20]. Artifacts still remaining in source space within individual subject data were removed using the Grubbs statistical test applied iteratively using spline interpolation - an option available within the MATLAB `isoutlier` function [21], and population outliers across all sessions and subjects source data were removed using the $>5SD$ criterion. ROIs were further grouped into canonical cognitive control networks that can undergo task-dependent modulation, i.e. the fronto-parietal network (FPN), cingulo-opercular network (CON) and the default mode network (DMN) [22–25]. Alpha band EEG data were trial-averaged for high vs. low consistency (i.e., attended vs. distracted) breath monitoring trials on the interoceptive attention task. These trials were compared for within-group pre vs. post activity differences in the fronto-parietal network (FPN), cingulo-opercular network (CON) and the default mode network (DMN) using paired t-tests. Effect sizes were also calculated for neural data, reported as Cohen's d , 0.2: small, 0.5: medium, 0.8: large [26]. Given that we have observed large effect size neural outcomes ($d > 0.8$) in our prior digital training studies [27–29], repeated measures analyses of variance (rm-ANOVA) were conducted to analyze between-group post vs. pre network effects; the Greenhouse–Geisser significance correction was applied to adjust for lack of sphericity. Finally, Spearman's correlations were used to analyze neurobehavioral associations.

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