



Cerebral blood flow changes associated with different meditation practices and perceived depth of meditation

Danny J.J. Wang^a, Hengyi Rao^{b,c}, Marc Korczykowski^{b,c}, Nancy Wintering^d, John Pluta^{b,e},
Dharma Singh Khalsa^f, Andrew B. Newberg^{g,*}

^aAlmanson–Lovelace Brain Mapping Center, University of California at Los Angeles, Los Angeles, CA, USA

^bDepartment of Neurology, University of Pennsylvania, Philadelphia, PA, USA

^cCenter for Functional Neuroimaging, University of Pennsylvania, Philadelphia, PA, USA

^dDepartment of Radiology, University of Pennsylvania, Philadelphia, PA, USA

^eDepartment of Psychology, University of Pennsylvania, Philadelphia, PA, USA

^fAlzheimer's Research and Prevention Foundation, Tucson, AZ, USA

^gMyrna Brind Center of Integrative Medicine, Thomas Jefferson University, Philadelphia, PA, USA

ARTICLE INFO

Article history:

Received 27 November 2009

Received in revised form 23 September 2010

Accepted 25 September 2010

Keywords:

Meditation

fMRI

Cerebral blood flow

Frontal lobe

Stress

Arterial spin labeling (ASL)

ABSTRACT

Our goal in this study was to advance the understanding of the neural pathways of meditation by addressing the cerebral blood flow (CBF) responses associated with two different meditation practices performed by the same individuals and how such changes related to the “stress” circuits in the brain. Ten experienced meditators performed two types of meditation, a “focused-based” practice and a “breath-based” practice. Subjects were scanned using perfusion functional magnetic resonance imaging (fMRI) during a baseline state, both meditation states, and a post meditation baseline state. Using general linear model, we found that the frontal regions, anterior cingulate, limbic system and parietal lobes were affected during meditation and that there were different patterns of CBF between the two meditation states. We observed strong correlations between depth of meditation and neural activity in the left inferior forebrain areas including the insula, inferior frontal cortex, and temporal pole. There were persistent changes in the left anterior insula and the precentral gyrus even after meditation was stopped. This study revealed changes in the brain during two different meditation practices in the same individuals and that these changes correlated with the subjective experiences of the practitioners.

© 2010 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

We previously described a model for the neurophysiologic activation during the complex neurocognitive task of meditation (Newberg and Iversen, 2003). This model is based, in part, on studies that have correlated brain function with specific behaviors, tasks, and experience. From this model, we have constructed the main hypotheses to be tested in this study. Specifically, this involves changes in activity in a number of brain structures that may be associated with specific elements of meditation practices.

It has been suggested that the prefrontal cortex and anterior cingulate gyrus are activated during meditation since an important element of meditation practice involves attentional focus (Newberg and Iversen, 2003; Cahn and Polich, 2006). Studies have generally shown that the prefrontal cortex and anterior cingulate gyrus areas are activated during attention focusing tasks (Posner and Petersen, 1990; Vogt et al., 1992). Using positron emission tomography (PET),

several investigators have shown activation of the prefrontal cortex in subjects performing purposely willed tasks, or tasks that required sustained attention (Frith et al., 1991; Pardo et al., 1991). Furthermore, focused attention on a mathematical task resulted in increased regional cerebral blood flow (rCBF) in the prefrontal cortex (Sammer et al., 2007).

Imaging studies of meditation performed by our group also suggest that the prefrontal cortex and anterior cingulate gyrus are activated during meditation. We observed increased rCBF (or metabolism) in the prefrontal cortex and anterior cingulate gyrus during several different types of meditation practices. These practices included Tibetan Buddhist meditation, Iyengar Yoga meditation, and Centering Prayer (Newberg et al., 2001; Newberg et al., 2003; Cohen et al., 2009). Herzog et al. (1990–1991) utilized PET with fluorodeoxyglucose (FDG) to measure glucose metabolism in eight subjects undergoing Yoga Meditative Relaxation. A significant increase in the frontal/occipital ratio of glucose metabolism was observed. However, the subjects did not experience a strong meditative state, and the glucose metabolism was not measured in specific cortical regions. A study utilizing functional magnetic resonance imaging (fMRI) of subjects performing a similar yoga relaxation technique designed to

* Corresponding author. 110 Donner Building, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA, 19104, USA. Tel.: +1 215 662 3092; fax: +1 215 349 5843.
E-mail address: andrew.newberg@uphs.upenn.edu (A.B. Newberg).

bring about “relaxation response,” demonstrated increased CBF in the frontal and limbic regions (Lazar et al., 2000).

In addition to frontal lobe activity, we have previously hypothesized and found support for altered activity in the limbic structures (Lazar et al., 2000; Cohen et al., 2009) which may be related to the emotional effects of meditation tasks (Brefczynski-Lewis et al., 2007; Lutz et al., 2008a,b; Goldin and Gross, 2010). We also hypothesized that there would be decreased activity in the parietal lobes during meditation. This is based in part upon several reports, including our own, that have demonstrated decreased activity in the parietal lobes during meditation practices (Newberg et al., 2001; Newberg and Iversen, 2003). It is also known that the parietal regions are associated with spatial processing (Silver et al., 2005; Zaehle et al., 2006), and since alterations in the sense of self and spatial orientation are subjectively changed during meditation practices, changes in the parietal lobes might be expected (Tagini and Raffone, 2010).

In spite of the growing number of studies on meditation, there were several important questions that have yet to be answered. For instance, it remains unclear whether a common brain activation pattern exists across various meditation tasks and different meditation stages. On the other hand, results from existing studies may be attributable to broader effects of attentional control rather than being specifically related to the effects of meditation on the brain (Brefczynski-Lewis et al., 2007; Lutz et al., 2008a,b; Raffone and Srinivasan, 2010). In the present study, we employed a perfusion based fMRI technique to continuously image the cerebral blood flow (CBF) responses before, during and following two types of meditation practice performed by experienced meditators. This design capitalized on the capability of perfusion fMRI for noninvasive, quantitative and repeatable CBF measurements (Aguirre et al., 2002; Wang et al., 2003). Using this technique, we have previously demonstrated the signature of the brain's response to psychological stress along with its ensuing effects which involved asymmetric prefrontal activity and increased CBF in several limbic structures (Wang et al., 2005a, 2007). It would be interesting to evaluate the meditation effect on CBF changes in the brain's “stress network”, given the stress relieving effect of meditation practice. The stress network more specifically refers to asymmetric prefrontal activation, the anterior cingulate cortex (ACC) and several limbic areas including amygdala, hippocampus and insula based on both our past studies on stress and other studies in the literature. In addition, studies have previously shown that meditation practices can regulate emotions associated with altered activation in the limbic structures (Lutz et al., 2008a,b).

Our primary goal in this study was therefore to make several significant advancements in the understanding of neural pathways mediating the meditation effect by addressing the “general” and “specific” CBF responses associated with meditation. To that end, we attempted to determine if 1) there were different CBF changes associated with different practices performed by the same individual; 2) there were correlations between CBF and the subjective depth of the meditation practices; 3) there were opposite effects of meditation and stress on CBF variations in specific brain regions, and 4) there were persistent effects on the brain after the meditation. We hypothesized that there would indeed be specific CBF changes associated with different practices when performed by the same individuals. We primarily expected increased activity in the frontal regions and limbic structures, but that the pattern would be distinct. This is a significant advancement since no studies to date have assessed the same individuals doing different types of meditation. We also hypothesized that the subjective experience during the meditation practices associated with depth of practice would correlate with CBF changes. Additionally, we hypothesized that the stress relieving effect of meditation was mediated through an altered CBF response representing enhancement of positive emotions and/or suppression of negative emotions and vigilance. Finally, we predicted that there would be a “washout” period after meditation is completed so that

there would be persistent changes in CBF after meditation. No studies have evaluated the after effects of meditation.

2. Materials and methods

2.1. Subjects

Ten healthy subjects (four females and six males, mean age = 53.7 years, range 43–62) who were experienced meditators participated in this study. They each performed meditation from the Kundalini yoga tradition for over 30 years (approximately 20,000 h) under the guidance of Yogi Bhajan. The particular meditation studied consisted of two basic types, both from the same tradition. The first was a “focused-based” practice called, Kirtan Kriya, in which subjects repeated several phrases (SA, TA, NA, and MA) while touching their thumb and fingers in sequence (Meditation 1). It is highly repetitive and is reported by the practitioners to enhance their attention capabilities, reduce stress, and increase awareness. The second meditation called, Shabad Kriya, was a “breath-based” practice in which the practitioner takes several deep breaths in and then repeats several phrases (SA, TA, NA, and MA) with each exhale. The goal of this second meditation is to induce a state of deep relaxation through the specified breathing exercises and internal repetition of the phrases (Meditation 2). This meditation is described by the practitioner to result in feelings of increased awareness and reduced stress. The primary difference is the first involves intense focusing of the mind and the second a relaxing of the mind. For this reason, we maintained the same order of the meditation practices. The first one creates an initial state of meditation while the second results in a consolidation and deepening of the practice.

All the subjects were screened for neurologic and psychiatric conditions. Written informed consent was obtained prior to all human studies according to an Institutional Review Board approval from the University of Pennsylvania.

2.2. MRI experimental procedure

The experimental protocol consisted of five perfusion fMRI scans performed with a fixed order: *Baseline 1, Control task, Meditation 1, Meditation 2 and Baseline 2*. Such design allowed us to simultaneously study the CBF changes during meditation (Meditation vs. Control), enduring CBF responses following meditation (Baseline 2 vs. 1), and the effect of two different styles of meditation practice (Meditation 2 vs. 1). In our experiment, the control task always preceded the two meditation conditions to avoid potential “carry over” effects caused by persistent CBF responses following meditation. During the first and second meditation scans, subjects were instructed to perform the focus-based and breath-based meditation practices respectively. As the control condition, subjects counted to four while touching their thumb and fingers (but not in sequence). Thus, the control condition was similar to the meditation sessions in that both required repeating a phrase (in this case numbers) and moving their fingers, but the control condition did not include the specific phrases or finger movements of the active meditation. Self reports of stress, depth of meditation, and the subjective “feeling of connectedness” levels (on the scale of 1 to 10) were collected between the five perfusion fMRI scans (total four samples). The feeling of connectedness was chosen since it is an experience that many meditators report and we have previously postulated that it might be associated with decreased activity in the parietal lobes. Because these concepts are such subjective measures, we asked the subjects to rate “5” as their usual level of stress, their usual depth of meditation, and their usual level of connectedness during their usual meditation. However, this element of the meditation experience has not been previously evaluated in a brain imaging study.

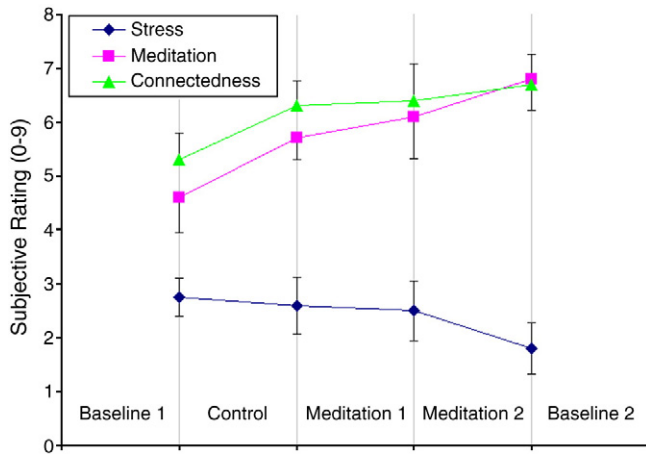


Fig. 1. Average subjective ratings of stress, depth of meditation, and connectedness during the time course of the experiment. Error bars indicate standard error.

MR scanning was conducted on a Siemens 3.0T Trio whole-body scanner (Siemens Medical Solution, Erlangen, Germany), using a standard Transmit/Receive head coil. A continuous arterial spin labeling (CASL) technique (Wang et al., 2005b) was used for perfusion fMRI scans, and imaging parameters were: FOV = 22 cm, matrix = 64×64 , TR = 5 s (long TR reduced scanning noise thereby facilitating meditation), TE = 17 ms, flip angle = 90° , 14–16 slices (6 mm thickness with 1.5 mm gap). Each CASL scan took 12 min (144 acquisitions) and 8 min (96 acquisitions) for the two meditation tasks and the rest three baseline/control conditions, respectively. A 3D MPRAGE volumetric scan was included to acquire high resolution T1-weighted anatomic images: TR = 1620 ms, TI = 950 ms, TE = 3 ms, flip angle = 15° , 160 contiguous slices of 1.0 mm thickness, FOV = $192 \times 256 \text{ mm}^2$, matrix = 192×256 , 1NEX with a total scan time of 6 min.

2.3. Data analysis

Behavioral ratings were analyzed using the repeated measures general linear model (GLM) of the SPSS 12.0 software package (SPSS Inc. Chicago, IL) to assess the effect of experimental condition. Perfusion fMRI data were analyzed offline using the VoxBo (www.voxbo.org) and SPM2 software packages (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). MR image series were first realigned to correct for head movements, co-registered with each subject's anatomical MRI, and smoothed in space with a 3D 12 mm FWHM (Full Width at Half Maximum) Gaussian kernel. All subjects showed tolerable head movements (maximum 6 mm along the x, y or z axis) throughout the experiment. Perfusion weighted image series were generated by pair-wise subtraction of the label and control images, followed by conversion to absolute CBF image series. Voxel-wise analyses of the CBF data were conducted in each subject, utilizing a GLM including the global time course as a covariate (first-level analysis). No temporal filtering or smoothing was involved. Four contrasts were defined in the GLM analysis, namely the CBF differences between the meditation and control conditions (*Meditation 1 – Control*; *Meditation 2 – Control*), the CBF difference between the two baseline conditions (*Baseline 2 – 1*), and the CBF difference between the two meditation conditions (*Meditation 2 – 1*).

Individual contrast images (β maps for each contrast) were normalized into a canonical space (Montreal Neurological Institute standard brain), and were analyzed using one-sample *t*-tests to obtain the activation pattern for the four defined contrasts using a random effects model that allows population inference (second-level analysis). Linear regression analyses were further carried out on these normalized individual maps to obtain the activation pattern correlated with differences in perceived stress, meditation and connectedness ratings, respectively. Areas of significant activation were defined at the cluster level if both criteria were met: *P* value < 0.001 (uncorrected) and the cluster extent size larger than 10 voxels ($2 \times 2 \times 2 \text{ mm}^3$). The above

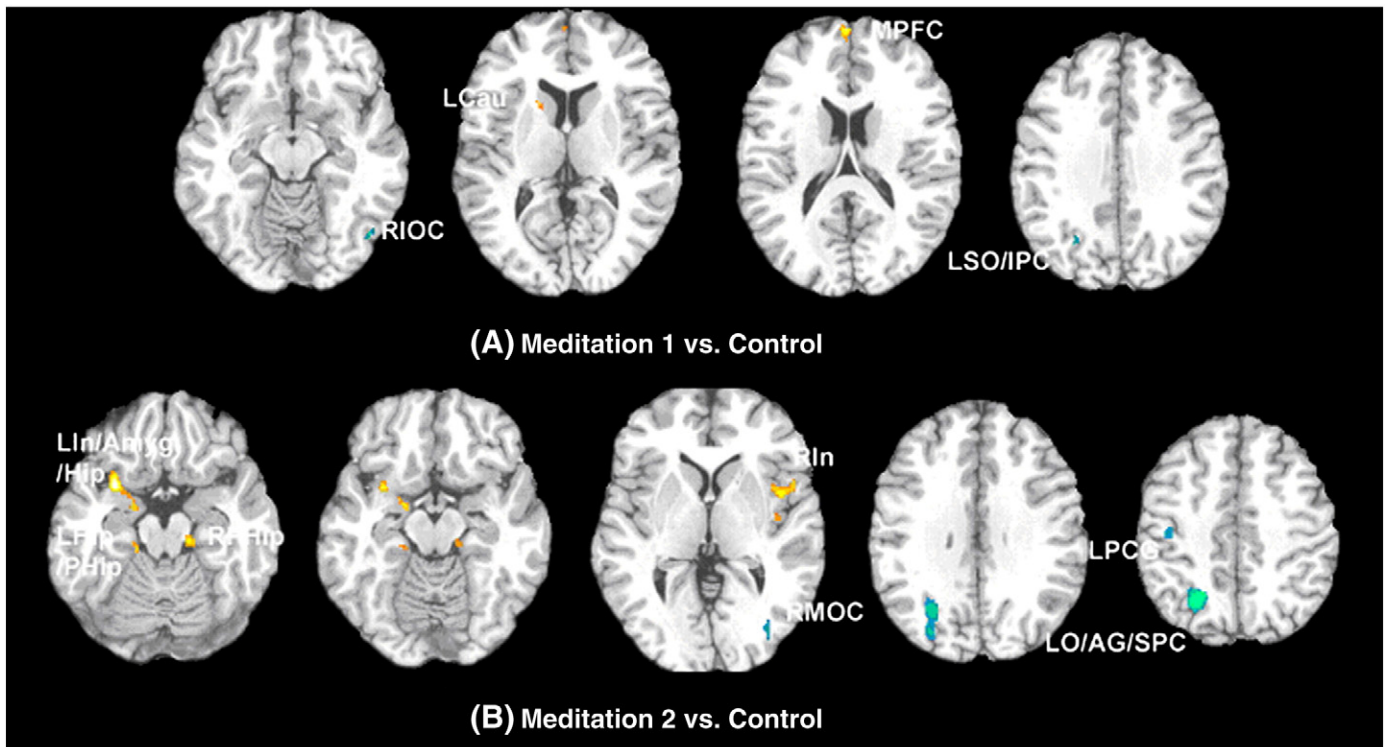


Fig. 2. Axial sections of group analysis results showing increased (red and orange) and decreased (blue and green) CBF during Meditation 1 relative to Control (A) and Meditation 2 relative to Control (B).

analyses were performed across voxels of the whole brain without correction for multiple comparisons. Based on the whole-brain analysis, regions of interest (ROIs) of activation clusters were generated using the SPM Marsbar toolbox. CBF changes in these ROIs were extracted and entered into a univariate GLM analysis using the SPSS software to investigate the effect size of each covariate.

3. Results

3.1. Behavioral data

During the course of experiment, mean subjective ratings of meditation and connectedness increased from the first baseline to the two meditation tasks whereas the mean perceived stress level decreased (Fig. 1). The main effect of experimental condition was significant for subjective ratings of meditation ($F(3, 27) = 3.17$, $P = 0.04$), and showed slight trend for lower stress ($F(3, 27) = 2.07$, $P = 0.13$). Post hoc analyses indicated a significant increase of meditation ratings between Baseline 1 and Meditation 2 conditions ($F(1, 9) = 14.2$, $P = 0.004$). Perceived stress was negatively correlated with subjective ratings of meditation ($R = -0.616$, $P = 0.002$) and connectedness ($R = -0.601$, $P = 0.003$), between which there was a strong positive association ($R = 0.883$, $P < 0.001$).

3.2. CBF responses during meditation tasks

Compared with the control, the first meditation task elicited significantly increased CBF in the medial prefrontal cortex (MPFC) and left caudate (LCau), while decreased CBF was observed in the left superior occipital and inferior parietal cortex, as well as in the right inferior occipital cortex (RIOC) (see Fig. 2A). The MNI coordinates and Z scores of detected clusters are listed in Table 1. The second meditation task, relative to the control condition, induced profound CBF activation in several limbic and paralimbic structures, including the left insula/amygdala/hippocampus (LIn/Amyg/Hip), right insula (RIn), left hippocampus and parahippocampus (LHip/PHip), right parahippocampus (RPHip), and left superior temporal cortex. CBF reduction was observed in the left occipital/angular gyrus/superior parietal cortex (LO/AG/SPC), right middle occipital cortex, and left pre and post-central gyrus (LPCG) (see Fig. 2B). The above results suggest that the two meditation tasks primarily activated forebrain areas (e.g. MPFC and caudate) and deeper limbic/paralimbic structures (e.g., hippocampus, insula and amygdala), respectively.

3.3. Brain activation differences between two meditation tasks

CBF responses during the two meditation tasks were further contrasted (Meditation 2–1). Meditation 2 showed greater CBF responses than Meditation 1 primarily in deeper limbic and forebrain structures in the left hemisphere, including the left hippocampus/parahippocampus/amygdala (LHip/PHip/Amyg), left insula/inferior frontal/superior temporal cortex (LIn/IF/STC), and left parahippocampus/fusiform gyrus. Increased CBF was also observed in the cerebellar vermis and right superior temporal cortex (RSTC) during Meditation 2 as compared to Meditation 1. Since the first meditation task involved greater medial prefrontal activation, reduced CBF was observed in the medial prefrontal cortex/anterior cingulate cortex (MPFC/ACC), and left orbitofrontal cortex (LorF) during Meditation 2. In addition, Meditation 2 showed reduced CBF in the left inferior parietal/supramarginal gyrus and motor areas including the left pre and post-central gyrus (LPCG) and right post-central gyrus (RPCG) (see Fig. 3A).

We further applied conjunction analysis to detect the common activation patterns between the two meditation tasks (see Fig. 3B). Interestingly, the LIn/IF/STC and RIn/STC are the only two brain regions showing common activation during the two meditation tasks

Table 1
Brain regions with significant findings in analyses of CBF data.

Brain regions	MNI coordinates			Z score	Cluster size	Activation/deactivation
	x	y	z			
<i>Meditation 1 vs. control (Fig. 2A)</i>						
MPFC	0	64	18	3.91	100	Activation
LCau	-18	14	10	3.52	21	Activation
RIOC	54	-68	-12	3.83	21	Deactivation
LSO/IPC	-28	-62	34	3.36	29	Deactivation
<i>Meditation 2 vs. control (Fig. 2B)</i>						
LIn/Amyg/Hip	-30	10	-22	5.23	451	Activation
RIn	44	-4	-4	3.79	413	Activation
LHip/PHip	-18	-34	-6	3.81	84	Activation
RPHip	18	-24	-22	3.87	94	Activation
LSTC	-50	-2	-4	3.36	10	Activation
LO/AG/SPC	-24	-58	46	5.50	840	Deactivation
RMOC	40	-78	2	5.53	64	Deactivation
LSPC	26	-57	63	5.23	52	Deactivation
LPCG	-44	-18	46	5.06	52	Deactivation
<i>Meditation 2 vs. Meditation 1 (Fig. 3A)</i>						
LHip/PHip/Amyg	-12	16	-28	4.16	141	Activation
LIn/IF/STC	-34	12	-20	4.00	129	Activation
LPHip/FG	-18	-32	-22	3.72	32	Activation
Vermis	-2	-48	-32	3.58	56	Activation
RSTC	44	16	-24	3.37	12	Activation
LPCG	-40	-22	52	4.55	201	Deactivation
LIP/SMG	-52	-44	54	4.36	67	Deactivation
MPFC/ACC	14	44	14	3.52	38	Deactivation
LorF	-14	40	-12	3.31	22	Deactivation
RPCG	38	-24	48	3.23	10	Deactivation
<i>Baseline 2 vs. Baseline 1 (Fig. 5)</i>						
LIn	-28	36	8	4.08	58	Activation
RPCG	38	0	56	4.09	36	Activation
Precuneus	4	-48	64	3.33	22	Activation

(Abbreviations for tables and figures: MPFC = medial prefrontal cortex; LCau = left caudate; RIOC = right inferior occipital cortex; LSO/IPC = left superior occipital and inferior parietal cortex; LIn/Amyg/Hip = left insula/amygdala/hippocampus; RIn = right insula; LHip/PHip = left hippocampus/parahippocampus; RPHip = right parahippocampus; LO/AG/SPC = left occipital/angular gyrus/superior parietal cortex; RMOC = right medial occipital cortex; LSPC = left superior parietal cortex; LPCG = left precentral gyrus; LHip/PHip/Amyg = left hippocampus/parahippocampus/amygdala; LIn/IF/STC = left insula/inferior frontal/superior temporal cortex; LPHip/FG = left parahippocampus/fusiform gyrus; RSTC = right superior temporal cortex; LPCG = left precentral gyrus; LIP/SMG = left inferior parietal/supramarginal gyrus; MPFC/ACC = medial prefrontal cortex/anterior cingulate cortex; RPCG = right precentral gyrus; LIn = left insula).

versus the control condition. Common deactivated regions include the posterior occipitoparietal cortex LO/AG/SPC and right medial occipital cortex. Consistent with our regression analysis results, the contrast and conjunction analysis of the two meditation tasks revealed that LIn/IF/STC was activated during both meditation tasks in contrast to the control condition, and its activity was increased in M2 compared to M1. In contrast, the mean CBF in the MPFC/ACC was decreased when comparing M2 to M1.

3.4. Correlation of CBF responses with behavioral ratings

Regression analyses were further carried out to detect significant associations between changes in regional CBF and behavioral ratings (depth of meditation, connectedness, and stress) from the control condition to the two meditation tasks respectively. Within brain regions demonstrating significant CBF responses to meditation in the group of 10 subjects, we found that CBF increase in the LIn/IF/STC region was positively correlated with changes in subjective ratings of connectedness and meditation from the control condition to the second meditation task ($P \leq 0.003$) (Fig. 4). In contrast, CBF changes in the MPFC/ACC were negatively correlated with depth of meditation

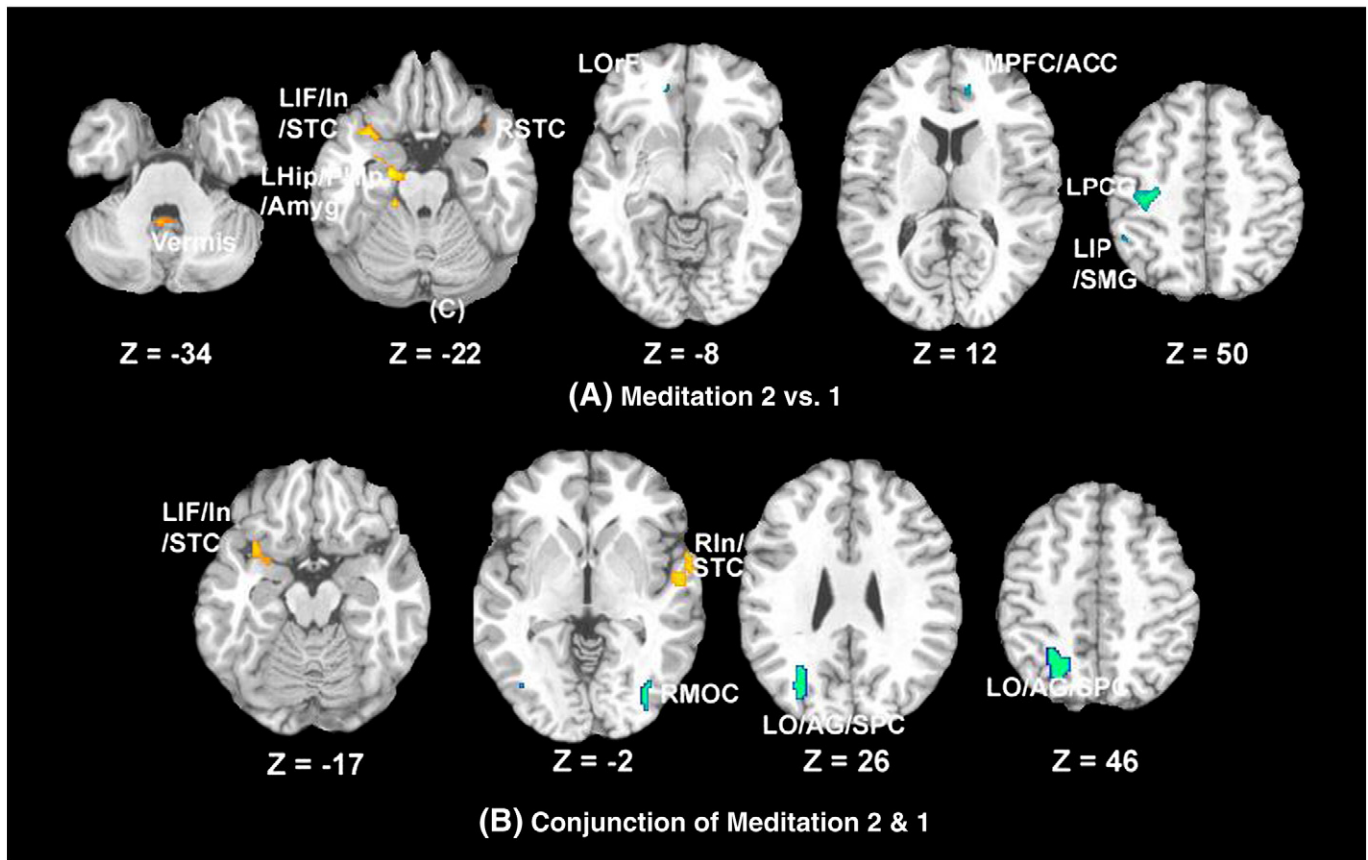


Fig. 3. Contrast of brain activations between the two meditation tasks (A), and conjunction analysis results of brain activation during Meditations 1 and 2 vs. the control condition (B). Note LIF/In/STC is detected in conjunction analysis, in contrast between Meditations 1 and 2, as well as in regression analysis with well-being, connectedness and stress, suggesting a pivotal role of this region in mediating meditation effects on stress.

and connectedness ratings ($P \leq 0.02$). Additionally, CBF changes in the LIn/IF/STC were negatively correlated with perceived stress ($P = 0.009$). These regression analysis results suggest that left inferior forebrain areas including the insula, inferior frontal cortex and superior temporal cortex (at the temporal pole) showed increased CBF responses during the second meditation task, which had positive associations with subjective ratings of both connectedness and depth of meditation as well as negative association with perceived stress. These relationships between CBF and behavioral ratings were generally reversed in MPFC/ACC. In the left parietal regions (LO/AG/SPC), we also found a trend for correlation between regional CBF reduction and increased connectedness ($P = 0.099$, see Fig. 4), supporting the hypothesized association of suppressed parietal function and perceived connectedness.

The above ROI analyses were based on activation clusters detected in a comparison of mean CBF responses between meditation and control conditions. We further performed voxel-based regression analysis between changes in regional CBF and behavioral ratings. Consistent with ROI based analyses, we detected significant correlations of CBF and subjective ratings of the depth of meditation in the ACC and LIn/IF/STC regions (see Fig. 4).

3.5. Sustained CBF responses following meditation tasks

Sustained CBF responses following meditation tasks were detected by comparing two baseline conditions (Baseline 2–1). Increased baseline CBF was observed in the left anterior insula (LIn), as well as the right precentral gyrus (RPCG) and precuneus (see Fig. 5). No decreased CBF at baseline was detected.

4. Discussion

Our primary goals for this study were to evaluate whether different meditation practices are associated with different CBF patterns in the brain, to correlate CBF changes with subjective experiences during meditation, to explore the relationship between meditation and stress in terms of brain activation patterns, and to determine if there are persistent effects following meditation.

While there have been several studies evaluating the performance of two different meditation practices using behavior or EEG measures (Dunn et al., 1999; Carter et al., 2005), this is one of the first fMRI study that reports individuals doing two different types of meditation practices. This allowed for the direct comparison of different practices to each other especially with regard to the depth of the experience. The results of this component of the study revealed several important findings. The areas we have previously proposed to be involved in the meditation practice, namely the frontal regions, anterior cingulate, limbic system and parietal lobes were affected in this study. We observed in the first meditation practice compared to the control condition, significantly increased CBF in the medial prefrontal cortex which we believe is associated with the intense focus-based component of the practice. The second practice is not focused-based per se, but dependent on breathing exercises. In this case, the prefrontal cortex was not particularly activated, but there were significant activations in the limbic structures of the hippocampus and amygdala in addition to the insula. These differences are interesting since the second meditation was reported by the subjects to be more intense. This may have been due to several factors which include less interference of the MRI noise with this particular practice (the first

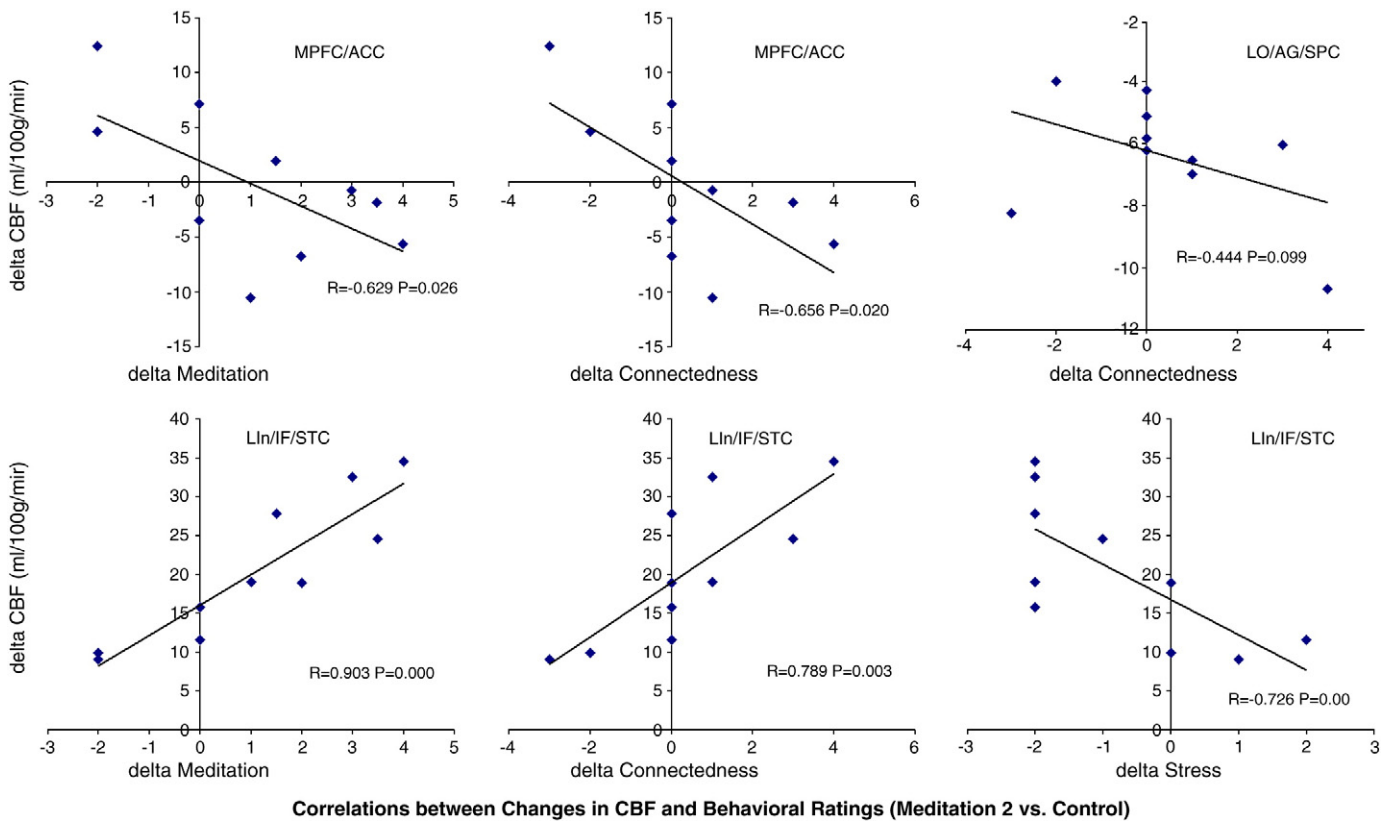


Fig. 4. Scatter plots of changes in CBF and behavioral ratings (meditation, connectedness and stress) between Meditation 2 and Control conditions. Mean CBF changes were extracted from MPFC/ACC and LIn/IF/STC regions in each individual subject and plotted across subjects.

practice was more rhythmic than the second and all of the subjects reported difficulty doing the first practice in conjunction with the MRI sounds), that it followed the first meditation, and that there are inherent features that make it more intense. We also have hypothesized, but never tested the notion that the initial stages of meditation would be associated with frontal lobe increases, but that with progressive meditation, the frontal lobes would decrease. It is possible that we have observed some support for this contention.

In other imaging studies of meditation, there have also been discrepant results regarding the frontal cortex. The first imaging study of meditation used FDG PET to measure regional glucose metabolism in eight subjects undergoing Yoga meditative relaxation (Herzog et al., 1990–1991). In this study there was a significant increase in the frontal:occipital ratio of cerebral metabolism. Specifically, there was a

mild increase in the frontal lobe, but marked decreases in metabolism in the occipital and superior parietal lobes. A study utilizing fMRI of subjects performing a similar yoga relaxation technique designed to bring about “relaxation response,” demonstrated increased CBF in the frontal and limbic regions (Lazar et al., 2000). PET imaging has been utilized to measure CBF changes in nine subjects performing Yoga relaxation techniques (Lou et al., 1999). That study did not report increases in the frontal areas, although the subjects were practicing a “passive” type of meditation. It might be that the breath-based practice studied in our study also represented a more passive, relaxation, type of meditation rather than intense focusing that might require prefrontal structures.

In addition to these studies, the prefrontal cortex and cingulate gyrus have been implicated in a number of social behavior tasks related

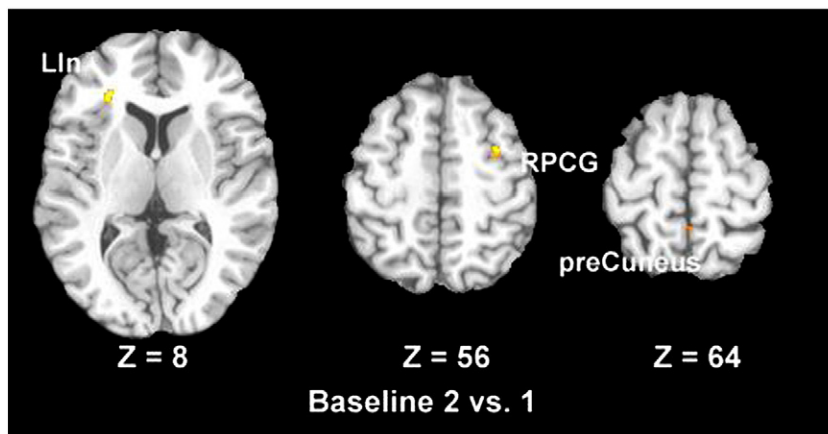


Fig. 5. Axial sections of group analysis results showing increased CBF following meditation tasks (between Baselines 2 and 1).

to Theory of Mind, empathy, moral reasoning, and evaluation of emotional states. The prefrontal cortex thus plays a crucial role in social cognitive skills (Declerck et al., 2006). For example, Mesulam (1998) describes how the prefrontal cortex is essential for flexible behavior because it inhibits the habitual responses that have become inappropriate. Imaging studies show that the prefrontal cortex, in addition to the cingulate gyrus, are consistently activated during theory of mind tasks such as those involving false belief (Stuss et al., 2001; Gallagher and Frith, 2003) or interpreting eye gazes (Calder et al., 2003). A meta-analysis of 80 studies on empathy suggests that the prefrontal cortex mediates human empathy by virtue of a number of distinctive processing nodes (Seitz et al., 2006). Damage to the prefrontal cortex also causes substantial impairments in moral judgment and social functioning (Koenigs et al., 2007; Wain and Spinella, 2007).

We have also hypothesized that there would be a relative decrease in the activity in the parietal areas associated with the sense of an altered experience of space during meditation (Newberg and Iversen, 2003). Several studies have shown that there are alterations in activity in the parietal lobes, particularly in association with increased activity in the prefrontal cortex, in subjects performing visual-spatial tasks (Cohen et al., 1996; D'Esposito et al., 1998). Thus, these studies not only suggest that the superior parietal lobe is associated with spatial processing, but that it interacts with the PFC during such processing. In both practices we studied, there were significant deactivations in the parietal lobes, more in the inferior parietal lobe during the first practice and the superior parietal lobe during the second. Interestingly, the second practice was associated with more intense feelings of connectedness, and there was a trend of correlation between CBF reduction and increased connectedness in left parietal regions, further supporting the importance of the parietal lobe in such subjective experiences.

The limbic system has also been postulated to be involved in meditation tasks and this study supports the importance of the limbic system, particularly the hippocampus and amygdala in meditation practices. Again the changes in the limbic system were more specifically involved during the second meditation which was typically reported as a more intense practice by the participants.

Thus, this study corroborated previous findings of involvement of the prefrontal cortex, limbic structures, and parietal lobes during meditation (Brefczynski-Lewis et al., 2007; Lutz et al., 2008a,b; Manna et al., 2010). However, this study further implicates the different activation states depending on the specific type of practice. This is particularly important when evaluating the physiological or clinical effects of different practices since they each might have a different affect on the brain.

Our second and third goals were to determine if there were correlations between subjective components of the meditation experiences and CBF, and further to explore the specific brain response to meditation and stress. Our subjective evaluation showed that with increasing meditation practice, there were increased feelings of connectedness and intensity of meditation along with decreased levels of stress. This was not particularly surprising, although we were able to correlate the subjective reports with changes in CBF. Particularly, there was a strong negative correlation between the MPFC/ACC activity and the intensity of meditation during the second meditation task. This supports the earlier notion that subjectively stronger effects of meditation may actually be associated with a lowered activity in the MPFC/ACC. The ACC was a primary brain region demonstrating stress response in our previous fMRI studies, with a hypothesized role of monitoring and regulating (negative) emotions as well as maintaining vigilance during stress responses (Wang et al., 2005a,b, 2007).

We also observed strong correlations between intensity of meditation and neural activity in the left inferior forebrain areas including the insula, inferior frontal cortex and temporal pole. CBF change in this region was negatively correlated with perceived stress. An asymmetric prefrontal activity related to emotion processing has long been hypothesized and received empirical support primarily from

electrophysiological studies, with the left and right prefrontal cortex associated with (approaching of) positive and (regulation of) negative emotions respectively (Davidson and Irwin, 1999; Davidson et al., 2000). In our earlier studies of psychological stress, reduced CBF in the left orbitofrontal and inferior frontal cortex was a primary finding and was interpreted as suppressed approach-oriented and hedonic goals during stress. The detected activation foci for correlations of CBF with meditation in the present study (see Fig. 4) and stress in our earlier studies ($x = -30$ $y = 30$ $z = -15$) were within a 1.5 cm distance. Therefore, our fMRI studies of meditation and stress adhere to each other and jointly suggest that meditation practice counteracts stress through enhancing positive emotions and facilitating hedonic behaviors (i.e., increasing CBF in the left prefrontal cortex).

The last goal of this study was to determine if the effects of meditation occurred only during meditation or lasted for some time afterwards. The data suggested that there were persistent changes in the left anterior insula and the precentral gyrus. The nature of these findings remains to be determined. Since the insula is particularly involved with emotional regulation, it may suggest the potential ability of meditation to cause longer term effects. Particularly, we noticed that the persistent insular activation extended into the left frontal regions that have been implicated with positive emotions. Future studies will need to determine how long such changes last and whether there is an additive effect.

One of the most limiting aspects of this study is the small sample size. This makes generalizing the findings to other types of practices and other types of individuals difficult. For example, novices might provide a different CBF pattern compared to the expert meditators evaluated in this study. Future studies will have to evaluate a larger population and also different types of practices. We also focused on specific structures based upon our initial hypotheses, and while we found evidence to support those hypotheses, but there may ultimately be other structures that are affected by specific practices which will have to be tested in a broader set of studies.

Another potentially confounding problem with this study, as with all meditation studies, is the fact that the subjective sense during the meditation is difficult to measure and it is difficult to ensure that individuals are meditating when you ask them to and not meditating when you ask them not to. We provided clear instructions to the subjects as to when to meditate and when to rest or perform the control task. However, all of the states could be associated with alterations in subjective experiences of stress or feelings of connectedness. We had subjects respond to a limited set of questions in order to provide data without distracting them significantly. All subjects felt that they had had an adequate meditation session, although they universally reported some difficulty with the first meditation and that the second meditation was more intense. Because of the nature of both meditation practices described above, we did not alter the order of the practices which also could be an important confounding variable. However, this problem might only limit the ability to differentiate the two meditation practices from each other on the basis that they are, in fact, different, rather than simply because the person was meditating for a longer period of time. A previous study by our group evaluated ASL in seven control subjects undergoing four sequential ASL perfusion MRI scans without performing tasks, carried out in a similar manner to the current study, while their subjective ratings of stress, heart rate, and salivary cortisol data were collected (Wang, 2005a). All the behavioral, physiological, and CBF measurements did not show significant changes across the time course of the experiment strongly indicating minimal habituation effect of MRI scanning. However, future studies might perform the study by having subjects perform the first meditation followed by a randomly assigned second meditation. The second meditation would be either a repeat of the first, focused-based practice, or the breath-based practice. This would better determine if the differences we observed in the second meditation are truly related to a different type of meditation practice

or merely the result of progressive meditation. Breathing itself, an important component of the second meditation, might be responsible for part or all of the effects observed in perfusion. A few studies have demonstrated the effect of hyperventilation/hyperoxia on CBF and generally found a slight reduction of global CBF (Floyd et al., 2003). In the present study, we attempted to control this potential confounding effect by including global CBF as a covariate in GLM analysis. Nevertheless, there might be regional CBF changes related to the modulational effect of breathing that need to be addressed in future studies. Functional MRI had important advantages for acquiring the data for this study, but the noise did impair some subjects from achieving an adequate practice during the first meditation. However, future efforts to make such techniques more amenable to the study of meditation may be fruitful in helping to better define the underlying physiological basis of such practices.

5. Conclusion

The results from this initial study have made a significant advancement in our understanding of the general and specific effects of meditation on the brain. We found that these two different meditation practices result in different CBF patterns. We also observed correlations between the CBF changes and the subjective experiences described by the practitioners. In particular, perceived depth of meditation and stress exerted opposite effects on neural activity in the left forebrain areas. Finally, we found tentative evidence for a washout period which might have potential implications from the perspective of utilizing meditation for various clinical conditions. If the effects of meditation last beyond the acute act of the practice, then one might expect longer term effects to occur. Future studies will have to explore these longer term effects.

Acknowledgements

We would like to thank Dr. Amishi Jha for her extensive efforts in helping to prepare this manuscript. This work was funded by a pilot grant from the Penn Comprehensive Neuroscience Center and NINDS P30NS045839, MH080892, and ARRA grant MH080892-S1.

References

- Aguirre, G.K., Detre, J.A., Zarahn, E., Alsup, D.C., 2002. Experimental design and the relative sensitivity of BOLD and perfusion fMRI. *Neuroimage* 15, 488–500.
- Brefczynski-Lewis, J.A., Lutz, A., Schaefer, H.S., Levinson, D.B., Davidson, R.J., 2007. Neural correlates of attentional expertise in long-term meditation practitioners. *Proceedings of the National Academy of Sciences USA* 104, 11483–11488.
- Cahn, B.R., Polich, J., 2006. Meditation states and traits: EEG, ERP, and neuroimaging studies. *Psychological Bulletin* 132, 180–211.
- Calder, A.J., Lawrence, A.D., Keane, J., Scott, S.K., Owen, A.M., Christoffels, I., Young, A.W., 2003. Reading the mind from eye gaze. *Neuropsychologia* 40, 1129–1138.
- Carter, O.L., Presti, D.E., Callistemon, C., Ungerer, Y., Liu, G.B., Pettigrew, J.D., 2005. Meditation alters perceptual rivalry in Tibetan Buddhist monks. *Current Biology* 15, R412–R413.
- Cohen, M.S., Kosslyn, S.M., Breiter, H.C., DiGirolamo, G.J., Thompson, W.L., Anderson, A. K., Bookheimer, S.Y., Rosen, B.R., Belliveau, J.W., 1996. Changes in cortical activity during mental rotation: a mapping study using functional MRI. *Brain* 119, 89–100.
- Cohen, D.L., Wintering, N., Tolles, V., Townsend, R.R., Farrar, J.T., Galantino, M.L., Newberg, A.B., 2009. Cerebral blood flow effects of yoga training: preliminary evaluation of 4 cases. *Journal of Alternative and Complementary Medicine* 15, 9–14.
- D'Esposito, M., Aguirre, G.K., Zarahn, E., Ballard, D., Shin, R.K., Lease, J., 1998. Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Research* 7, 1–13.
- Davidson, R.J., Irwin, W., 1999. The functional neuroanatomy of emotion and affective style. *Trends in Cognitive Science* 3, 11–21.
- Davidson, R.J., Jackson, D.C., Kalin, N.H., 2000. Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. *Psychological Bulletin* 126, 890–909.
- Declerck, C.H., Boone, C., De Brabander, B., 2006. On feeling in control: a biological theory for individual differences in control perception. *Brain and Cognition* 62, 143–176.
- Dunn, B.R., Hartigan, J.A., Mikulas, W.L., 1999. Concentration and mindfulness meditations: unique forms of consciousness? *Applied Psychophysiology and Biofeedback* 24, 147–165.
- Floyd, T.F., Clark, J.M., Gelfand, R., Detre, J.A., Ratcliffe, S., Guvakov, D., Lambertsen, C.J., Eckenhoff, R.G., 2003. Independent cerebral vasoconstrictive effects of hyperoxia and accompanying arterial hypocapnia at 1 ATA. *Journal of Applied Physiology* 95, 2453–2461.
- Frith, C.D., Friston, K., Liddle, P.F., Frackowiak, R.S., 1991. Willed action and the prefrontal cortex in man. a study with PET. *Proceedings. Royal Society of London* 244, 241–246.
- Gallagher, H.L., Frith, C.D., 2003. Functional imaging of “theory of mind”. *Trends in Cognitive Science* 7, 77–83.
- Goldin, P.R., Gross, J.J., 2010. Effects of mindfulness-based stress reduction (MBSR) on emotion regulation in social anxiety disorder. *Emotion* 10, 83–91.
- Herzog, H., Lele, V.R., Kuwert, T., Langen, K.-J., Kops, E.R., Feinendegen, L.E., 1990–1991. Changed pattern of regional glucose metabolism during Yoga meditative relaxation. *Neuropsychobiology* 23, 182–187.
- Koenigs, M., Young, L., Adolphs, R., Tranel, D., Cushman, F., Hauser, M., Damasio, A., 2007. Damage to the prefrontal cortex increases utilitarian moral judgements. *Nature* 446, 908–911.
- Lazar, S.W., Bush, G., Gollub, R.L., Fricchione, G.L., Khalsa, G., Benson, H., 2000. Functional brain mapping of the relaxation response and meditation. *NeuroReport* 11, 1581–1585.
- Lou, H.C., Kjaer, T.W., Friberg, L., Wildschiodtz, G., Holm, S., Nowak, M., 1999. A 150–H2O PET study of meditation and the resting state of normal consciousness. *Human Brain Mapping* 7, 98–105.
- Lutz, A., Brefczynski-Lewis, J., Johnstone, T., Davidson, R.J., 2008a. Regulation of the neural circuitry of emotion by compassion meditation: effects of meditative expertise. *PLoS ONE* 3, e1897.
- Lutz, A., Slagter, H.A., Dunne, J.D., Davidson, R.J., 2008b. Attention regulation and monitoring in meditation. *Trends in Cognitive Sciences* 12, 163–169.
- Manna, A., Raffone, A., Perrucci, M.G., Nardo, D., Ferretti, A., Tartaro, A., Londei, A., Del Gratta, C., Belardinelli, M.O., Romani, G.L., 2010. Neural correlates of focused attention and cognitive monitoring in meditation. *Brain Research Bulletin* 82, 46–56.
- Mesulam, M.M., 1998. From sensation to cognition. *Brain* 121, 1013–1052.
- Newberg, A.B., Iversen, J., 2003. The neural basis of the complex mental task of meditation: neurotransmitter and neurochemical considerations. *Medical Hypothesis* 61, 282–291.
- Newberg, A.B., Alavi, A., Baime, M., Pourdehnad, M., Santanna, J., d'Aquili, E.G., 2001. The measurement of regional cerebral blood flow during the complex cognitive task of meditation: a preliminary SPECT study. *Psychiatry Research: Neuroimaging* 106, 113–122.
- Newberg, A., Pourdehnad, M., Alavi, A., d'Aquili, E., 2003. Cerebral blood flow during meditative prayer: preliminary findings and methodological issues. *Perceptual and Motor Skills* 97, 625–630.
- Pardo, J.V., Fox, P.T., Raichle, M.E., 1991. Localization of a human system for sustained attention by positron emission tomography. *Nature* 349, 61–64.
- Posner, M.I., Petersen, S.E., 1990. The attention system of the human brain. *Annual Review of Neuroscience* 13, 25–42.
- Raffone, A., Srinivasan, N., 2010. The exploration of meditation in the neuroscience of attention and consciousness. *Cognitive Processing* 11, 1–7.
- Sammer, G., Blecker, C., Gebhardt, H., Bischoff, M., Stark, R., Morgen, K., Vaitl, D., 2007. Relationship between regional hemodynamic activity and simultaneously recorded EEG-theta associated with mental arithmetic-induced workload. *Human Brain Mapping* 28, 793–803.
- Seitz, R.J., Nickel, J., Azari, N.P., 2006. Functional modularity of the medial prefrontal cortex: involvement in human empathy. *Neuropsychology* 20, 743–751.
- Silver, M.A., Ress, D., Heeger, D.J., 2005. Topographic maps of visual spatial attention in human parietal cortex. *Journal of Neurophysiology* 94, 1358–1371.
- Stuss, D.T., Gallup, G.G., Alexander, M.P., 2001. The frontal lobes are necessary for “theory of mind”. *Brain* 124, 279–286.
- Tagini, A., Raffone, A., 2010. The ‘I’ and the ‘Me’ in self-referential awareness: a neurocognitive hypothesis. *Cognitive Processes* 11, 9–20.
- Vogt, B.A., Finch, D.M., Olson, C.R., 1992. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. *Cerebral Cortex* 2, 435–443.
- Wain, O., Spinella, M., 2007. Executive functions in morality, religion, and paranormal beliefs. *The International Journal of Neuroscience* 117, 135–146.
- Wang, J., Aguirre, G.K., Kimberg, D.Y., Roc, A.C., Li, L., Detre, J.A., 2003. Arterial spin labeling perfusion fMRI with very low task frequency. *Magnetic Resonance in Medicine* 49, 796–802.
- Wang, J., Rao, H., Wetmore, G.S., Furlan, P.M., Korczykowski, M., Dinges, D.F., Detre, J.A., 2005a. Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. *Proceedings of the National Academy of Science USA* 102, 17804–17809.
- Wang, J., Zhang, Y., Wolf, R.L., Roc, A.C., Alsup, D.C., Detre, J.A., 2005b. Amplitude modulated continuous arterial spin labeling perfusion MR with single coil at 3T-feasibility study. *Radiology* 235, 218–228.
- Wang, J., Korczykowski, M., Rao, H., Pluta, J., Fan, Y., Gur, R., McEwen, B., Detre, J.A., 2007. Gender difference in neural response to psychological stress. *Social Cognitive and Affective Neuroscience* 2, 227–239.
- Zaehle, T., Jordan, K., Wüstenberg, T., Baudewig, J., Dechent, P., Mast, F.W., 2006. The neural basis of the egocentric and allocentric spatial frame of reference. *Brain Research* 1137, 92–103.