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From state-to-trait meditation: Reconfiguration of central executive and default mode networks

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Abstract

While brain default mode network (DMN) activation in human subjects has been associated with mind wandering, meditation practice has been found to suppress it and to increase psychological well-being. Additionally to DMN activity reduction, experienced meditators during meditation practice show and increased connectivity between the DMN and the central executive network (CEN). However, the gradual change between DMN and CEN configuration from pre-meditation, during meditation, and post-meditation are unknown. Here we investigated the change in DMN and CEN configuration by means of brain activity and functional connectivity analyses in experienced meditators across three back-to-back functional magnetic resonance imaging scans: Pre-meditation baseline (trait), meditation (state), and post-meditation (state-to-trait). Pre-meditation baseline group comparison was also performed between experienced meditators and healthy controls. Meditation trait was characterized by a significant reduction in activity and functional connectivity within DMN and increased anticorrelations between DMN and CEN. Conversely, meditation state and meditation state-to-trait periods showed increased activity and functional connectivity within the DMN and between DMN and CEN. However, the latter anticorrelations were only present in experienced meditators with limited practice. The interactions between networks during these states by means of Positive Diametric Activity (PDA) of the fractional Amplitude of Low-Frequency Fluctuations (fALFF) defined as $\overline{CEN\ fALFF} - \overline{DMN\ fALFF}$ revealed no trait differences, but significant increases during meditation state that persisted in meditation state-to-trait. The gradual reconfiguration in DMN and CEN suggest a neural mechanism by which the CEN negatively regulates the DMN and is probably responsible for the long-term trait changes seen in meditators and reported psychological well-being.

Significance Statement

We introduce a Positive Diametric Activity (PDA) metric to measure the relation between two anticorrelated rs-fMRI networks in experienced meditators. PDA as well as functional connectivity (FC) are increased during meditation compared to resting state and persists in the post meditation resting state. Conversely, meditation trait is characterized by positive PDA but with significant reduction in activity and functional connectivity within Default Mode Network (DMN) and increased anticorrelations between DMN and central executive network (CEN). PDA and FC between DMN and CEN distinguish meditation state-to-trait effects.

1. Introduction

What does the mind do when all physiological needs are taken care of and there are no immediate demands? Does it part into an empty void, a dormant state to conserve resources until something disturbs it and activity is needed? We all know that this is not the case. Every moment of our waking experience challenges this explanation of mental life. When nothing requires active cogitative processing, our mind generally tends to think about what is *not* going on in the present moment, i.e., it wanders, recapitulates events that happened in the past, or fantasizes about what might happen in the future, jumping from one thought to the next with amazing speed and apparent randomness (Mason et al., 2007). Undeniably, this never stopping stream of consciousness appears to be our brain's idle mode of being, our default mode when not otherwise engaged (Christoff et al., 2016; Kane et al., 2017; Mason et al., 2007). Although this ability is as an evolutionary achievement that allows us to learn, reason, and plan (Mantini et al., 2013; Rilling, 2014), it swiftly fails to serve its adaptive function, and turns into a risk factor for health and psychological well being whenever it becomes a rigid and inflexible pattern with tremendous emotional costs (Jazaieri et al., 2015; Killingsworth and Gilbert, 2010a; Ottaviani et al., 2013; Simon and Engström, 2015; Smallwood et al., 2009). Consequently, the underlying mental processes that keep the brain active when not otherwise engaged have been a source of significant theoretical surmise. Since the advent of neurophysiological recordings, it has been determined that the brain is never truly at rest (Berger and Hans, 1933). From a functional imaging perspective, the remarkable properties of the brain's intrinsic activity were first noted by Biswal and colleagues (1995). They observed that the ‘‘noise’’ in the spontaneous functional Magnetic Resonance Imaging (fMRI) blood oxygen level dependent (BOLD) signal exhibited striking patterns of spatial coherence corresponding, in their case, to the sensorimotor regions of the cerebral cortex. Subsequently, Raichle and colleagues first took notice that during the commonly used “baseline” in research paradigms, the synchronous behavior of a number of anatomic regions were observed to deactivate during task and thus initially identified as a network of task-specific deactivations, later named the default mode network (DMN) (Buckner et al., 2008; Gusnard et al., 2001). Soon it was determined that these task specific deactivations of the DMN also showed patterns of coherent activation during periods of rest that included anterior (medial prefrontal cortex, MPFC) and posterior midline structures (posterior cingulate, PCC) as well as lateral temporal cortex (LTC) and the hippocampus. Additionally, in healthy individuals, DMN activity has been shown to be anticorrelated (negatively correlated) with brain regions activated during attention demanding tasks (e.g., the central executive network) (Fox et al., 2005; Fransson, 2005a; Greicius et al., 2002; Kelly et al., 2008; Uddin et al., 2009). Specifically, the Central Executive Network (CEN), typically including the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC), supports these attention demanding tasks, i.e. attentional control and working memory. Across individuals greater magnitude of DMN-CEN anticorrelations is associated with superior cognitive function such as complex working memory (Hampson et al., 2010a; Keller et al., 2015a; Whitfield-Gabrieli et al., 2009). (Hampson et al., 2010b; Keller et al., 2015b; Whitfield-Gabrieli et al., 2009). Abnormal DMN activity – such as competitive, antagonistic DMN activation during CEN activity or changes in connectivity between subregions of the DMN – has also been associated not only with lower levels of happiness (Killingsworth and Gilbert, 2010b; Smallwood and O'Connor, 2011), but with a number of psychological disorders such as anxiety (Zhao et al., 2007), depression (Sheline et al., 2009), schizophrenia (Bastos-Leite et al., 2015; Camchong et al., 2011; Garrity, 2007; Pomarol-Clotet et al., 2008; Whitfield-Gabrieli et al., 2009), epilepsy (Liao et al., 2011), autism (Assaf et al., 2010), attention deficit hyperactivity disorder (ADHD; Uddin et al., 2008), and Alzheimer's disease (AD; Greicius et al., 2004; Sheline and Raichle, 2013). Recent studies further suggest that abnormal DMN activity and connectivity plays a role in neuropsychiatric disorders (Raichle, 2015; Whitfield-Gabrieli and Ford, 2012). These associations have led to the suggestion of using the DMN as method by which to study mental disorders, resulting in a growing body of literature concerning disorder-specific variations within the DMN (Arens et al., 2003; Broyd et al., 2009; Fox and Greicius, 2010; Greicius, 2008; Simon and Engström, 2015; Whitfield-Gabrieli and Ford, 2012).

Given the interrelationship between mind-wandering, DMN activity, and the risk to health and psychological well being, a question arises: Is it possible to change this maladaptive mode into one that is more pleasant and healthier? According to many philosophical and contemplative traditions, yes, this is possible. Thus, these teach that happiness is to be found by "living in the moment", i.e, to be here and now without losing oneself in past or future thought.

For more than two millennia, meditation has been practiced as a means of achieving this ephemeral mind state, psychological equanimity and self-awareness, yet it has only recently become the target of systematic western-world research for its relevance to mental and physical health in fields such as medicine, psychology, and neuroscience (Van Dam et al., 2017). Undeniably, meditation is becoming increasingly well regarded for its therapeutic promise (Buchholz, 2015; Creswell, 2015; Gu et al., 2015; Simon and Engström, 2015) and meditation methods have been beneficial in the treatment of psychological disorders such as schizophrenia (Chien and Thompson, 2014), depression (Eisendrath et al., 2008; Kuyken et al., 2008; Ma and Teasdale, 2004; Teasdale et al., 2000; Yang et al., 2016), anxiety (Baer, 2003; Grossman et al., 2004; Ludwig and Kabat-Zinn, 2008; Shen et al., 2014), addiction (Bowen et al., 2014), alcoholism (Garland et al., 2010; Witkiewitz et al., 2005), smoking (Tang et al., 2013), mild cognitive impairment (MCI; Wells et al., 2013), and attention-deficit/hyperactivity disorder (Bueno et al., 2015; Janssen et al., 2015; ADHD; Zylowska et al., 2008). Preliminary findings have suggested that the effects of meditation include better emotion regulation (Lutz et al., 2014; Prakash et al., 2015; Turner, 2014), self-regulation (Tang et al., 2014), awareness and self-perception (Hölzel et al., 2011b), memory and cognition (Zeidan et al., 2010), attention (Moore et al., 2012), working memory (Banks et al., 2015; Mrazek et al., 2013), as well as gray and white matter differences in experienced meditators (Fox et al., 2014; Hölzel et al., 2011a; Luders et al., 2009). Functional imaging studies on meditation practice have examined two distinct effects of meditation. The first, called a state effect, refers to the short-term consequences of meditation practice on the individual's state. This would include short lived changes in bodily awareness, relaxation, emotion regulation, attention and in BOLD activation or functional connectivity (FC) when measured with fMRI. During this active state of meditation, studies have consistently found that within-network connectivity of the DMN as well as between-network connectivity of DMN, CEN and salience network (SAL) are increased (Brewer et al., 2011; Garrison et al., 2014; Jang et al., 2011; Jao et al., 2016). The second, called a trait effect, refers to long-lasting changes in these same dimensions, which continue after practice and during the meditator's daily life (Lutz et al., n.d.). However, the findings for this trait effect have not been so clear when measured with resting state functional connectivity (rsFC), with mixed results (for a recent review see Mooneyham et al., 2016). Furthermore, little to nothing is known about the activity and connectivity change of DMN and CEN that intertwine the transitory state effects of meditation with the lasting trait effects of meditation practice.

Here we hypothesized that activity of the CEN is an important modulator of DMN activity and connectivity, both during the meditation state and during the transition phase post meditation. Support for this idea comes on the one hand from correlational neuroimaging studies looking into attentional and cognitive control (Anticevic et al., 2012; Dosenbach et al., 2007; Fox et al., 2005; Fransson, 2005b; McKiernan et al., 2003; Northoff et al., 2007; Sonuga-Barke and Castellanos, 2007; Sridharan et al., 2008), but specifically from a study by Chen et al (2013) that provides direct evidence for this neural mechanism. In their study, they specifically tested this mechanism by exciting or inhibiting nodes within the CEN using noninvasive brain stimulation and observed the results using simultaneous brain imaging. They found that the DMN is under inhibitory control specifically from a node in CEN (posterior middle frontal gyrus pMFG;BA 9/10). Accordingly, we predicted that brain activation in nodes of the CEN during meditation would: (i) modulate activity of the DMN and increase connectivity between DMN and CEN, (ii) this changes would persist after meditation and finally, (iii) that there are trait differences in DMN and CEN activity and connectivity characteristic of meditation experience. To test these predictions, we conducted three back-to-back functional magnetic resonance imaging (fMRI) runs in experienced meditators: Pre-meditation baseline (trait), meditation (state), and post-meditation (state-to-trait). The pre-meditation baseline was also performed on a group of healthy controls as a comparison.

2. Materials and Methods

2.1. Participants

After standard exclusion criteria for fMRI research were applied, 16 experienced meditators (EM; 6 female, mean age 41.12 years, SD 10.5, average of 1677 h +/- 367 h of Vipassana meditation experience) and 17 meditation naive healthy controls (HC; 7 female, mean age 35.70 years, SD 4.7) participated in the study. There was no significant age difference between groups (t(21) = -1.68, p = .10). All subject groups were recruited and scanned in the same time period as part of the same experiment and all subjects gave informed consent for the experimental procedure, and the protocol had IRB approval.

2.2. Experiment Design

BOLD fMRI data were collected from all participants during a five-minute, eyes-open resting-state period (rsBase). In addition, immediately following the rsBase scan, EM participants were also scanned during a 20-minute, eyes-open period while engaged in vipassana meditation (Med). Vipassana meditation emphasizes focused attention typically involving the deliberate focus of attention to a chosen target—such as general body sensations or sensations related to breathing— and the voluntary redirection of attention each time it lapses (Hart, 2011). Finally, EM underwent a second five-minute eyes-open resting-state period (rsPost).

2.3. Meditation Trait, State and State-to-Trait Operationalizations (Austin, 1999; Shapiro (Jr.) and Walsh, 1984; West, 2016)**:**

Meditation Trait: the *lasting changes* in sensory, cognitive, and self-referential awareness and their underlying brain activity and connectivity that persist in the meditator irrespective of being actively engaged in meditation. Contrast HC rsBase < EM rsBase (Figure 1.C.a).

Meditation State: Refers to the altered sensory, cognitive, and self-referential awareness that can arise *during* meditation practice and their underlying brain activity and connectivity. In the present study this will correspond to the contrast EM rsBase < EM Med (Figure 1.C.b).

Meditation State-to-Trait: Refers to the changes in sensory, cognitive, and self-referential awareness and their underlying brain activity and connectivity that persist in the meditator *after* an active engaged meditation session. Contrast EM rsBase < EM rsPost (Figure 1.C.d).

2.4. MRI Data Acquisition

MRI imaging was performed on a 3.0T GE MR750 instrument (General Electric, Waukesha, WI) using a 32-channel head coil. Functional imaging for resting state included 35 slices, acquired using a T2*-weighted EPI sequence with TR/TE 2000/40 ms, a 64x64 matrix and 4-mm slice thickness, resulting in a 4x4x4 mm^3 isometric voxel and a total of 151 volumes. For meditation imaging included 35 slices, acquired using a T2*-weighted EPI sequence with TR/TE 1500/40 ms, a 64x64 matrix and 4-mm slice thickness, resulting in a 4x4x4 mm^3 isometric voxel and a total of 804 volumes. The shorter TR during meditation was chosen according to the parameters in Hasenkamp et al. (2012a) to adhere to additional experiential sampling during meditation and thus needed a faster acquisition. Importantly, this discrepancy has been shown not to affect fractional ALFF (fALFF) nor functional connectivity correlation coefficients (CC) since multiple repetition times have been empirically compared to address the issue of temporal mismatch (Wu et al., 2011). Additionally, High-resolution structural 3D-T1-weighted images were acquired for anatomical localization (resolution of 1x1x1 mm^3, TR = 2.3 s, TE = 3 ms) covering the whole brain. The images were acquired with an acceleration factor = 2.

2.5. Preprocessing

The preprocessing of resting state images was done using SPM 12 software (http://www.fil.ion.ucl.ac.uk/spm) implemented in a MATLAB suite (Mathworks, Inc., Natick, Massachusetts). It included slice time correction, head motion correction, co-registration to subjects' structural images, segmentation, normalization, linear detrending and smoothing (FWHM = 8 mm).

2.6. Brain Activity Analysis

In order to detect regional brain activity changes we used an improved approach of the Amplitude of Low Frequency Fluctuations (ALFF) method, fractional ALFF (fALFF) (Zou et al., 2008). This method takes the ratio of power spectrum of low-frequency (here: 0.008-0.09 Hz) to that of the entire frequency range. fALFF analysis was carried out with AFNI's 3dRSFC (Taylor and Saad, 2013). Similar to the procedures of previous literature (Kong et al., 2015; Shpaner et al., 2014; Zou et al., 2008), the time series of each voxel was transformed to a frequency domain after the linear trend was removed without band-pass filtering. The square root was then calculated at each frequency of the power spectrum, and finally the sum of amplitude across 0.008-0.09 Hz was divided by that across the entire frequency range (0–0.25 Hz for TR = 2 sec and 0-0.33 Hz for TR = 1.5 sec, see fMRI Data Acquisition) to obtain fALFF. Importantly, the TR discrepancy has been shown not to affect fractional ALFF (fALFF) since multiple repetition times have been empirically compared to address the issue of temporal mismatch (Wu et al., 2011). Next, we obtained the Meditation Trait differences of the fALFF maps of HC and EM at baseline (rsBase) using two sample t-tests. The thresholded images were then converted into binarized masks and were used as the target Regions of interest (ROI's) from which to extract the mean fALFF maps for all subjects and states. All imaging analysis were performed with FSL's randomise tool for nonparametric permutation (5000 permutations) inference on neuroimaging data (Winkler et al., 2014) and masked with the binarized DMN & CEN templates of Yeo et al (2011) and Threshold-Free Cluster Enhancement (TFCE: Smith and Nichols, 2009) cluster corrected ($P < 0.05$) . We first obtained the meditation trait differences of the fALFF maps of HC and EM at baseline (rsBase) using two-sample t-test and then extracted the mean fALFF maps for all subjects and states. The extracted values were converted to normally distributed Z-scores to allow for second-level analyses using multilevel modeling one-way repeated measures analysis of variance (ANOVA) and post hoc Tukey test. Statistical analysis was performed with the open-source R package (www.R-project.org).

2.7. Positive Diametric Activity

To further assess the information processing during meditation we introduce a Positive Diametric Activity (PDA) metric in order to determine the activation change of CEN and DMN according to their mean fALFF. The PDA metric is based on the hypothesis that there is a causal neural mechanism by which the CEN negatively regulates the DMN (Chen et al., 2013). This is to say that when CEN activity is increased this produces an inhibitory effect on the DMN and its activity is decreased. Accordingly, we define the PDA as follows:

$$PDA \ = \underline{CEN\,fALFF} - \underline{DMN\,fALFF}$$

Where PDA will always be positive as long as the mean activity of CEN is greater than the mean activity of DMN, reflecting precisely this negative relation between CEN and DMN. Meditation trait differences of the PDA for HC and EM at baseline (rsBase) was assessed using two-sample t-tests. The PDA for EM rsBase, Med and rsPost were analyzed using multilevel modeling one-way repeated measures analysis of variance (ANOVA) and post hoc Tukey test.

2.8. Functional Connectivity Analysis

Functional connectivity analysis was performed using a seed-driven approach with in-house, custom software CONN 16.b (Chai et al., 2012; Whitfield-Gabrieli et al., 2012). We performed seed-voxel correlations by estimating maps showing temporal correlations between the BOLD signal from the target ROIs and that of every brain voxel (i.e. Whole-Brain analysis). The specific target ROI clusters were obtained from the previous fALFF analysis two sample t-tests between HC and EM at rsBase for the DMN and CEN respectively (see Brain Activity Analysis section). This yielded seed ROIs for the DMN in the medial prefrontal cortices (see clusters 1 & 2 in Figure 1.A.a and Table 1), which are nodes that have been implicated in processing of self-referential stimuli and in generating a model of the self (Northoff and Bermpohl, 2004) and for the CEN in bilateral inferior frontal gyrus and inferior parietal lobule (see clusters 3, 4 & 5 in Figure 1.A.a and Table 1). Physiological and other spurious sources of noise were estimated and regressed out using the anatomical CompCor method (aCompCor) (Chai et al., 2012). Global signal regression, a widely used preprocessing method, was not used because it artificially creates negative correlations that prevent the interpretation of anticorrelation (Behzadi et al., 2007; Chai et al., 2012; Whitfield-Gabrieli et al., 2012) and can contribute to group differences in positive correlations (Saad et al., 2012). Instead, aCompCor allows for interpretation of anticorrelations and yields higher specificity and sensitivity compared with global signal regression (Chai et al., 2012). A temporal band-pass filter of .008 Hz to .09 Hz was applied simultaneously to all regressors in the model.We used methods that minimize the influence of motion and artifact and that allow for valid identification of correlated and anticorrelated networks (Behzadi et al., 2007; Chai et al., 2012; Whitfield-Gabrieli et al., 2012). To address the spurious correlations in resting-state networks caused by head motion we used quality assurance software Artifact Detection Tools (http://www.nitrc.org/projects/artifact_detect; http://www.nitrc.org/projects/conn) (Whitfield-Gabrieli et al., 2012) to identify problematic time points during the scan. Specifically, an image was defined as an outlier if the head displacement in x, y, or z direction was greater than .5mm from the previous frame, or if the global mean intensity in the image was greater than 3 standard deviations from the mean image intensity for the entire resting scan. A single regressor for each outlier image was included in the first level general linear model along with motion parameters and first order derivatives (there were no significant differences between groups and runs, see Fig.S1). The anatomical image for each participant was segmented into white matter, grey matter, and cerebrospinal fluid (CSF) masks using SPM8. To minimize partial voluming with grey matter, the white matter and CSF masks were eroded by one voxel, which resulted in substantially smaller masks than the original segmentations (Chai et al., 2012). The eroded white matter and CSF masks were then used as noise ROIs. Signals from the white matter and CSF noise ROIs were extracted from the unsmoothed functional volumes to avoid additional risk of contaminating white matter and CSF signals with grey matter signals. Previous results showed that aCompCor signals were considerably different from the global signal, as regressing higher order principal components of the global signal diminished both positive and negative correlations whereas regressing aCompCor signals resulted in stronger anticorrelations and eliminated spurious correlations

(Behzadi et al., 2007). Time series of all the voxels within each seed were averaged, and first-level correlation maps were produced by extracting the residual blood oxygen level–dependent time course from each seed and computing Pearson correlation coefficients between that time course and the time course of all other voxels. Correlation coefficients were converted to normally distributed Z-scores using the Fisher transformation to allow for second-level general linear model analyses. Meditation Trait differences of HC and EM at baseline (rsBase) were compared using two-sample t-tests. Second-level analyses for EM rsBase, Med and rsPost, were compared using with a one-way repeated measures analysis of variance (ANOVA) implemented in CONN. All contrasts are nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$, unless otherwise stated.

2.9. Correlation between PDA and FC

In order to assess if there is a relationship between Brain Activity (fALFF) and Functional Connectivity (FC) we correlated the individual Positive Diametric Activity (PDA) scores (see above) with differences in FC of DMN and CEN ROI's for the different meditation states.

3. Results

3.1. Meditation Trait Effects

3.1.1. fALFF analysis

DMN: EM showed reduced activity in the left Medial Temporal Gyrus (MTG; BA 21), right Superior Frontal Gyrus (SFG; BA 6), left Medial Prefrontal Cortex (MPFC; BA 10, see Figure 1.A.a.1 and 1.A.a.2, blue box plots in 1.B [HC rsBase < EM rsBase] rs Base and Table 1).

CEN: EM showed reduced activity in bilateral Dorslolateral Prefrontal Cortex (DLPFC; BA 9, see Figure 1.A.a.3 and 1.A.a.4; red box plots [HC rsBase < EM rsBase] in 1.B, Table 1) and left

Inferior Parietal Lobule (IPL; BA 40, Figure 1.A.a.5, Table 1). For this and all other fALFF significant MNI coordinates see Table 1.

3.1.2. FC analysis

DMN: EM showed reduced connectivity with left Superior Frontal Gyrus (SFG; BA 11), right Medial Frontal Gyrus (MFG; BA 10), Inferior Parietal Lobule (IPL;BA 40) and Superior Temporal Gyrus (STG; BA 38). Figure 2.A.a; blue box plots [HC rsBase < EM rsBase] in 2.B and Table 2. For this and all other significant connectivity coordinates see Table 2.

CEN: No differences were found.

3.1.3. PDA analysis

No significant differences were found.

3.1.4. Correlations between PDA and FC

DMN: No significant correlations were found.

CEN: No significant correlations were found.

3.1.5. Correlations between Hours of Meditation practice and FC

DMN: No significant correlations were found.

CEN: Whole-Brain FC analysis revealed a significant correlation (R = .87) between the hours of meditation practice and connectivity between CEN and MPFC at rsBase for EM (See Figure 4.A).

To better understand this positive correlation between meditation experience and increased connectivity between CEN and MPFC, which also has been reported in other studies comparing novice vs. expert meditators (Brewer et al., 2011; Jang et al., 2011; Shaurya Prakash et al., 2013), we divided our EM group into two sub-groups (Median = 1130 hrs): experienced meditators with more than 1130 hrs of daily practice (EM>1130; ~3 years) and intermediate meditators (EM <1130) and conducted a multilevel modeling one-way repeated measures ANOVA and post hoc Tukey test for the connectivity Z-scores between CEN and MPFC. The results confirmed a significant difference between HC (mean = .13) and EM<1130 (mean = -.04, b = -0.16, p < 1e-3) but no difference between HC and EM>1130 (mean = .04, b = -.09, p = .08). Furthermore, there was also a significant difference between EM<1130 (Median = -0.25) and EM>1130 (Median = -.07, b = .17, p = .04). (Figure S2).

3.1.6. Correlations between Hours of Meditation practice and PDA

No significant correlations were found for Meditation Trait, State or State-to-Trait PDA and meditation hours.

3.2. Meditation State Effects

3.2.1. fALFF analysis

DMN: No significant differences were found.

CEN: The multilevel modeling one-way repeated measures ANOVA yielded significant variation among rsBase, Med and rsPost, $X^2(2) = 24.57$, $p < 1e-04$. The post hoc analysis showed that CEN fALFF was significantly increased in bilateral Dorslolateral Prefrontal Cortex (DLPFC; BA 9, Figure 1.A.b) during Med (M = .3) compared to rsBase (M = -0.55, b = .84, p <1e-04). See red box plots [EM rsBase < Med] in Fig.1.B.

3.2.2. FC analysis

DMN: No significant differences were found.

CEN: EM showed increased connectivity of Posterior Cingulate Gyrus (PCC; BA 31) and Inferior Parietal Lobule (IPL; BA 40). Figure 2.A.b and red box plot [EM rsBase < Med] of 2.B.

3.2.3. PDA analysis

The multilevel modeling one-way repeated measures ANOVA yielded that there was significant variation among rsBase, Med and rsPost, $X^2(2) = 12.54$, $p = .005$. The post hoc analysis showed that PDA was significantly increased during Med (M = .65) compared to rsBase (M=0.23, b = .57, p <.003) and rsPost (M = 0.36, b = 0.42, p <.02). See green box plots [EM rsBase < Med] in Fig.1.B.

3.2.4. Correlations between PDA and FC

DMN: No significant correlations were found.

CEN: There was positive correlation (R = .91, parametric stats with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$) between PDA during Med and FC during Med of bilateral Dorsolateral Prefrontal Cortex (DLPFC;BA 9) and left Posterior Cingulate Gyrus (PCC;BA 31), left Inferior Frontal Gyrus (IFG;BA 45), left Superior Temporal Lobe (STG;BA 22) and left Inferior Parietal Lobe (IPL;BA 40). See Figure 3.A. For this and all other significant correlation analysis coordinates see Table 3.

3.2.5. Correlations between Hours of Meditation practice and FC

DMN: Whole-Brain FC analysis showed a significant correlation (R = .87) between the hours of meditation and the increase in connectivity between rDLPFC and MPFC during meditation (See Figure 4.B).

CEN: No significant correlations were found.

3.2.6. Correlations between Hours of Meditation practice and PDA

No significant correlations were found for Meditation Trait, State or State-to-Trait PDA and meditation hours.

3.3. Meditation State-To-Trait Effects

3.3.1. fALFF analysis

DMN: No significant differences were found.

CEN: The multilevel modeling one-way repeated measures ANOVA yielded that there was significant variation among rsBase, Med and rsPost, $X^2(2) = 24.57$, $p < 1e\text{-}04$. The post hoc analysis showed that CEN fALFF was significantly increased in bilateral Dorsolateral Prefrontal Cortex (DLPFC; BA 9, Fig.1.A.c) during rsPost ($M = .09$) compared to rsBase ($M = -0.55$, $b = 0.63$, $p = .006$; red box plots [EM rsBase < EM rsPost] in 1.B).

3.3.2. FC Analysis

DMN: No differences were found.

CEN: EM showed increased connectivity ($X^2(2) = 14.47$, $p < .001$) with the Precuneus (BA 23) and right Angular Gyrus (BA 39) at rsPost compared to rsBase (Figure 2.A.c and red box plots [EM rsBase < EM rsPost] of 2.B).

3.3.3. PDA analysis

PDA: The multilevel modeling one-way repeated measures ANOVA yielded no significant differences. However a two-sample paired t-test showed a significant increase relative to rsBase ($t(15) = 1.97$, $p = .03$, green box plots [EM rsBase < EM rsPost] of 1.B, uncorrected).

3.3.4. Correlations between PDA and FC

DMN: There was a significant negative correlation (R = -.70) between the change in PDA from rsBase to rsPost and the change in functional connectivity from rsBase to rsPost between Medial Prefrontal Cortex (MPFC; BA 10) and Posterior Cingulate Cortex (PCC; BA 31), Precuneus (BA; 19) and Limic Lobe (BA 20) (See Figure 3.B).

3.3.5. Correlations between Hours of Meditation practice and FC

DMN: No significant correlations were found.

CEN: Whole-Brain FC analysis showed a significant correlation (R = .63) between the change in CEN and PCC connectivity from rsBase to rsPost and the hours of meditation practice (See Figure 4.C).

3.3.6. Correlations between Hours of Meditation practice and PDA

No significant correlations were found for Meditation Trait, State or State-to-Trait PDA and meditation hours.

4. Discussion

Meditation trait was characterized by a significant reduction in activity and functional connectivity within the DMN and increased anticorrelations between DMN and CEN in experienced meditators. However, the latter anticorrelations were only present in meditators with less than 3 years of practice. Conversely, the meditation state and the meditation state-to-trait periods showed increased activity and functional connectivity within the DMN and between DMN and CEN. While there were no meditation trait Positive Diametric Activity metric (PDA) differences, we found significant increase during meditation state that persisted in meditation state-to-trait. The gradual reconfiguration in DMN and CEN suggest a neural mechanism by which the CEN negatively regulates the DMN and is probably responsible for the long term trait changes seen in meditators and reported psychological well-being.

To our knowledge, no previous study has directly compared trait, state and state-to trait conditions in experienced meditators using fALFF and FC. In so doing, our findings demonstrate the following for each stage:

Meditation Trait:

We found that meditation trait is characterized by a (i) significant reduction in brain activity of specific nodes of the DMN, most prominently the MPFC and MTG as well as CEN nodes in the right and left DLPFC and (ii) a reduction in functional connectivity, both within DMN and between DMN and CEN. Thus, the former reduction in intrinsic DMN connectivity would speak for trait reduced synchrony of DMN regions for meditators and is in accordance with previous studies (Doll et al., 2015; Hasenkamp and Barsalou, 2012b) which found that a region in MPFC showed decreased connectivity with the PCC in mindfulness experts compared to novices. Similarly, the latter finding of reduced FC between DMN and CEN for meditators in the baseline resting state is in accordance with two recent studies (Doll et al., 2015; Kemmer et al., 2015), suggesting a critical interplay between DMN and CEN for repeated engagement of attention on present moment experience. Hence, DMN activity and FC, instead of being engaged in task-unrelated thought or mind-wandering, resulting in activation and synchronization of the DMN (Mason et al., 2007), rather is again and again suppressed to re-engage in present moment awareness and hence reflects the stronger anti-correlated coupling between CEN and DMN (Marusak et al., 2017; Mooneyham et al., 2017). This is idea is in accordance with preliminary analysis using dynamic functional connectivity on the Meditation State data that suggest that meditation trait is characterized by more transitions between brain states (mindful vs. mind-wandering) over time, and thus meditators probably spent overall less time in a mind-wandering or a mindless state (Martinez et al., 2018). However, and most importantly, the additional finding of a positive correlation between meditation experience and increased connectivity between CEN and MPFC, which also has been reported in other studies comparing novice vs. expert meditators (Brewer et al., 2011; Jang et al., 2011; Shaurya Prakash et al., 2013) and, which at first seems to contradict the increase in anticorrelations for meditators in general, rather is a subtle difference that points to additional network reconfiguration occurring as practice increases for expert meditators (Brewer et al., 2011; Hasenkamp and Barsalou, 2012b). We then disentangled this finding by searching for the differences between intermediate (<1130 hrs of practice, ~3 years of 1 hour daily practice) and more experienced meditators (>1130 hrs) functional connectivity in these nodes. The finding, hence suggests that the trait state of intermediate meditators is characterized by a stronger reduction in DMN connectivity and significant increases in anticorrelations between CEN and MPFC. In more experienced meditators (>1130 hrs of practice) the reduction in DMN connectivity still remains, however the anticorrelations have returned to a pre-meditation state. This finding, we think, is of major importance and points to the evolution of brain activity and connectivity changes as meditation progresses from an intermediate to more advanced stages, and that this change is rather a slow one, with the final sole reduction of DMN activity and connectivity independent of CEN suppression of at least 3 years of practice and can even evolve to a sustained increase in connectivity between CEN and DMN in meditators with more than 3 years of experience (Brewer et al., 2011; Creswell et al., 2016). Additionally, we think that this trait suppression of

DMN in more experienced meditators independent of anticorrelations with the CEN, is the ultimate network reconfiguration without any active and repeated suppression of the DMN by the CEN and thus, a more effective, consolidated effortless baseline, reflecting a completely transformed and stable mindful state with suppression of DMN without the more active and repeated transitions between mindful vs. mind-wandering brain states in intermediate meditators. However, this hypothesis has to be tested in longitudinal studies.

Meditation State:

We found that meditation state is characterized by: (i) increase in the activity of specific CEN nodes (bilateral DLPFC), (ii) increased FC between CEN nodes and DMN nodes (MPFC and PCC), (iii) increased PDA, (iv) PDA positively correlates with the strength in FC between the CEN and the DMN and (v) that meditation experience (meditation hours) positively correlates with connectivity between MPFC and right DLPFC during meditation. These findings are in accordance with previous literature (Brewer et al., 2011; Hasenkamp and Barsalou, 2012b) and suggest that the neural mechanisms underlying the active meditation state is associated with differential activation and connectivity of CEN nodes modulate activity and connectivity of the DMN. Importantly, although we cannot rule out that other brain networks mediate the effect of CEN on the DMN, our results indicate that activity in the CEN, specifically in the DLPFC effects on the activity and connectivity of the DMN hub nodes, i.e. MPFC and PCC. This hypothesis is in line with previous meditation studies (Brewer et al., 2011; Hasenkamp et al., 2012; Hasenkamp and Barsalou, 2012b) but is of particularly interest given a study by Chen et al. (2013) where they used TMS and fMRI to demonstrate a directional causal relationship by which a DLPFC node situated within the CEN inhibits the MPFC portion of the DMN. This in turn is further supported by evidence of monosynaptic projections between CEN and DMN structures in rhesus monkeys, which indicate that these efferent pathways are part of an elaborate anatomical circuit which could mediate aspects of attention, memory, and external or internal perception (Selemon and Goldman-Rakic, 1988). What is more, recent evidence has shown that there is a direct relation between GABA-ergic inhibition within the mPFC and the reactivity of amygdala during emotional processing. Delli Pizzi et al (2017) investigated the mPFC-amygdala circuit both with resting-state fMRI (rs-fMRI) and proton MR spectroscopy (MRS) as well as trait anxiety. Their results showed that the rs-fMRI signals of the amygdala and the mPFC were significantly anti-correlated and that this negative functional coupling between the two regions was inversely correlated with the GABA+/tCr level within the MPFC and the STAI-Y2 scores. This suggests a close relationship between MPFC GABA levels and functional interactions within the MPFC-amygdala– circuit. Although this is still an open question and needs additional research with simultaneous MRS acquisition during and after meditation, we propose that a meditation state: 1) increases activity within the CEN, 2) this increase in CEN activity directly downregulates the two major DMN nodes (i.e. MPFC and PCC), 3) this down regulation of MPFC is coupled with a reduction in GABA+/tCr levels and reduced amygdala reactivity which, 4) have a direct impact on anxiety scores and the physiology of emotion regulation.

Meditation State-to-Trait:

We found that the meditation state-to-trait is characterized by shoeing remnants of the meditation state effect both in activity and connectivity. Specifically, (i) increased activity of the CEN, (ii) increased FC between CEN nodes and DMN, although only with the PCC, which has been suggested to be more related to internal meditation practices (Scheibner et al., 2017) and (iii) a increased PDA. Moreover, the change in PDA from rsBase to rsPost was negatively correlated with change in intrinsic connectivity of the DMN (MPFC & PCC), i.e. the greater the increase in PDA the less the intrinsic connectivity of the DMN at rsPost. This is also in line with previous studies that suggest that the post-task resting state network activity and connectivity reflect an aspect of the immediately preceding brain state (Waites et al., 2005) and that these brain changes support the role of learning from a recently performed task as a concomitant process in expertise development (Muraskin et al., 2016). Hence, it further supports the hypothesis that the activity within CEN nodes (specifically DLPFC) actively suppresses DMN nodes and that this suppression carries over during a restful state after meditation, although it shifts to a more posterior node, namely the PCC, probably because this node is more engaged in this particular type of meditation, i.e. internal focused meditation (Scheibner et al., 2017). Finally, we found that meditation experience positively correlates with change in CEN-DMN connectivity. Hence, the more experienced meditators seem to have a larger homeostatic rebound after meditation in CEN-DMN connectivity (for a discussion of this hypothesis see below).

Finally, and because of the design of the present study, we propose that both, the increased PDA as well as the increased connectivity between DMN and CEN during meditation, as well as the remnants after meditation, at the beginning of practice, effectively produce a “homeostatic rebound” to what we identify as the meditation trait, namely the reduced activity and connectivity within DMN and between DMN and CEN. We think that brain activity, brain connectivity and long term ensurance of homeostasis depend on intrinsic properties that determine the functionality of these neuronal networks. Homeostatic factors are inherently important and involve complex self-regulatory mechanisms (Davis, 2013). Consequently, it seems reasonable to view this “homeostatic rebound” as the plasticity that results from a repeated meditation practice within a context of otherwise stable network configurations. First, without the existence of potent mechanisms that perturb this normal balance between networks, and secondly, similarly potent mechanisms that in turn stabilize this perturbation, our capacity to learn and change brain function would be lost. Hence, we suggest, that there is a two stage reconfiguration or homeostatic plasticity (Davis, 2013; Hellyer et al., 2016), that evolves with meditation practice. First, as meditation practice begins, it produces stronger anti-correlated coupling between CEN and DMN (Marusak et al., 2017; Mooneyham et al., 2017) and thus increases the frequency of repeated periods of DMN suppression, even without being actively engaged in meditation, resulting in increased number of moments during the day of engagement in present moment awareness and less mindlessness. This initial change is in accordance with additional evidence showing that increased anticorrelations between DMN and CEN are associated with a healthy development (Chai et al., 2014) and aging (Esposito et al., 2017; Keller et al., 2015c), cognitive reserve (Franzmeier et al., 2017), superior cognitive performance (Chai et al., 2014), reduced risk of psychopathology (Andrews-Hanna et al., 2014; Whitfield-Gabrieli et al., 2009), increased emotional stability (Servaas et al., 2017), and overall physiological and psychological well being (Fountain-Zaragoza and Prakash, 2017). As meditation increases, a second reconfiguration occurs where the frequency of repeated periods of DMN suppression start to overlap and rather become prolonged periods of engagement in present moment awareness up until the point where it is just continued present moment awareness. Once this point has been reached, we think that there is no more need of active monitoring if one is in a mindless state or mindful state and thus the anticorrelations start to return to a normal pre-meditation level.

The plasticity resulting from a repeated meditation practice, i.e. the suggested "homeostatic rebound", may also be the underlying mechanism of many of the benefits reported with meditation practice (Goldberg et al., 2018) that depend on the top-down regulation of the DMN by CEN (Chen et al., 2013; Garrison et al., 2015). In doing so, it is possible that functional abnormalities in cortical and subcortical regions involved in emotion regulation such as anxiety, depression or other types of psychopathology that relate to deficiencies in noradrenergic and serotonergic function are also recalibrated and thus enhancing brain noradrenergic or serotonergic transmission (Whitfield-Gabrieli and Ford, 2012; Willner et al., 2013). Meditation training, thus, with time, may lead to observable changes in the brain and in neurotransmitter levels (Guglietti et al., 2013; Jindal et al., 2013) accounting for its antidepressant effects and use in psychotherapy. However, this last hypothesis has to be corroborated with further studies that particularly look at this process.

We also want to note some limitations of this study. First off, when we talk about “activity” in the present study we do this with complete knowledge of the limitations of Blood oxygenation level dependent (BOLD) imaging as the standard technique used to generate images in fMRI studies, and that relies on regional differences in cerebral blood flow to indirectly delineate regional activity (Arthurs and Boniface, 2002; Huettel, 2004). Thus, “activity” in the present study refers to BOLD activity. There were a modest number of participants. In turn, this motivated a region-of-interest approach focused on specific nodes from the DMN and CEN, based on the prior literature, so that a conservative level of statistics could be employed. A strength of this study is that it represents a first step in elucidating the potential neurobehavioral mechanisms mediating the practice of meditation on DMN activity and the FC. Specifically it suggests that “homeostatic rebound” of anticorrelated DMN and CEN networks after meditation could be the compensatory mechanisms operating in the brain that may account for the trait changes in meditators. Finally,

5. Conclusion

Here we examined the brain changes underlying the State-to-Trait experience and training of meditation. We focused on the activity and connectivity of the default and executive networks given their respective roles in internal cognition, self-regulation, and awareness. The findings presented reveal that active meditation practice deliberately engages networks related to cognitive and attentional control that effectively directs the focus of attention and curbs our usual mode of getting carried away by the endless stream of internal and external distractions. Furthermore, we showed that this active state is carried over to an immediate and passive restful state with similar network relationships than the active state. The trait effects of meditation suggest a recalibration and reconfiguration of network structure, or homeostatic plasticity (Davis, 2013; Hellyer et al., 2016), that produces in particular reductions in DMN activity and connectivity. However, the way this suppression is achieved depends on the stage of meditation. Intermediate meditators show stronger anti-correlated coupling between CEN and DMN (Marusak et al., 2017; Mooneyham et al., 2017), which suggests increased frequency between states of mindlessness and mindfulness and thus moments of DMN suppression, even without being actively engaged in meditation. Finally, with more experience in meditation, the moments of mindfulness become so frequent that no more transitions are needed and thus become the new default mode with sustained reduction in DMN activity and connectivity without effort. These, we think are the trait characteristics that ultimately underlie the beneficial effects of meditation, yet allowing the initial practitioner to increase the number of moments of mindful and clear reality to finally achieve a sustained mindful state —even to see reality as it actually is, without the perturbing vail of past or future illusion.

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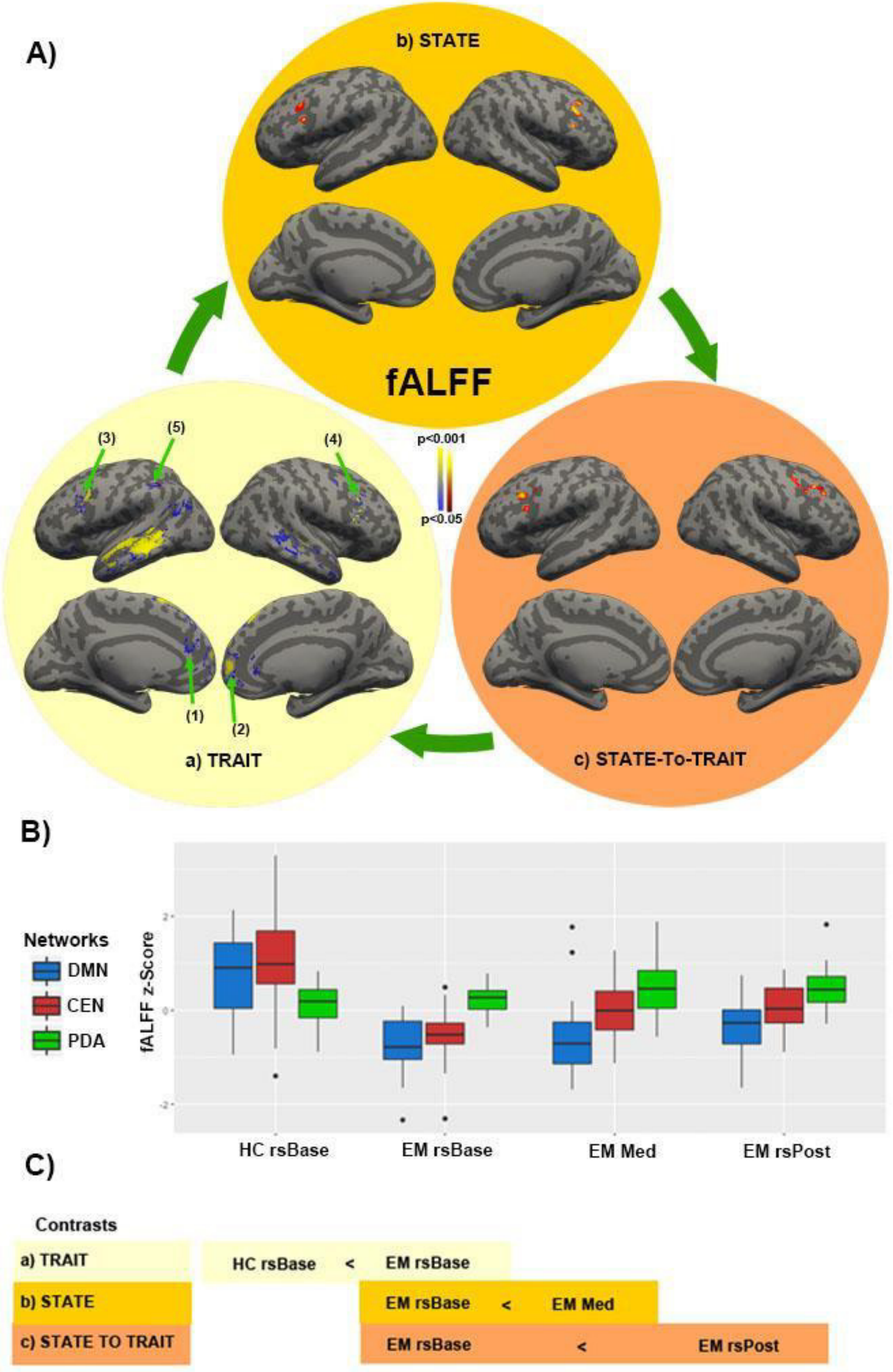
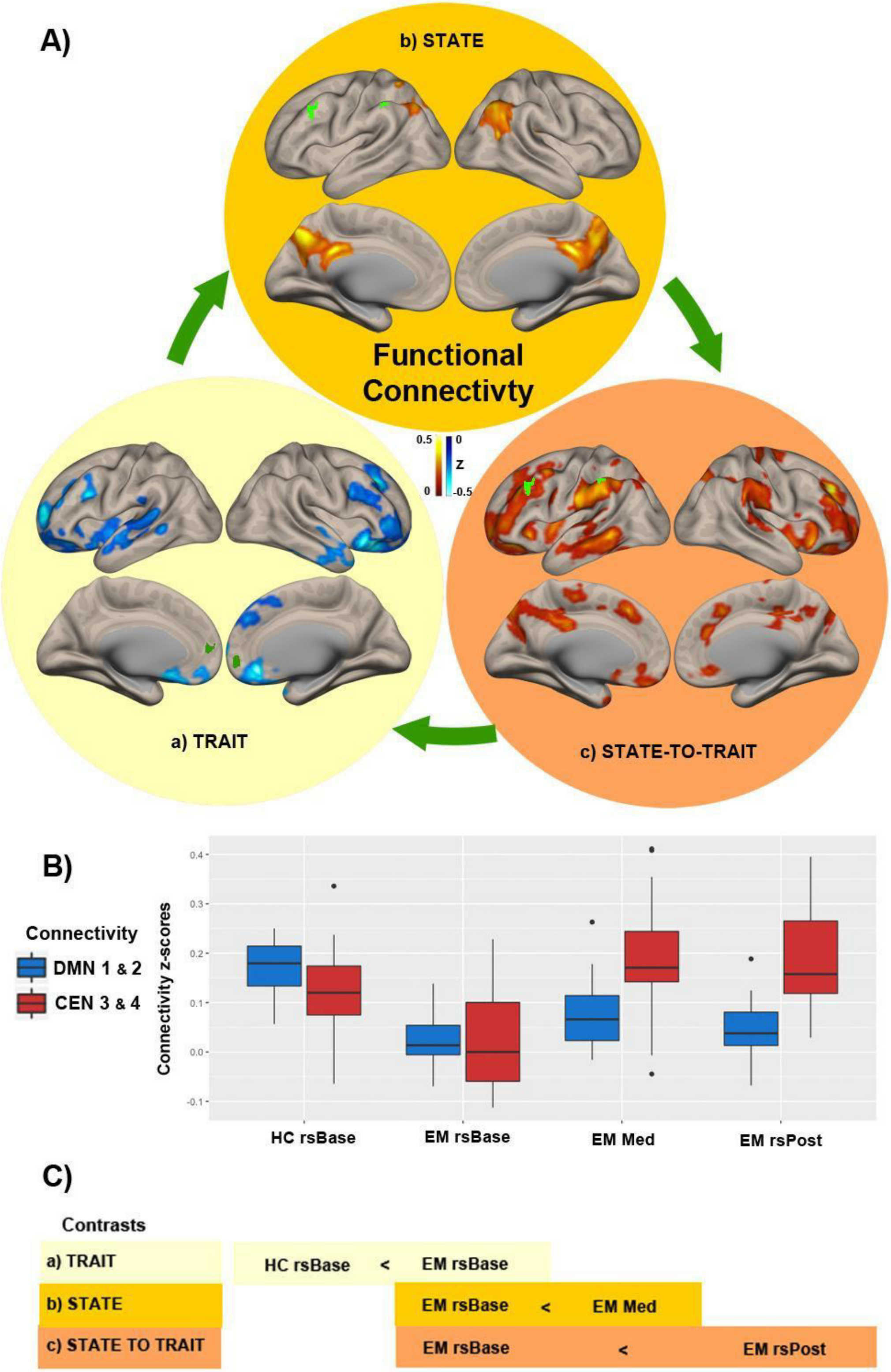

A)
b) STATE
fALFF
p<0.001
p<0.05
(3)
(5)
(4)
(1)
(2)
a) TRAIT
c) STATE-To-TRAIT
B)
Networks
DMN
CEN
PDA
fALFF z-Score
2
0
-2
HC rsBase
EM rsBase
EM Med
EM rsPost
C)
Contrasts
a) TRAIT
HC rsBase < EM rsBase
b) STATE
EM rsBase < EM Med
c) STATE TO TRAIT
EM rsBase < EM rsPost

Figure 1.

State-To-Trait meditation brain activity changes of the Fractional Amplitude of Low Frequency Fluctuations (fALFF). **A.a)** Brain regions showing trait changes in fALFF between meditators and healthy controls at baseline (HC rsBase < EM rsBase). **A.b)** Brain regions that show significant changes in fALFF during the meditation state in meditators (EM rsBase < EM Med). **A.c)** Brain regions that show significant changes in fALFF during the transition from state-to-trait meditation in meditators (EM rsBase < EM rsPost). **B)** Boxplot showing the mean fALFF z-scores in blue (DMN) and red (CEN) and Positive Diametric Activity scores in green during baseline (rsBase), meditation (Med) and post meditation (rsPost) for healthy controls (HC) and experienced meditators (EM). **C)** Schematic representation of State-To-Trait contrasts. All stats shown are nonparametric (5000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$. Black dots represent subjects that lie beyond the whiskers.



Contrasts

a) TRAIT	HC rsBase	<	EM rsBase		
b) STATE			EM rsBase	<	EM Med
c) STATE TO TRAIT			EM rsBase	<	EM rsPost

Figure 2.

State-To-Trait meditation functional connectivity changes (FC). **A.a)** Brain regions showing trait FC changes between meditators and healthy controls at baseline (HC rsBase < EM rsBase). **A.b)** Brain regions that show significant FC changes during the meditation state in meditators (EM rsBase < EM Med). **A.c)** Brain regions that show significant FC changes during the transition from state-to-trait meditation in meditators (EM rsBase < EM rsPost). Dark green (DMN ROIs 1 & 2) and light green (CEN ROIs 3 & 4) clusters show in each case the seeds used to determine the shown contrast (see Figure 1.A.a). **B)** Boxplot showing mean FC z-scores in blue (DMN 1 & 2) and red (CEN 3 & 4) during baseline (rsBase), meditation (Med) and post meditation (rsPost) for healthy controls (HC) and experienced meditators (EM). **C)** Schematic representation of State-To-Trait contrasts. All stats shown are nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$. Black dots represent subjects that lie beyond the whiskers.

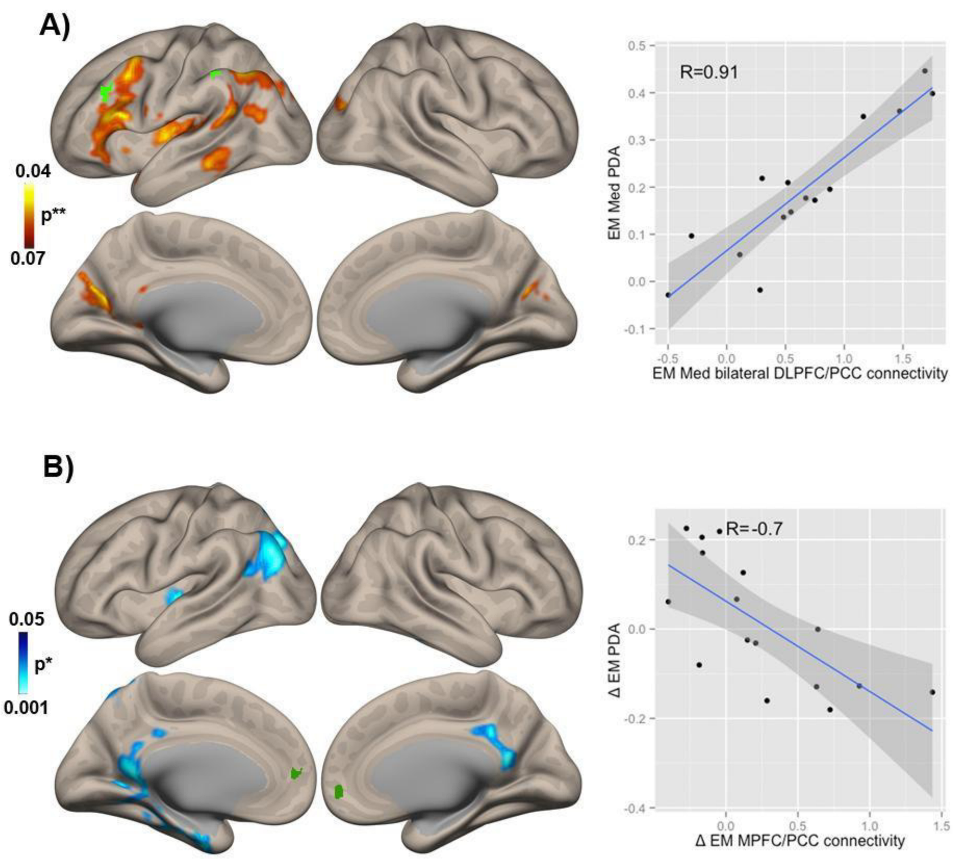


Figure 3.

Correlations between Positive Diametric Activity (PDA) and Functional Connectivity (FC). **A)** Brain regions that show significant correlation between PDA and FC during the meditation state in meditators (EM Med). **B)** Brain regions that show significant correlation between the change in PDA and change in FC during the transition from state-to-trait meditation (**Δ**EM=rsBase-rsPost). Dark green (DMN ROIs 1 & 2) and light green (CEN ROIs 3 & 4) clusters show in each case the seeds used to determine the shown contrast (see Figure 1.A.a).

*nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$.

** parametric stats with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$.

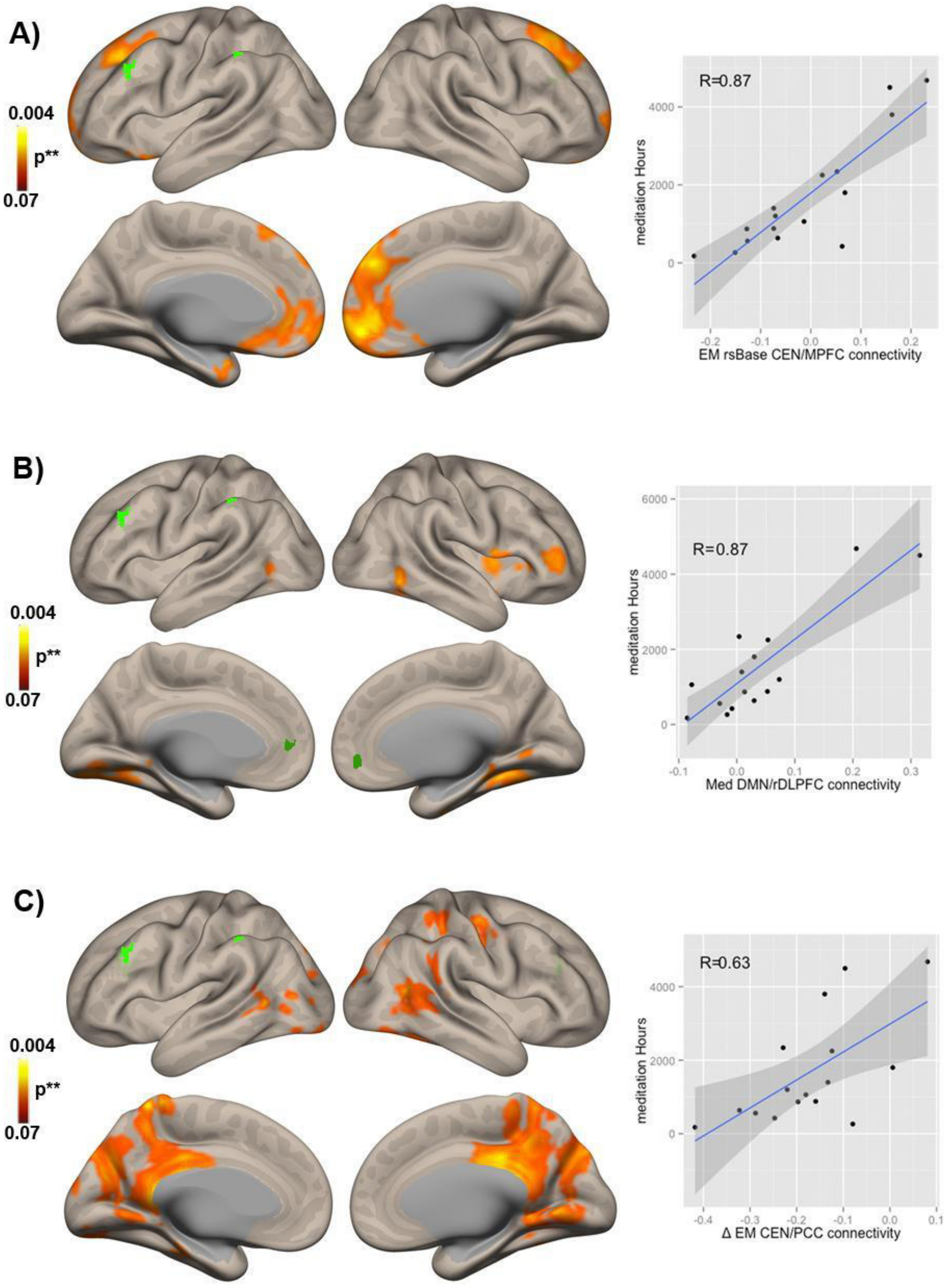
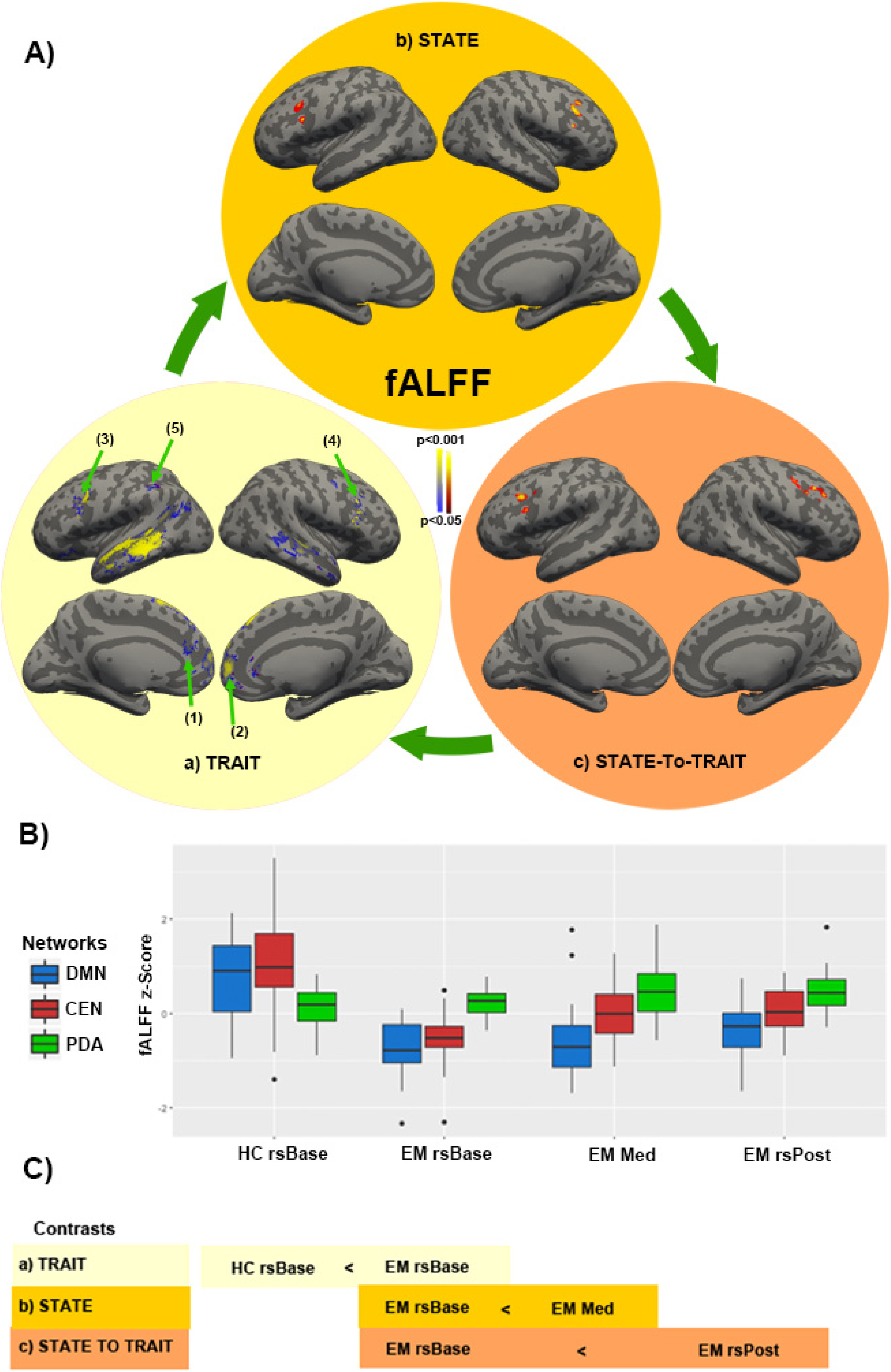
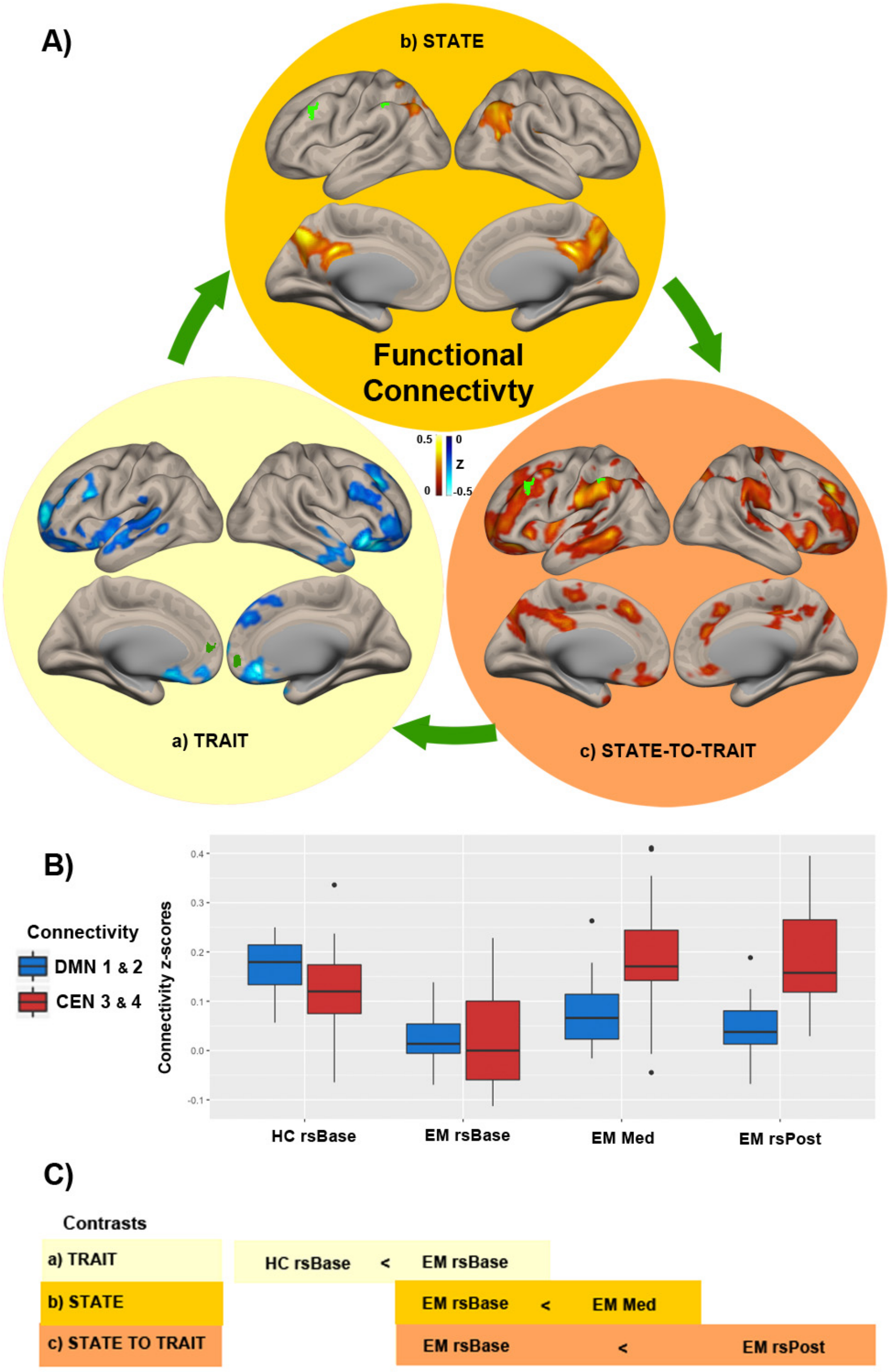

A)
0.004
p**
0.07
R=0.87
meditation Hours
0
2000
4000
-0.2
-0.1
0.0
0.1
0.2
EM rsBase CEN/MPFC connectivity
B)
0.004
p**
0.07
R=0.87
meditation Hours
0
2000
4000
6000
-0.1
0.0
0.1
0.2
0.3
Med DMN/rDLPFC connectivity
C)
0.004
p**
0.07
R=0.63
meditation Hours
0
2000
4000
-0.4
-0.3
-0.2
-0.1
0.0
0.1
Δ EM CEN/PCC connectivity

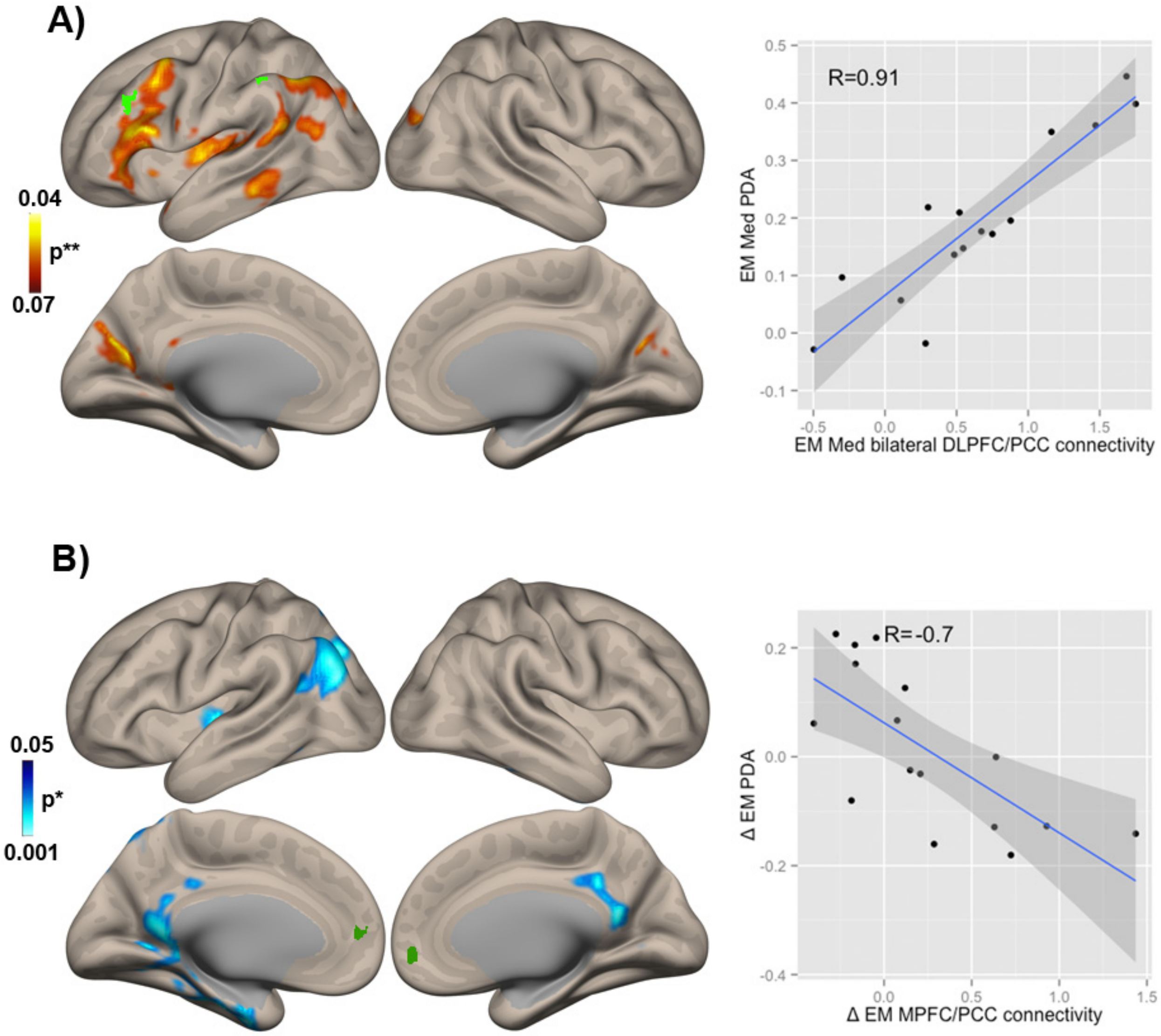
Figure 4.

Correlations between meditation hours (MedHrs) and Functional Connectivity (FC). **A)** Brain regions showing the correlation of MedHrs and FC at baseline for meditators. **B)** Brain regions that show significant correlation between MedHrs and FC during the meditation state in meditators (EM Med). **C)** Brain regions that show significant correlation between MedHrs and the change in FC during the transition from state-to-trait meditation in meditators ((**Δ**EM=rsBase-rsPost). Dark green (DMN ROIs 1 & 2) and light green (CEN ROIs 3 & 4) clusters show in each case the seeds used to determine the shown contrast (see Figure 1.A.a). ** nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$.


A)
b) STATE
fALFF
p<0.001
p<0.05
(3)
(5)
(4)
(1)
(2)
a) TRAIT
c) STATE-To-TRAIT
B)
Networks
DMN
CEN
PDA
fALFF z-Score
2
0
-2
HC rsBase
EM rsBase
EM Med
EM rsPost
C)
Contrasts
a) TRAIT
HC rsBase < EM rsBase
b) STATE
EM rsBase < EM Med
c) STATE TO TRAIT
EM rsBase < EM rsPost



Contrasts			
a) TRAIT	HC rsBase	<	EM rsBase
b) STATE	EM rsBase	<	EM Med
c) STATE TO TRAIT	EM rsBase	<	EM rsPost


A)
0.04
p**
0.07
R=0.91
EM Med PDA
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
-0.5
0.0
0.5
1.0
1.5
EM Med bilateral DLPFC/PCC connectivity
B)
0.05
p*
0.001
R=-0.7
Δ EM PDA
0.2
0.0
-0.2
-0.4
0.0
0.5
1.0
1.5
Δ EM MPFC/PCC connectivity

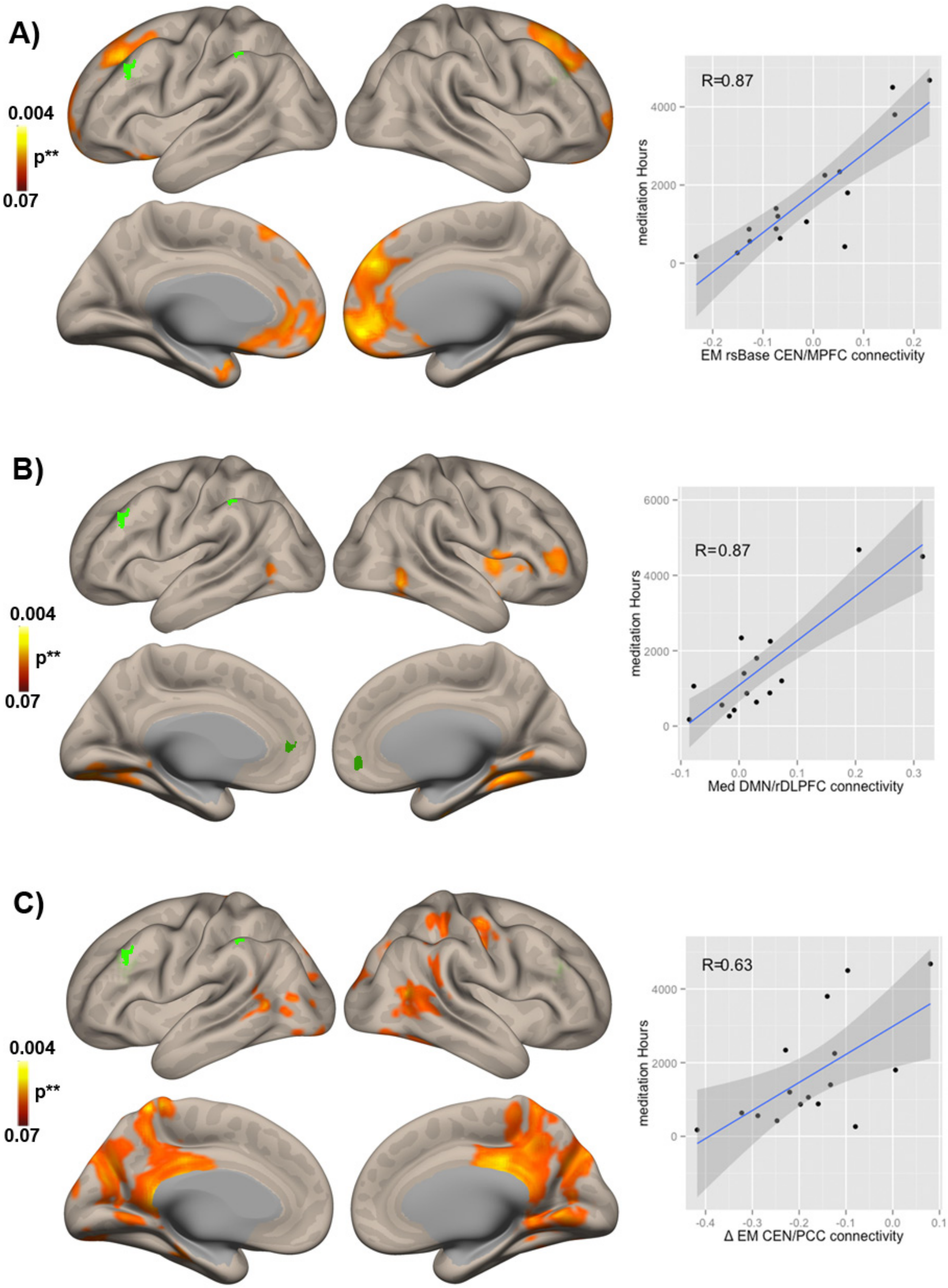

A)
0.004
p**
0.07
R=0.87
meditation Hours
4000
2000
0
-0.2
-0.1
0.0
0.1
0.2
EM rsBase CEN/MPFC connectivity
B)
0.004
p**
0.07
R=0.87
meditation Hours
6000
4000
2000
0
-0.1
0.0
0.1
0.2
0.3
Med DMN/rDLPFC connectivity
C)
0.004
p**
0.07
R=0.63
meditation Hours
4000
2000
0
-0.4
-0.3
-0.2
-0.1
0.0
0.1
Δ EM CEN/PCC connectivity

Table 1 Differences in fractional Amplitude of Low Frequency Fluctuations (fALFF) for the different meditation states

Region	BA	Voxels	MNI (x,y,z mm)	p Value*
Meditation Trait Effects				
HC rsBase > EM rsBase				
DMN				
Medial Temporal Gyrus	L 21	1302	-66,-34 -6	0.02
Medial Prefrontal Cortex[1]	R 10	18	6, 60, 26	0.01
Medial Prefrontal Cortex[2]	L 10	147	-2,58,12	0.05
CEN				
Inferior Frontal Gyrus[3]	L 9	405	-34,6,34	0.01
Inferior Frontal Gyrus[4]	R 9	144	54,20,20	0.03
Inferior Parietal Lobule[5]	L 40	74	-54,-38,50	0.05
Meditation State Effects				
EM Med > EM rsBase				
DMN				
No significant differences	N/A	N/A	N/A	N/A
CEN				
Inferior Frontal Gyrus	R 9	115	46,18,30	0.02
Inferior Frontal Gyrus	L 9	82	-44,10,26	0.03
Meditation State-To-Trait Effects				
EM rsPost > EM rsBase				
DMN				
No significant differences	N/A	N/A	N/A	N/A
CEN				
Inferior Frontal Gyrus	L 9	17	-46,18,34	0.02

*All statistics are nonparametric (5000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$

Inferior Frontal Gyrus	R 9	4	50,28,38	0.05

Table 2 Differences in Functional Connectivity for the different meditation states

Region	**Connectivity**	**BA**	**Voxels**	**MNI (x,y,z mm)**	**p Value**
<u>Meditation Trait Effects</u>					
EM rsBase > HC rsBase					
DMN $^{\text{seeds 1 \& 2}}$					
Superior Frontal Gyrus	Reduced	L 11	>1000	-16,60,26	0.01
Middle Frontal Gyrus	Reduced	L 9	>200	-26 26 32	0.01
Inferior Parietal Lobule	Reduced	L 40	>200	-38,-48,26	0.02
Superior Temporal Gyrus	Reduced	R 38	>200	48,16,-20	0.03
CEN $^{\text{seeds 3, 4 \& 5}}$					
No significant differences	N/A	N/A	N/A	N/A	N/A
<u>Meditation State Effects</u>					
EM Med > EM rsBase					
DMN $^{\text{seeds 1 \& 2}}$					
No significant differences	N/A	N/A	N/A	N/A	N/A
CEN $^{\text{seeds 3, 4 \& 5}}$					
Middle Frontal Gyrus	Increased	L 10	>200	-29,48,15	0.02
Middle Frontal Gyrus	Increased	R 10	>200	31,52,12	0.02
Anterior Cingulate Gyrus	Increased	L 32	>200	4,30,24	0.02
Posterior Cingulate Gyrus	Increased	R 31	>200	3,-31,38	0.03
Inferior Parietal Lobe	Increased	L 40	>200	-38,-46,46	0.03
<u>State-To-Trait Effects</u>					
EM rsPost > EM rsBase					
DMN $^{\text{seeds 1 \& 2}}$					
No significant differences	N/A	N/A	N/A	N/A	N/A
CEN $^{\text{seeds 3, 4 \& 5}}$					
Precuneus	Increased	L 23	>1000	-2,-42,28	0.02
Angular Gyrus	Increased	R 39	>1000	50,-66,33	0.02

* nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$

Table 3 Correlation between Positive Diametric Activity (PDA) and Functional Connectivity (FC)

Region	**BA**	**Voxels**	**MNI (x,y,z mm)**	**p Value***
Meditation State Effects				
EM Med PDA & EM FC				
DMN $^{\text{seeds 1 \& 2}}$				
No corr	N/A	N/A	N/A	N/A
CEN $^{\text{seeds 3, 4 \& 5}}$				
Inferior Frontal Gyrus	L 45	>200	-56,14,18	0.01
Superior Temporal Lobe	L 22	>200	-46,-16,8	0.03
Posterior Cingulate Gyrus	L 31	>200	-12,43,23	0.01
Inferior Parietal Lobe	L40	>200	-48,-64,50	0.02
State-To-Trait Effects				
Δ PDA & Δ FC				
DMN $^{\text{seeds 1 \& 2}}$				
Posterior Cingulate Cortex	L 31	>200	0,-36,34	0.02
Precuneus	L 19	>200	-35,-74,34	0.02
Limbic Lobe, Uncus	L 20	>200	-28,-22,-34	0.03
CEN $^{\text{seeds 3, 4 \& 5}}$				
Medial Frontal Lobe	L 6	>200	-16,-12,60	0.02
Superior Temporal Lobe	R 22	>200	56,2,6	0.01

* nonparametric (1000 permutations) with height threshold p<0.05 and Cluster-Size FDR-corrected p<0.05

Table 4 Correlation between meditation hours and Functional Connectivity (FC)

Region	R	BA	Voxels	MNI (x,y,z mm)	pValue*
Meditation State Effects					
DMN $^{\text{seeds 1 \& 2}}$					
Middle Frontal Gyrus	0.87	R 10	>200	45, 44, 12	0.02
CEN $^{\text{seeds 3, 4 \& 5}}$					
No Correlations	N/A	N/A	N/A	N/A	N/A
State-To-Trait Effects					
DMN $^{\text{seeds 1 \& 2}}$					
No Correlations	N/A	N/A	N/A	N/A	N/A
CEN $^{\text{seeds 3, 4 \& 5}}$					
Posterior Cingulate Cortex	0.63	L 29	>200	-06, -44, 14	0.03
Trait Effects					
DMN $^{\text{seeds 1 \& 2}}$					
No Correlations	N/A	N/A	N/A	N/A	N/A
CEN $^{\text{seeds 3, 4 \& 5}}$					
Medial Frontal Gyrus	0.87	L 10	>200	-06, 44, 8	0.01

* nonparametric (1000 permutations) with height threshold $p<0.05$ and Cluster-Size FDR-corrected $p<0.05$