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Cerebral blood flow differences between long-term meditators and non-meditators

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abstract

We have studied a number of long-term meditators in previous studies. The purpose of this study was to determine if there are differences in baseline brain function of experienced meditators compared to non-meditators. All subjects were recruited as part of an ongoing study of different meditation practices. We evaluated 12 advanced meditators and 14 non-meditators with cerebral blood flow (CBF) SPECT imaging at rest. Images were analyzed with both region of interest and statistical parametric mapping. The CBF of long-term meditators was significantly higher ($p < .05$) compared to non-meditators in the prefrontal cortex, parietal cortex, thalamus, putamen, caudate, and midbrain. There was also a significant difference in the thalamic laterality with long-term meditators having greater asymmetry. The observed changes associated with long-term meditation appear in structures that underlie the attention network and also those that relate to emotion and autonomic function.

1. Introduction

Meditation, in general, is a complex neurocognitive task that is often associated with alterations in body physiology and psychological measures. Over the past 30 years, there have been a number of studies which have explored the physiological correlates of different types of meditation. It is important to note here that meditation refers to a large variety of practices that range from purely relaxation based to those performed with the goal of attaining powerful spiritual experiences. This variation, in itself, makes the study of such practices difficult. However, we have tried to find similarities among these practices, and feel that enough prior studies have demonstrated changes associated with these practices, that it seems worthwhile to continue to explore them.

We have previously argued that meditation practices might be regarded as "belief promoting" practices since their content – e.g. Buddhist or Christian ideals – are what the participants focus upon. If such practices alter beliefs and cognitions, then one would expect differences in brain function in individuals who performed such practices for many years compared to those who have not performed these practices. For e.g. the frontal lobes play an important role modulating emotions, engaging cognitive processes, and developing a sense of self. Neuroimaging studies have generally shown increased frontal

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lobe activity during meditation practices suggesting that meditation may promote beliefs and help reinforce specific religious or spiritual ideals. In addition, meditation techniques often result in alterations in the state of consciousness of the individual (Baijal & Srinivasan, 2010; Lehmann et al., 2001; Travis, Tecce, Arenander, & Wallace, 2002). Such alterations may be mild, such as a state of relaxation or alertness (Lazar et al., 2000). Sometimes meditation results in profound changes in consciousness leading individuals into trance-type states, states of self-hypnosis, or mystical states (Newberg & Iversen, 2003; Travis et al., 2002). It is also possible that over time, repetitive meditation practice might produce permanent changes in the state of the brain with respect to consciousness (Lutz, Brefczynski-Lewis, Johnstone, & Davidson, 2008; Lutz et al., 2009). Furthermore, it has been suggested that meditation affects the brain's default network (Travis et al., 2010) which is associated with baseline brain function and mediates many basic brain functions. Its subsystems include part of the medial temporal lobe for memory, part of the medial prefrontal cortex for mental simulations, and the posterior cingulate cortex for integration, along with the adjacent precuneus and the medial, lateral and inferior parietal cortex (Buckner, Andrews-Hanna, & Schacter, 2008; Raichle et al., 2001). If meditation does result in long term changes in brain activity, one might expect that the default network is also changed.

Neuroimaging studies utilizing positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI) have all demonstrated specific changes in cortical and sub-cortical structures when subjects were actively meditating (Herzog et al., 1990–1991; Lou et al., 1999; Lazar et al., 2000; Newberg, Pourdehnad, Alavi, & d'Aquili, 2003; Newberg et al., 2001). However, we are aware of a limited number of neuroimaging studies that have evaluated the long-term effects of meditation practices. A study by Lutz, Greischar, Rawlings, Ricard, and Davidson (2004) suggested that the practice of meditation for a period of time can cause longer lasting changes in the brain. Another study (Davidson et al., 2003) showed that there were significant changes over time in the brain's electroencephalogram. In addition, a study by Lazar et al. (2005) utilizing structural MRI demonstrated that long-term meditators had thicker cerebral cortexes than non-meditators. Other studies showed increased gray matter concentration in meditators compared to non-meditators in the insula, inferior temporal lobe, frontal lobe, and hippocampus (Hölzel et al., 2008; Luders, Toga, Lepore, & Gaser, 2009). A different study found that long-meditators did not experience a significant negative correlation between brain volumes and aging as did non-meditating controls subjects (Pagnoni & Cekic, 2007).

This current study retrospectively evaluated all of the meditation subjects that we have studied to date using SPECT imaging and compared the cerebral blood flow (CBF) to whole brain ratios during the baseline (or resting) scan between long-term meditators and non-meditators. In this way, we hoped to evaluate whether there were differences in specific brain areas in long-term meditators compared to non-meditators. If such differences are observed, there remain two intriguing possibilities. One possibility is that meditators have brains that are fundamentally different to begin with which predisposed them to finding such practices beneficial. This might have contributed substantially to these individuals seeking out such practices and making them an important part of their daily lives. The second possibility is that the meditators affected their brains over the course of many years of performing their practice. In either case, if the brains of long-term meditators are different from non-meditators, this finding has potentially important implications for understanding the relationship between the brain and meditation practices.

The purpose of this study was to determine the differences in the brain associated with those individuals performing meditation for many years. What is not yet known is whether changes observed during the acute phase of meditation practice will become more permanent and will be in a similar direction of either increased or decreased activity. Based upon specific areas of the brain previously observed to be affected during meditation and also based upon areas observed to be structurally different in long-term meditators, we elaborated several hypotheses that would be the focus of this study: (1) we expected to observe relatively higher baseline frontal lobe CBF in long-term meditators because we have previously observed increased activity in the frontal lobe regions during active meditation (Newberg, Pourdehnad, Alavi, & d'Aquili, 2003; Newberg et al., 2001) and because existing studies have found differences in these structures between meditators and non-meditators (Lazar et al., 2005; Luders et al., 2009); (2) we expected to see relatively lower baseline parietal lobe activity in long-term meditators since meditation is also associated with alterations in the subjective experience of personal space and we have postulated and have found decreased activity in the parietal lobes during active meditation (Newberg, Pourdehnad, Alavi, & d'Aquili, 2003; Newberg et al., 2001; Herzog et al., 1990–1991); (3) we expected differences in the midbrain since this structure is related to autonomic changes associated with meditation (Jevning, Wallace, & Beidebach, 1992; Sudsuang, Chentanez, & Veluvan, 1991); (4) we expected to see higher baseline CBF in the basal ganglia and limbic system since these areas are related to emotional processing which has been found to be an important component of meditation (Luders et al., 2009; Lutz et al., 2008); and (5) we expected to see higher thalamic activity since this structure is involved with sensory processing and also for integrating higher cognitive processes and has previously been shown to be activated during meditation (Newberg & Iversen, 2003; Newberg et al., 2001).

2. Methods

2.1. Subjects and imaging acquisition

The study protocol and consent form were approved by the human Institutional Review Board. Twelve long-term meditators, with no history or clinical evidence of medical, neuropsychological, or drug abuse that would potentially alter cere-

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bral blood flow, were recruited to participate in this study. Seven were women and five men with ages ranging from 38–52 years with a mean age of 45 years. Each subject described himself or herself as practicing meditation or prayer for more than fifteen years experience. As such, all individuals practiced a focus based meditation which involved either imagery or various words or mantras. All subjects reported daily practice of 30–60 min and all had participated in extended retreats throughout their training (e.g. 1–3 months). Some subjects were recruited as subjects who were part of previously reported studies of Tibetan Buddhist meditators (Newberg et al., 2001) and Franciscan nuns (Newberg, Pourdehnad, Alavi, & d'Aquili, 2003). Other subjects were recruited separately. Subjects were instructed not to meditate the day of the scan so that the baseline represented a true baseline and not a post-meditation scan. Subjects had an intravenous canula (IV) placed in one arm approximately 20 min prior to the baseline scan. The subjects reported minimal discomfort from the IV that resolved prior to initiating the remainder of the study. The subject was instructed to rest in the room with their eyes closed and ears unoccluded for 5–10 min at which time they were injected through the IV with 7–10 mCi of ^{99m}TC-HMPAO (Amersham International, Arlington Heights, IL) or ^{99m}TC Bicisate (Bristol-Myers Squibb Medical Imaging, N. Billerica, MA), prepared as specified by the manufacturers. Approximately 15 min following the injection, the subject was scanned for 45 min in a Picker-Prism (Picker Inc, Cleveland, OH) triple-headed rotating gamma camera using high resolution fanbeam collimators. Projection images were obtained at three-degree angle intervals on a 128×128 matrix (pixel size $3.56\ \text{mm} \times 3.56\ \text{mm}$) over 360° by rotating each head 120°. These SPECT images were reconstructed in the transaxial, coronal, and sagittal planes using filtered backprojection, followed by a low pass filter and 1st order Chang attenuation correction (attenuation coefficient 0.11 cm^{-1}).

Fourteen non-meditating subjects (seven female and seven male, with a mean age of 43 and an age range from 22 to 60), recruited as a group of healthy controls for other activation studies on acupuncture, massage, and yoga, had undergone a similar baseline SPECT imaging scan as those described above. The baseline scans of the control subjects were then compared to the baseline scans of the meditators to assess baseline differences in the meditation subjects.

2.2. Image analysis and statistics

Two different statistical approaches were used in order to evaluate differences between the long-term meditators and non-meditators.

3. Region of interest analysis

The scans were reconstructed and resliced, using an oblique reformatting program, according to the anterior-posterior commissure line so that all scans were at comparable orientations for the analysis. A previously validated template methodology consisting of regions of interest (ROI) corresponding to the major cortical and sub-cortical structures was placed over the baseline scan (Resnick, Karp, Tretsky, & Gur, 1993). For the purposes of this study, we examined the CBF as measured in a selected number of ROIs which was hypothesis driven. The ROIs examined were the inferior frontal, superior frontal, prefrontal cortex, orbitofrontal, dorsal medial cortex, inferior temporal, superior parietal, inferior parietal, occipital, and sensorimotor areas, as well as the caudate, thalami, midbrain, cerebellum, and cingulate gyrus. Each ROI (which are small and therefore represents a "punch biopsy" of any given area) had its placement adjusted manually in order to achieve the best fit according to the atlas. Counts per pixel in each ROI were normalized to the whole brain activity. This provided a CBF ratio for each ROI compared to the whole brain. Such ratios are presented without units and have been reported in a variety of prior articles utilizing SPECT imaging demonstrating good test–retest reliability (Newberg, Saffer, Farrar, Pourdehnad, & Alavi, 2005; Newberg et al., 2001).

A laterality index (Li) for the thalamus, which had previously been observed to be asymmetric in long-term meditators, was also calculated to determine the relative activity of homologous regions in the left and right hemisphere using the following equation:

$$\mathrm{Li} = \frac{(\mathrm{Right} - \mathrm{Left})}{1/2 \times (\mathrm{Right} + \mathrm{Left})} \times 100$$

Mean values for the long-term meditators and non-meditators in each of the ROIs and for the LIs were compared using unpaired *t*-tests. We corrected the CBF data analysis for multiple comparisons using the False Discovery Rate method (Benjamini & Hochberg, 1995) which controls for the expected proportion of incorrectly rejected null hypotheses.

4. Statistical parametric mapping (SPM)

The image volumes of transverse slices were made compatible with SPM by creation of usable headers for the images. For each image, a file was created that contained data on image size, number of slices, pixel depth, maximal pixel value, and voxel size. All slices of a brain image were sampled and averaged to arrive at a mean pixel intensity for that image. The intensity threshold was set at 60% of the whole brain value. The images were spatially normalized in SPM to a standardized stereotactic space based on the Talairach and Tournoux (1998). The normalization process included further isotropic smoothing to a total of 12 mm. The long-term meditator and non-meditator groups were compared using the t-test comparison with

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the significance threshold set at $p < .001$ ($Z > 3.20$) (Friston et al., 1995). The location and peaks of significant increases and decreases between the groups were obtained. The cerebral structures were identified by their Talairach coordinates.

5. Results

Using the ROI analysis, the CBF ratios of long-term meditators was found to be significantly higher ($p < .05$) compared to non-meditators in the prefrontal cortex (see Fig. 1), parietal cortex, thalamus, putamen, caudate, inferior temporal lobe, cerebellum, and brainstem regions (see Table 1).

SPM analysis confirmed many of these regions to be affected (see Table 2). In particular, SPM found significant higher CBF in the long-term meditators in the parietal lobes, cerebellum, middle frontal lobes, left insula, and brain stem.

There was also a significant difference in the thalamic laterality index (see also Fig. 1) with the mean Li in meditators 9.0 ± 6.5 and that in the non-meditators 5.5 ± 4.4 ($p = .03$). Thus, long-term meditators had significantly greater asymmetry in their thalamic activity although five had right greater than left and seven had left greater than right. The middle frontal cortex had marginally significantly greater asymmetry, with a left predominance, in the long-term meditators compared to non-meditators (6% vs. 2% respectively, $p = .05$).

6. Discussion

Overall, the findings of this study suggest that long-term meditators have significantly different patterns of CBF at baseline compared to non-meditators. Regarding our initial hypotheses, the first was that we expected to observe a higher level of activity in the frontal cortices in long-term meditators. There have been several studies that have examined the effects of the complex neurocognitive task of meditation on brain activity. Several brain imaging studies have shown changes in frontal lobe activity during meditation practices (Herzog et al., 1990–1991; Newberg, Pourdehnad, Alavi, & d'Aquili, 2003; Newberg et al., 2001; Lazar et al., 2001; Lou et al., 1999).

In this SPECT study, the results support the hypothesis that long-term meditation is associated with higher activity in the frontal areas, particularly in the PFC and middle frontal cortex. Davidson et al. (2003) showed that there were significant changes over time in the brain's electroencephalogram. In particular, they observed that an eight week mindfulness based meditation program resulted in increases in left-hemispheric anterior activation. Our finding of marginally increased left frontal lobe activity in long-term meditators supports this earlier EEG finding. Lazar et al. (2005) used structural MRI to find that long-term meditators had thicker cerebral cortexes in the right anterior insula, right middle and superior frontal sulci, left superior temporal gyrus than in controls. This finding was supported by several other studies that also demonstrated

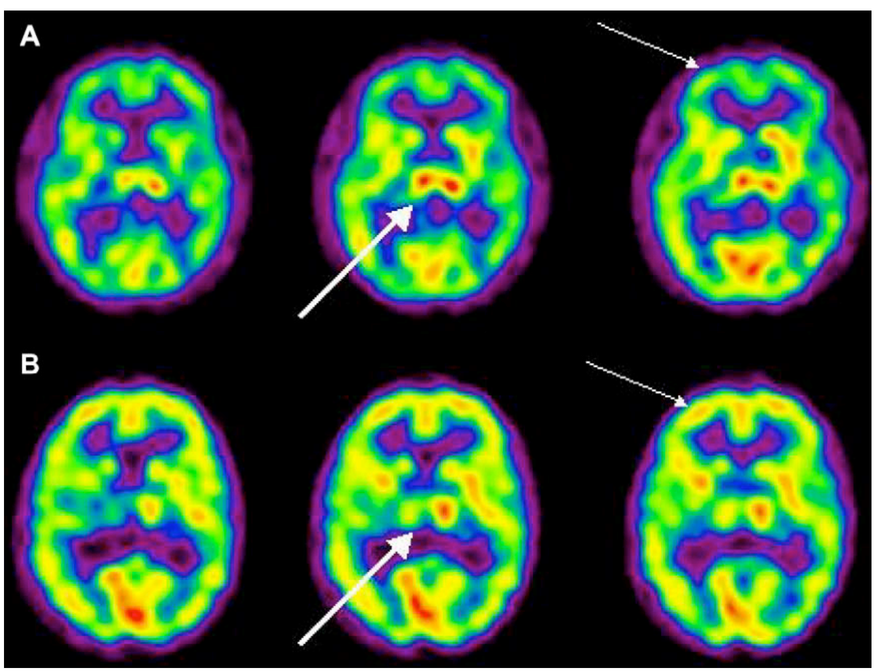

Fig. 1. This figure shows three transaxial slices of SPECT scans (Z levels 16, 8, and 0 respectively; with CBF represented as red > yellow > green > blue) from a non-meditator (A) and a long-term meditator (B). These images demonstrate increased CBF in the frontal lobes bilaterally (thin arrows) in the long-term meditator compared to the non-meditator. Also, there is a marked asymmetry in the thalamic activity (thick arrows) in the long-term meditator rather than relatively symmetric thalamic activity in the non-meditator. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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Table 1
Assessing the difference in baseline CBF between long-term meditator and non-meditator based on ROI analysis. The values are expressed as the ratio of the mean counts in the region divided by the mean whole brain counts.

Brain structure	*p*-value	Non-meditators		Meditators	
		Mean	SD	Mean	SD
Right prefrontal cortex	.002*	1.15	0.14	1.29	0.10
Left prefrontal cortex	.009*	1.22	0.10	1.30	0.06
Right parietal	<.0001*	1.13	0.04	1.27	0.07
Left parietal	<.0001*	1.13	0.03	1.26	0.08
Right putamen	.01*	1.27	0.09	1.37	0.15
Left putamen	.01*	1.26	0.10	1.36	0.12
Right cerebellum	<.0001*	1.05	0.12	1.23	0.05
Left cerebellum	<.0001*	1.09	0.10	1.21	0.06
Right caudate	.001*	1.13	0.10	1.28	0.12
Left caudate	.03	1.16	0.13	1.25	0.13
Right amygdala	.01*	0.89	0.09	0.99	0.10
Left amygdala	.03	0.90	0.11	1.01	0.15
Right inferior temporal	.005*	1.06	0.05	1.22	0.19
Left inferior temporal	.002*	1.08	0.10	1.25	0.10
Right thalamus	.02	1.19	0.07	1.32	0.20
Left thalamus	.04	1.27	0.09	1.37	0.17
Midbrain	.04	0.97	0.10	1.11	0.20

* Still significant after correction for multiple comparisons.

Table 2
Location and peaks of significantly ($p < 0.001$) higher resting regional cerebral blood flow in long-term meditators compared to non-meditators based on the SPM analysis.

Structure	Coordinates			*Z* score
	x	*y*	*z*	
Right parietal	56	−62	34	4.62
Left parietal	−14	−40	50	5.29
Right cerebellum	18	−38	−38	4.06
Left cerebellum	6	−80	−16	4.66
Left insula	−46	−26	18	3.83
Right middle frontal	34	12	52	3.81
Left middle frontal	−8	44	12	3.95
Midbrain	−2	16	−2	4.11

increased brain volume or gray matter concentration in the frontal lobes (Hölzel et al., 2008; Luders et al., 2009). The frontal lobes are intimately connected with the limbic areas and help to mediate attention, emotions, and memory. Thus, the overall higher frontal lobe activity may play an important role in why these individuals pursue such practices.

Our second hypothesis was that there would be relatively lower CBF in the superior parietal areas since these are associated with visuo-spatial orientation (Cohen et al., 1996; D'Esposito. et al., 1998) and perhaps also the altered experience of space during meditation (d'Aquili and Newberg, 1993). This parietal lobe, in conjunction with the temporal lobe, has also been implicated in out-of-body experiences (Bunning & Blanke, 2005). Interestingly, we found higher CBF in the parietal regions in long-term meditators. We might speculate that this baseline difference is associated with a stronger decrease during the actual practice (Newberg, Pourdehnad, Alavi, & d'Aquili, 2003; Newberg et al., 2001) and that this amplifies the experience of losing the sense of space.

Our third hypothesis was that there would be differences in the midbrain since this region can ultimately be involved in autonomic function and also sensory processing. We did observe significantly higher midbrain CBF in long-term meditators compared to non-meditators. This suggests that there may be longer term processes affecting important midbrain functions. It will be helpful for future studies to compare altered midbrain, as well as hypothalamic function, with measures of autonomic activity in these subjects in order to better determine the effect of such practices on the autonomic nervous system (Jevning et al., 1992; Sudsuang et al., 1991). This is particularly important since studies have found evidence to suggest a strong autonomic effect during meditation (Jevning et al., 1992; Peng et al., 1999).

Our fourth hypothesis was that there would be higher CBF in the basal ganglia and limbic structures. In long-term meditators, we did observe greater activity in the putamen and caudate nucleus than in non-meditators. There was also mildly higher uptake in the amygdala. Since these regions are known to be involved in emotional regulation, and since religious and spiritual practices have a substantial effect on emotions, it makes sense that there are more permanent differences in these areas when individuals take part in these practices.

The final hypothesis was that there would be alterations in the thalamus. The long-term meditation group had significantly greater activity in the thalamus and also a significantly different thalamic laterality index compared to non-meditators. The thalamus plays an important role in sensory processing and also higher cognitive processes. That the thalamus is significantly different in long-term meditators suggests that this may also be involved in the various perceptions of these individuals.

The results of this study support the hypothesis that long-term meditators have different activity patterns in their brain compared to non-meditators. However, it might be that long-term meditators have baseline frontal lobe activity that was conducive to practicing meditation in the first place and that is why these individuals sought out such a practice. On the other hand, meditation might induce such changes in brain activity over a period of time. In either case, the implication is that different patterns of baseline brain function are associated with different religious and spiritual practices. We have previously argued that beliefs in religious and spiritual concepts may result from specific patterns of brain activity and the results of this study are at least consistent with this possibility. The results from this study might also suggest that meditation-based practices affect beliefs and experiences through a fronto-parietal network since these structures have consistently been involved in both the acute practice of meditation and, now, in the long-term effects of such practices. In addition, the frontal lobes have been suggested as an important mediator in the sense of self and altered states of consciousness (Dietrich, 2003; Legrand & Ruby, 2009). Future studies will ideally evaluate larger numbers of subjects and also more specifically include measures of religiosity, spirituality, and other subjective beliefs.

There are several important limitations to this study. One issue is that the subjects come from several different traditions which arguably might result in different brain changes. However, this should have made it more difficult to produce significant group findings. Thus, it is interesting that these practitioners from different traditions still had similar results when pooled together. This suggests that the practices employed by these individuals were associated with similar brain changes. It also should be noted that the subjects all did a similar type of focused-based practice whether the focus was more visually (e.g. Buddhists) or verbally (e.g. nuns) based. Another potentially interesting confounding problem is trying to determine the actual state of the individual during the baseline scan. It has been argued by expert practitioners that ideally, an individual is meditating persistently. For some of our subjects, therefore, it is possible that even at baseline, they were in some degree of a meditative state. Subjects were clearly instructed regarding the importance of not meditating during the baseline scan since it would interfere with interpretation of the meditation state. Future studies might try to place subjects in a neutral condition such as counting as another type of baseline. Overall, this study shows that long-term meditators have differences in CBF compared to non-meditators.

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