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Neural correlates of meditation: a review of structural and functional MRI studies

Rui Ferreira Afonso[1], Inessa Kraft[1], Maria Adelia Aratanha[1], Elisa Harumi Kozasa[1]

[1]Hospital Israelita Albert Einstein, Sao Paulo, SP, Brazil, [2]Department of Psychiatry and Psychotherapy, University of Marburg, Marburg, Germany

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1. ABSTRACT

Here, we review the neurophysiological and neuroimaging changes that mediation induces in structural and functional MRI. The available evidence from structural studies suggests that mediation impacts neuronal plasticity and the functional MRI suggest that there are changes in gray and white matter in subjects who meditate. FMRI studies show that meditation is associated with decreased activity of default mode network and activation of brain regions involved in cognitive and emotional control. Together, the available imaging techniques have revealed that rather than impacting specific brain regions, meditation causes structural and functional changes in large-scale brain networks.

2. INTRODUCTION

Due to diversity of practices, many attempts have been made to define meditation. Some authors define a specific technique as mindfulness: "*paying attention in a particular way: on purpose, in the present moment, nonjudgmentally*" (2) or "*mindfulness meditation involves the self-regulation of attention and involves adopting a particular orientation toward one's experiences in the present moment*"(3). Others define meditation by its neurobiological correlates, suggesting it is a "*a complex neural practice that induces changes in neurophysiology and neurochemistry of the brain, resulting in altered neurocognition and behavior in the practitioner*" (4), that is, in this case technique and effect become tangled. Some authors, however, aim at encompassing several types of meditation in a broader definition, as defined by Cardoso *et al.* (5): "*Meditation is a procedure which should encompass a specific technique, clearly defined, involving muscle relaxation in some point of the process and "logic relaxation"; it is a self-induced state, using a self-focus skill (coined "anchor")*. This definition was reinforced by Bond *et al.(6)*.

Even though meditation is currently in practice, it originated in ancient times, being present in the *Vedas*, one of the first manuscripts of humankind, which has been practiced, throughout history. Willard Johnson suggested in 1982 (7) that meditation may have arisen concurrently with early domestication of fire. According to this author, humankind had its first experiences on altered consciousness states while still living in caves, sitting around fires and watching its flames.

Meditation has been brought to us through the context of spirituality, embedded in rituals of different religions such as Buddhism, Hinduism and Christianity, and others. Due to positive effects of mediation on human health, there has been an increase in the number of meditation practitioners (8), (9). Andrade *et al.* points out that about 30% of the inhabitants of a large metropolis suffer from mental disorders (10). Several meta-analysis have also shown that meditation can be used for treatment different psychological disorders with positive outcomes (11), (12). In this scenario, the use of adequate scientific methodology and instruments to observe the phenomena associated with meditation becomes important and allows health professionals to encourage meditation practice (13).

Although there may be some differences between meditation practices such as focused attention (FA) and open monitoring (OM) and their correlates *dharana* (concentration) and *dhyana* (meditation) in the ancient texts (14), such techniques share many similarities. Here, we will review, the effects of meditation on brain structure and function, raise some methodological questions and will not discuss semantic differences. For example, in cross-sectional studies, conclusions about the results of meditation might be mistaken for pre-existing individual differences. Moreover, if we take the effects of meditation into account, we should also consider state and trait (15), where state encompasses the alterations caused during some practice, while trait encompasses those that transform baseline patterns and remain even when the individual is not meditating. In the present scenario, researches are more focused on the psychobiological effects of meditation as a cognitive training than on the reports of the mystical states of trance described as *nirvana* or *samadhi,* which were precursors for the first meditation studies (16), (17).

The aim of this study was to review structural and functional magnetic resonance imaging studies about meditation.

3. EVIDENCE FROM STRUCTURAL MRI

Brain imaging studies show growing evidence that meditation can induce changes in the brain structure and thus it can be assumed that its practice leads to neuronal plasticity (18). For treating age related cognitive decline and accompanying thinning of the cortex, meditation rises as a method that is associated with increased cortical thickness and offers the possibility of protecting the brain against natural aging decline processes as well as some mental disorders (19). It seems that meditation can act as a mental training to specific regions that, similarly to learning of new skills like juggling (20), can lead to structural neuroplasticity. But what is really known about the causal effects of meditation on morphometric brain alteration? Several studies already showed evidence of meditation-training induced neuroplasticity in some specific brain regions.

One of the first studies analyzing the cortical thickness of meditators was published by Lazar *et al.* in 2005 (21)(Tables 1-2). Twenty long-term meditators who practiced insight meditation (adapted form of Vipassana) were recruited to participate in that study. A central element of the Vipassana meditation, in the context of insight meditation, is the attention to the sensory stimuli that come up during the process. Lazar and her colleagues found the right anterior insula and the right middle and superior frontal sulci to be significantly thicker in meditators than in controls. A correlation of cortical thickness and the change in respiration rate, which served as an objective indicator of the amount of meditation practice, pointed to the inferior occipito-temporal visual cortex as a significant region. Particularly, after being controlled for age which could have an effect especially on frontal regions of older meditators (22), this region remained significant. A significant correlation between respiration rate and the cortical thickness in the insula was also found after the authors controlled for age. Thus, they conclude that the thickness of the occipito-temporal visual cortex and the insula increases with the amount of meditation practice. In the Brodmann area (BA) 9/10 meditation seems to slow down cortical thinning, as 40- and 50- year old meditators compared to 20-30 year old meditators and controls showed the same average thickness. This could be linked to its function in integrating emotion and cognition. Due to its largest significant group difference, the study brings out the insula as a brain region that is significantly activated, probably in experienced practitioners as well as in meditation beginners, as it is responsible for the awareness of interoceptive stimuli such as breathing and other sensory stimuli. The insula showed to be active during the attention to bodily

Table 1. Main MRI studies

Meditation	MRI analysis	Main results(meditation x control)	Reference
insight meditation (vipassana)	cortical thickness	Greater cortical thickness in the right anterior insula and in the right middle and superior frontal sulci.	Lazar *et al*., 2005 (21)
Vipassana	voxel-based morphometry	Greater gray matter volumes in the left inferior temporal gyrus, the right anterior insula and the right hippocampus.	Hölzel *et al*., 2008 (24)
Dzogchen	voxel-basedmorphometry	Altered gray matter densities in the medulla oblongata, left superior frontal gyrus, the left inferior frontal gyrus, the left mid-ventrolateral prefrontal cortex, bilaterally the anterior lobe of the cerebellum and the left fusiform gyrus.	Vestergaard-Poulsen *et al*., 2009 (28)
Zen mediation	Cortical thickness	Thicker cortices in the dorsal anterior cingulate cortex and bilaterally in the secondary somatosensory cortex.	Grant *et al*., 2010 (31)
integrative body mind training	fractional anisotropy	Increased fractional anisotropy values in the left anterior corona radiata, body and genu of the corpus callosum, superior corona radiata and superior longitudinal fasciculus.	Tang *et al*., 2010 (33)
Shamatha, Vipassana, andZazen	Diffusion Tensor Imaging	Larger fractional anisotropy in fiber tracts such as the anterior thalamic radiation, cingulum-hippocampus, corticospinal tract, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, temporal component of superior longitudinal fasciculus, uncinate fasciculus and forceps minor.	Luders *et al*., 2011 (37)
Mindfulness-based stress reduction	voxel-based morphometry	Increase in gray matter concentration in a region of interest within the left hippocampus; increases of gray matter concentration. In whole brain analysis, increase in gray matter concentration in the posterior cingulate cortex, the left temporo-parietal junction and the cerebellum.	Hölzel *et al*., 2011 (40)
several disciplines	Diffusion Tensor Imagin	Increased fractional anisotropy in several regions of the corpus callosum.	Luders *et al*., 2012 (39)
Brain Wave Vibration	cortical thickness/Diffusion Tensor Imaging	Increased cortical thickness in the bilateral ventromedial prefrontal cortex, superior frontal cortex, temporal pole, middle and inferior temporal cortices, left fusiform cortex and medial prefrontal cortex on meditators. Meditators showed higher fractional values in the cuneus, precuneus and occipital regions and the ventromedial prefrontal cortex and lower fractional anisotropy values in the right medial prefrontal cortex, posterior cingulate cortex and right occipital regions	Kang *et al*., 2013 (43)
Sahaja Yoga Meditation	voxel-basedmorphometry	Larger gray matter volume overall and with regional enlargement in the right inferior temporal gyrus and bilaterally the anterior insula and left ventrolateral prefrontal cortex, the right ventromedial orbitofrontal cortex.	Hernández *et al*., 2016 (19)
Loving-kindness meditation	voxel-based morphometry	Greater gray matter volume in the right angular gyrus, right posterior parahippocampal gyrus, left inferior temporal gyrus and middle temporal gyrus	Leung *et al*., 2013 (52)
several disciplines	voxel-based morphometry	Larger left hippocampal volume.	Luders *et al*., 2013 (57)
several disciplines	cortical gyrification	Enlargement in the pre and post central gyrus, central sulcus, left inferior/middle temporal gyrus, angular gyrus, parieto-occipital fissure, fusiform gyrus, parietal operculum and cuneus and the right anterior dorsal insula.	Luders *et al*., 2012 (58)
soham meditation	voxel-based morphometry	Higher gray matter volume in the left ventral pallidum, left supplementary motor area and brainstem.	Kumar *et al*., 2014 (60)

sensations and visceral awareness and therefore fits well into the meditators' practice (23). In general, the team found regions to be thicker in the right hemisphere that corresponds to its role for sustaining attention. They suggest differences between beginners and advanced practitioners. Advanced practitioners focus their awareness on thoughts and emotions or external stimuli as sounds, whereas beginners start by concentrating their awareness on interoceptive stimuli. In this context they conclude that other meditation forms will affect slightly different brain structures and patterns. Lazar and her

Table 2. Main functional MRI studies

Meditation	**Condition**	**Main results**	**Reference**
Kundalini	during meditation	Increased activity in putamen, midbrain, pregenual, anterior cingulate cortex, and hippocampal/parahippocampal formation	Lazar *et al*., 2000 (66)
ACEM meditation	during meditation task	Meditavion vs Waiting interval: increased activity in the left superior temporal gyrus Meditation vs control task: increased activity in the left inferior frontal gyrus Meditation vs word sequence generation task: increased activity in the left superior temporal gyrus	Davanger *et al*., 2010 (68)
Tibetan Buddhist tradition	meditation vs resting state	Increased activity in the frontal parietal regions, insula, lateral occipital, thalamic nuclei, basal ganglia and cerebellum in expert meditators and novice meditators during meditation x resting. Novice meditators and most expert meditators (skill acquired) showed less effort during meditation while least expert meditators showed greater activation of attention-related brain regions.	Brefczynski-Lewis *et al*., 2007 (65)
focused attention-to-breath	meditation and passive viewing during cued aversive pictures	Decreased amygdala activity and increased prefrontal integration of the amygdala.	Doll *et al*., 2016 (69)
Soham meditation	meditation vs control task - classify geometric Figures between blue and yellow.	During meditation: increased activity in the left mPFC, left inferior frontal gyrus, supplementary motor area and left precuneus control task: increased activity in the left middle and superior middle temporal, left inferior parietal and left post-central gyrus.	Guleria *et al*., 2013 (70)
compassion meditation (CM)	CM or reappraisal during film clips (negative or neutral stimuli)	CM vs negative stimuli: increased activity in the left prefrontal cortex and frontal cortex, supplementary motor area, areas in parietal lobules, and temporal gyrus, anterior cingulate cortex, posterior cingulate cortex, thalamus, hypothalamus, ventral pallidum, globus pallidus, caudate, putamen, portions of the cerebellum and right amygdala. CM vs. reappraisal: meditation had increased activity in the ventromedial prefrontal cortex, medial orbitofrontal cortex, gyrus rectus, portions of anterior cingulate cortex, frontopolar cortex, supplementary motor area, mid-cingulate, precuneus, bilateral superior temporal gyrus and inferior frontal gyrus/operculum, right fusiform gyrus, bilateral amygdala, hypothalamus, caudate, globus pallidus, putamen, right hippocampus and portions of the thalamus. Reappraisal, increased activity in the middle temporal gyrus, posterior cingulate/precuneus and cerebellum, bilateral medial frontal gyrus and left inferior frontal gyrus, pre-supplementary motor area/medial superior frontal gyrus, left calcarine gyrus.	Engen and Singer 2015 (71)
Mindful Attention Training (MAT), Cognitively-Based Compassion Training (CBCT)	IAPS database	CBCT vs. MAT and control: negative correlation to negative images and depression scores in amygdala activity. MAT vs. control: decreased activity in the right amygdala for all images of the IAPS. Also decreased activity in right amygdala throughout the 8 weeks of intervention in response to all images and positive valence images of the IAPS.	Desbordes *et al*., 2012 (74)

colleagues argue that the specific thickening of the cortex is caused by meditation as those regions correspond to specific activities in which meditators engage in the course of their training. However, they emphasize that they expect structural changes in diverse regions, caused by other meditation techniques and mental exercises.

Hölzel *et al.* (24) extended the findings of Lazar *et al.* (21). They investigated if regions that show typical functional activation during meditation will also show an increased gray matter concentration (GMC). A voxel based morphometric (VBM) region of interest (ROI) analysis was applied, enabling analysis of gray matter concentration in cortical and subcortical structures. They tested 20 meditators trained in Goenka'sVipassana meditation which showed greater gray matter volumes in the left inferior temporal gyrus, the right anterior insula and the right hippocampus in comparison to the other 20 controls evaluated. Other hypothesized structures tested, did not reach significance. In addition, they tested whether the number of daily hours spent on meditation practice had an effect on the GMC. In doing so, they found a significant correlation only for the left inferior temporal gyrus region, whereas other regions showed only a trend (right anterior amygdala) or no significance (hippocampus). In a whole brain analysis, they tried to find out more regions that could also show a correlation with the amount of practice. This revealed the bilateral rectus gyrus and the medial orbitofrontal cortex as significant regions. As the orbitofrontal cortex is assumed to down regulate the amygdala, it could be involved in emotion processing (25), (26) similarly to the hippocampus. since the meditators also practiced Vipassana as in Lazar *et al.* (21), it is not surprising that the team discovered an increased gray matter volume in the right anterior insula. This effect could thus be the result of the similar meditation practice used in both studies. The structural changes and correlation with the amount of practice in the left inferior temporal gyrus first indicates a temporal region of the brain to be involved in meditation practice. In terms of meditation, this region is often linked to deep mystical and religious experiences (27). The cortical thickening of the hippocampus is linked to its strong anatomical connection to the amygdala and therefore its potential influence on emotional processes (25). The research team of Hölzel could not address the problem about the causal direction of structural brain changes in meditators, and neither could Lazar *et al.*. We assume that this "chicken-or-egg problem" could only be solved by long-term studies in the future. Furthermore, they notice the different method (VBM) used to Lazar *et al.* (21) and point out that their results are not directly comparable. In summary, Hölzel's group expanded the set of regions that are associated with structural changes caused by meditation.

Very impressive was the finding of Vestergaard-Poulsen *et al.* (28), who showed structural changes especially in the brain stem of long-term meditators who practiced the Dzogchen tradition of Tibetan Buddhism, a meditation form which is dominated by open awareness. Those researchers applied VBM to the whole brain and evaluated the gray matter density and volume. Their results showed altered gray matter densities especially in the medulla oblongata and several other regions as the left superior frontal gyrus, the left inferior frontal gyrus, the left mid-ventrolateral prefrontal cortex, bilaterally the anterior lobe of the cerebellum and a small part of the left fusiform gyrus in meditators compared to controls. As meditation practice often includes attention to one's own respiration, the medulla oblongata apparently shows structural changes due to its physiological involvement in the control of the respiratory flow (29). However, in comparison to the right hemispherical characteristic of Lazar's (21) findings, they found left forebrain regions such as the left superior frontal gyrus and the left mid-ventrolateral prefrontal cortex to be structurally changed in their group of meditators. Indeed, this could be because they used participants with different meditation styles and analyses methods (cortical thickness and VBM). Reasoning that a ceiling effect could hide a possible correlation between the accumulated hours of practice and differences in gray matter density, they assume that morphometric brain alterations can proceed fast, so that this correlation fails to appear in long-term practicing meditators.

Mindfulness-based stress reduction (MBSR) programs have become widespread, especially in the improvement of symptoms in stressed and chronic pain patients (2), (30). This positive impact on pain-processing was also tested for the practice of Zen mediation by Grant *et al.* (31). The study team investigated 17 Zen practicing meditators and 18 control subjects who underwent a thermal pain sensitivity testing. They supposed that the uncomfortable cross-legged posture during meditation would act as a regularly practiced nociceptive stimulation – and thus would lead to lowered pain sensitivity effects that could structurally be proven by anatomical changes in the brain. And indeed, Grant and his team first figured out that meditators showed significantly lower pain sensitivity than controls and demonstrated further that this was associated with thicker cortex in the anterior cingulate cortex in meditators compared to controls. ROI analyses revealed thicker cortices in pain processing areas such as the dorsal anterior cingulate cortex and bilaterally in secondary somatosensory cortex in meditators in comparison to controls. They demonstrated that the increase of meditation practice experience is associated with the increase in the thickness of the gray matter in the dorsal anterior cingulate cortex. This region is strongly considered to be involved in emotional processes and nociception and arbitrates pain based on affective aspects (32). The authors suppose that some kind of control instance is settled in this region, responsible for pain control. Higher cortical thickness would therefore be linked to corresponding higher pain control and probably lower pain sensitivity. Besides the dorsal anterior cingulate cortex as an emotion related brain region, they also found the secondary somatosensory cortex related region to be thicker in relation to reduced pain sensitivity. The correlation analysis between hours of meditation and cortical thickness brought up the lower leg areas in the bilateral primary somatosensory cortex and could be associated with pain in the knees and ankles of the meditators. However, this conclusion lacked in the missing correlation between pain sensitivity and primary somatosensory (31).

Until then several studies showed that meditation is linked to grey matter changes in diverse brain regions. Tang and his colleagues (33) however, tried to answer the question of whether the brains of meditators are thus also characterized by enhanced connectivity apparent by fiber tracts or rather higher fractional anisotropy (FA) levels between these regions. Based on their previous study (34)that assessed integrative body mind training (IBMT) practitioners, where they revealed improved executive and alerting attention after 11 hours of IBMT training over one month, Tang and his colleagues hypothesized in their following study that this training would also show effects on FA, especially in the anterior corona radiata which connects striatum and anterior cingulate cortex. The anterior cingulate cortex, as part of the conflict monitoring system, is integrated in emotion regulation processes (35), (36). To explore this, they had 45 participants undergo either the IBMT program or a parallel relaxation training program that served as a control condition. The IBMT training is characterized by mindfulness and mental imagery training. The training was conducted for 30 minutes during the week and for one month (11 hours of training in total). Several areas, , including the left anterior corona radiata, showed to be significantly increased after IBMT in comparison to relaxation training. Furthermore, increased FA values were found in the body and genu of the corpus callosum, superior corona radiata and superior longitudinal fasciculus after IBMT training. They did not find any gray matter differences in either group and thus speculate that gray and white matter differ in the time they need to undergo structural changes. The authors discuss whether FA value changes indicate myelination changes or restructuring in white matter tracts and consider the training a way to ease symptoms of several disorders with anterior cingulate cortex deficits. The increases in FA in the corpus callosum are interpreted as a possible increase in the interhemispheric connection of the ventral and the dorsal anterior cingulate.

Based on the findings of Tang *et al.* (33) and the assumption that meditation should, in addition to gray matter, affect white matter, Luders and his team (37) evaluated a multimodal imaging approach combining Diffusion Tensor Imaging (DTI) measurement with tract mapping methods. They measured 27 meditators experienced in several disciplines compared to 27 controls. As they found out, meditators seem to have larger FA in fiber tracts such as the anterior thalamic radiation, cingulum-hippocampus, corticospinal tract, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, temporal component of superior longitudinal fasciculus, uncinate fasciculus and forceps minor (frontal projection of corpus callosum). Grouped by hemisphere interaction, the analysis revealed cingulum – cingulate gyrus, cingulum-hippocampus and temporal component of superior longitudinal fasciculus and a trend for superior longitudinal fasciculus. Left and right hemisphere comparisons showed larger FA in right cingulum – cingulate gyrus and cingulum-hippocampus but not in the left hemisphere of meditators. Temporal component of superior longitudinal fasciculus and superior longitudinal fasciculus were found to have larger FA with stronger effects for the left hemisphere in meditators compared to controls. A correlation analysis revealed no significant results correlating the number of meditation years or frequency (minutes per week) and FA values in selected ROIs. The correlation of age with FA was significantly negative, however less pronounced in meditators than in controls in all ROIs selected, except the left and right cingulum-hippocampus and left cingulum – cingulate gyrus. The missing correlation between years of practice and FA value could presumably not be significant since the fibers are subject to age related decline. Furthermore, they argue that the difference in meditation styles of the participants evaluated can lead to the missing correlation. As the superior longitudinal fasciculus passes through the inferior temporal gyrus, it can be well connected to the results of previous structural studies that show thickening in the temporal lobe or larger GMV in the inferior temporal gyrus, especially in the left hemisphere, which was also confirmed by this study with stronger effects for the left hemisphere (21), (24). As the uncinate fasciculus links the amygdala and the hippocampal gyrus to the orbitofrontal cortex the authors conclude that the finding of enlarged FA in this region is connected to larger GMV in the regions found in previous studies (28), (38). Fiber tracts connecting motor areas and somatosensory areas require further research, as remarked by the research group. Larger tracts of the corticospinal tract could be linked to Vestergaard-Poulsen's (28) finding of structural changes in the medulla oblongata, since the corticospinal tract also passes through it. The findings of the study team bring up the question whether disease symptoms that underlie demyelination processes, as in multiple sclerosis, can be relieved or reduced by meditation practice (39).

Hölzel *et al.* (40) investigated gray matter concentration changes in the brain of sixteen non-meditators after performing an 8- week MBSR program. Using voxel-based morphometry they revealed increases in gray matter concentration in a region of interest within the left hippocampus of the MBSR group, but not between the groups, as the control group did not show any structural changes in selected regions. The changes showed no correlation with the amount of practice time. In a whole brain analysis, they could further demonstrate increases of gray matter concentration in the posterior cingulate cortex, the left temporo-parietal junction and the cerebellum, of which one cluster was extended to the brainstem positioned in the locus coeruleus and nucleus raphe pontis in the MBSR group. No clusters were found for the whole brain analysis after a correlation analysis between GMC and amount of practice in days. The cerebellum area did not conform with the cerebellum area found by Vestergaard-Poulsen *et al.* (28), but rather to a region important for norepinephrine (locus coeruleus) and serotonin (nucleus raphe pontis) production. Deficits in neurotransmitter production of these regions were associated with dysfunctions related to behavior, cognition and mood (41). The posterior cingulate cortex is commonly mentioned in research about the default mode network, as it is one of the core regions and contributes to self-referential processes and past and future thinking (42). Even though the MBSR program includes meditation, it proposes several other strategies that increase relaxation and reduce stress and can, hence, influence the results based on this treatment (30). Hölzel and her team realized that they need to control for unspecific effects or evaluate a program that is based only on meditation to analyze effects caused only by meditation and mindfulness. Otherwise results could be more dependent on diverging participant characteristics.

Based on the finding of their previously conducted DTI study, where they detected larger FA values in the forceps minor and showed differed fiber structures, Luders *et al.* (39) conducted a further study focusing on more sections of the corpus callosum this time evaluating changes in thickness influenced by meditation. Changes in fiber structures of the corpus callosum were also confirmed by Tang *et al.* (33). To evaluate this, they measured 30 long-term meditators practicing various meditation styles and compared them with 30 controls. This time they extended their analysis not only by using DTI but also thickness and area size measurements. Area analysis for five callosal segments was conducted and revealed increased thickness at the border between anterior midbody and anterior third of the corpora callosa which, however, did not survive FDR correction. The DTI analysis showed increased FA in several regions of the corpus callosum of meditators compared to controls (rostral body of the anterior third, the anterior midbody and even slightly extending into the posterior midbody, while sparing isthmus and splenium, as well as the genu and rostrum of the callosal anterior third). Contrary to the F Major, they found significantly larger FA values in the forceps minor of meditators compared to controls and assumed that meditation influences posterior parts of the corpus callosum. Discussing the findings of Tang *et al.* that reported meditation-induced increases of FA in the “genu”, which is also a part of the anterior third and was not found to be active here, they suppose that the chosen meditation-naïve subjects of the longitudinal study of Tang and colleagues might have more impact on the structure of the corpus callosum than long-term practitioners who had already acquired their skill to meditate. They further suppose that different meditation styles could also differently affect corpus callosum regions. Luders and his colleagues suppose that their findings, reflecting a change at a microscopic level (fiber number, density, or myelination) that was seen in increased FA within anterior corpus callosum of meditators, could lead to alterations on a macroscopic level (callosal thickness) as well. The evidence for that was demonstrated in their study by revealing thicker corpora callosa in meditators. However, this did not survive FDR correction. Nonetheless it could also support the assumption that there are more fibers in the corpus callosum caused by meditation. In summary, Luders *et al.* found further indication for the assumption that meditation could lead to an increased inter-hemispheric connectivity and a better integration of information. Their study showed that it is important to integrate different imaging approaches (structural MRI and DTI) to find more robust results.

Kang *et al.* (43) employed a whole brain cortical thickness analysis together with a DTI analysis on Brain Wave Vibration (BWV) meditation practitioners, which combines rhythmic movements with the focus on arising body events in their practice. Thus, they extended the changes of structural analysis from gray to white matter by adding the analysis of the connectivity between regions provided by the investigation of the fractional anisotropy degree of white matter. This was previously carried out by Tang *et al.* (33) and Luders *et al.* (37). Based on their functional study dealing with the default mode network (DMN), they focused their hypothesis on the medial prefrontal cortex, orbitofrontal cortex and parietal areas. The large sample size, with 46 meditators and 46 controls used for this study, is remarkable. The authors found a significantly increased cortical thickness in the bilateral ventromedial prefrontal cortex, superior frontal cortex, temporal pole, middle and inferior temporal cortices, left fusiform cortex and medial prefrontal cortex on meditators, compared to controls. This result partially confirmed their previous hypothesis. Interestingly, they also analyzed the thinning of the cortex, and found that meditators showed significantly thinner cortices in the bilateral postcentral and inferior parietal cortices, right middle occipital cortex, left posterior cingulate cortex and left cuneus. This anterior-posterior difference with thicker cortex in anterior and thinner cortex in posterior parts of the brain was explained with the finding of Kanai and Rees (44) and Takeuchi *et al.* (45), who showed decreased grey matter volume associated with increased cognitive functions. Thus, they justify that meditation practice is related to cortical thinning due to the enlargement of specific cognitive skills as attention and emotion regulation strengthen during meditation. Furthermore, as shown by Boyke *et al.*, (46), the increase of grey matter volume is followed by a decrease, after intensive and long-lasting training. This led Kang *et al.* (43) to question the conclusion that higher meditation experience is automatically associated with thickening of the cortex, as considered in many other previous studies. These thinner cortexes are especially located in posterior brain regions, particularly occipital and parietal regions that show regions of the DMN and thus are connected to self-referential processing. The medial prefrontal cortex participates in motor functions and is linked to the movements of the BWV (47). In contrast, the DTI data showed higher FA values in the cuneus, precuneus and occipital regions and the ventromedial prefrontal cortex and lower FA values in the right medial prefrontal cortex, posterior cingulate cortex and right occipital regions of meditators, as compared to control participants. Therefore, higher FA values can be linked to higher cortical thickness. Increasing fibers could in turn lead to reduced FA values that link regions with thinner cortex. As meditators had mainly increased FA values in hub regions, the authors speculate that meditation increases the amount of cross fibers. A positive, but weak correlation between the mean cortical thickness and the duration of meditation practice was revealed in the left superior frontal cortex. Based on a ROI analysis, they found that mean FA values differed significantly in the left ventromedial prefrontal cortex, left lateral prefrontal cortex, left temporal cortex, left posterior cingulate cortex and right middle occipital cortex of meditators compared to controls. As this is another study with cross-sectional design, it is still not clear whether the effects observed can be completely explained only by meditation training.

Furthermore, a recent study conducted by Hernández *et al.* (19) showed that long-term practice of Sahaja Yoga Meditation (SYM) which is mainly based on loving kindness and mindfulness meditation techniques, is associated with larger gray matter volume overall and with regional enlargement, especially in right hemispheric cortical regions as the right inferior temporal gyrus and bilaterally the anterior insula and left ventrolateral prefrontal cortex, the right ventromedial orbitofrontal cortex and a tendency in the right angular gyrus. Consequently, those authors confirm the finding of structural changes happening in regions responsible for attention control and interoception. By finding changes in the ventrolateral prefrontal cortex and the insula, they confirmed their previously conducted functional MRI study that showed activation due to SYM meditation in these regions, which are assumed to be linked to emotional intelligence (48), (49). The ventromedial orbitofrontal cortex is interpreted in relation to top down emotional regulation due to its connection with the amygdala and hence could be interpreted as stronger affective control relating to negative emotions (50). The angular gyrus is linked to facilitated empathy in social life, since it also contains the temporo-parietal junction that relates to these facets (51). The enhanced structural changes of the right hemisphere are referred to stronger connection to the limbic system and the depth of thoughtless awareness. Further they found significantly larger gray matter volumes across the whole brain in SYM practitioners compared to controls, which was not until then found in other meditation techniques (19).

Another form of meditation, the Loving-kindness meditation (LKM), is based on the cultivation of positive emotions such as love, compassion and empathy toward self and others, which distinguishes this technique from other meditation forms and consequently can further social cognition. Furthermore, based on the assumption that meditation forms that work with emotions could have an effect on the emotion-processing system, Leung *et al.* (52) measured 10 long-term LKM practitioners and compared them to 15 control subjects without meditation experience who underwent a total of seven hours of training in basic meditation self-practice. Using an automated voxel-based morphometry for the whole brain they found out that LKM practitioners showed more gray matter volume in the right angular gyrus, right posterior parahippocampal gyrus, left inferior temporal gyrus and middle temporal gyrus. As the structural changes of the inferior temporal gyrus were also found in other studies and the LKM practice starts with general attention and mindfulness practice, this region seems to be affected through general mindfulness and attention meditation. The right angular gyrus gray matter volume was found to be negatively correlated with the hours of meditation practice. The authors explained this by know-how adoption that does not require any more effort in training (53). The focus of the study is on the right angular gyrus, since it includes various different regions such as the temporo-parietal junction which plays a role in social cognition, empathy and metallization, as already discussed in the study of Hernandez *et al.* (19). They strengthen their argumentation citing Lutz *et al.* (54), who found a greater functional activity in the right angular gyrus of the temporo-parietal junction that they linked to interaction with others at emotional and rational levels. The finding in the right posterior parahippocampal gyrus was linked to its function in the paralimbic system and is connected to the amygdala and higher cognitive centers (55). The middle temporal gyrus represents again a region in the temporal lobe as already demonstrated by Holzel *et al.* (24) and Luders *et al.* (56) and thus seems to be subject to changes in various forms of meditation. Due to the small sample size and different practice stages of meditators, this study also presents limitations.

With a sample of 30 long-term meditators and 30 controls, Luders and his team (57) contributed once again to the clarification of morphological changes due to meditation by conducting a study about hippocampal anatomical changes. Using a combination of traditional ROI-based approach with measurement of the hippocampal volume they found, through a global measurement based on the number of voxels in the hippocampus, that the left hippocampal volume was significantly larger in meditators than in controls. With up to 15% larger radial distances, especially in left hippocampal subregions in meditators compared to controls, revealed by local analysis to evaluate the hippocampal surface, they demonstrated once again that the hippocampus is subject to structural changes probably caused by meditation. They also correctly mentioned the problem of other ignored variables in the lifestyle of the participants that can influence the result in the hippocampus and impact on the group difference observed.

Using cortical measurements different from those in other studies conducted to characterize the structural changes in meditators once again, Luders and his colleagues (58) examined the cortical folding degree, a process called gyrification, in a large-size sample of meditators. Analyzing the degree of gyrification in 50 meditators with various types and years of meditation experience and comparing them to 50 controls, they found an enlargement in several regions in meditators as the pre and post central gyrus, central sulcus, left inferior/middle temporal gyrus, angular gyrus, parieto-occipital fissure, fusiform gyrus, parietal operculum and cuneus and the right anterior dorsal insula. Furthermore, they found positive correlations between gyrification and years of meditation experience in left and right lateral surfaces and left medial surface, with a pronounced expression in the right posterior temporal lobe and the right anterior dorsal insula. Decreased gyrification together with increased number of practice years (negative correlation) indicated regions in the right medial surface. The larger gyrification in the left precentral gyrus was put into the context of regions surrounding motor cortices which have a relationship with the interoceptive function of the insula. Luders and his team (39) interpreted the anterior dorsal insula in its role in interoceptive function (23). Altered cuneus and right fusiform gyrus were interpreted in association with the visual information processing (59). In their interpretation, they focused especially on the course of the formation of the shape of gyri and sulci that changes over the years, speculating that sulci developed earlier are less susceptible the structural changes caused by environmental factors. The problem of the measurement of the gyrification in this approach, as mentioned by the team, is that it does not allow the distinction between sulci and gyri and, for age related changes in clinical studies, this method should be further developed in the areas of regional specificity and spatial resolution (58).

Evaluating structural changes in meditators practicing “SOHAM” meditation, Kumar *et al.* (60) used voxel-based morphometry to analyze 14 long-term meditators and 14 controls. They detected changes especially in breathing related regions since SOHAM meditation concentrates on respiration while repeating the word "SO-HAM" synchronized with the breathing rhythm. Indeed, they found higher gray matter volume in the left ventral pallidum, left supplementary motor area and brainstem in meditators compared to controls. These results seem reasonable and are in line with other studies, since the brain stem entails regions responsible for cardio-respiratory function and regulation. Increased gray matter in the left ventral pallidum was linked to the role of reward and emotion regulation and interpreted as a strengthen in meditators through its increase in gray matter concentration (61). Difficulties in the interpretation of supplementary motor area in meditators were linked to a possible role in attention and awareness due to its anatomic localization. By controlling the basic rhythm of respiration and mediating behavioral respiratory control its increase in gray matter in SOHAM meditators seem to be plausible.

Due to its different meditation technique it can however hardly be compared with other meditation studies.

All studies presented differed in analysis methods, sample sizes and meditation styles, bringing highly inconsistent results. In the meta-analysis conducted by Fox *et al.* (62) the authors tried to sum up the conclusions that can be drawn out of past morphometric studies related to meditation regarding their practical (clinical) relevance expressed by effect size. Conclusively, they found changes in nine consistently reported brain regions in meditators compared to controls. These contain the following gray matter regions: rostrolateral prefrontal cortex, anterior/mid cingulate cortex, insular cortex, somatomotor cortices, inferior temporal gyrus, hippocampus and the following white matter regions: corpus callosum and superior longitudinal fasciculus. Their analysis revealed that long-term meditators received more attention in past studies than meditation novices. The finding that mean effect sizes for gray and white matter are different, led the authors conclude that meditation influences more changes in gray rather than in white matter. This assumption, however, was refuted due to the large sample size available in the analysis. Surprisingly, Fox *et al.* (62) showed that experience in practice and effect sizes are not positively correlated as expected. The negative correlation between the two factors supports the assumption that age-related factors play an important role in the finding of significant results. It could also be explained by unchangeable morphology caused by the perfectionism of long-term practitioners. Mentioning the fact that increases in white or gray matter structures are mostly interpreted as cognitive increases linked to neurodegenerative diseases and age-related decline, they also elucidated that decreases in the structures can be associated with synaptic pruning. This process is characterized by the reduction of irrelevant portions between the associations of neurons and the degradation of irrelevant neurons, enabling an improved network cooperation and enhanced efficiency that plays an important role in learning processes (63). They call attention to several points that future research should concentrate on to improve consistency in their findings. Among them they mention the inclusion of more demographic variation in participants, comparison of various meditation styles and their connected changes, more longitudinal and follow-up studies and emphasize the importance of calculating an effect size to draw conclusions out of the results (62).

4. EVIDENCE FROM FUNCTIONAL MRI

As the techniques for brain function analysis and activity develop, so does the understanding of the neurobiological correlates of meditation. In the 1970s there was a predominance of EEG use in meditation studies. While EEG measures electrical activity in the cortical surface, with high temporal resolution, fMRI accesses deeper layers of the brain through the Blood Oxygenation Level-Dependent (BOLD) contrast. BOLD contrast relies on different metabolic and hemodynamic factors as the result of change in deoxyhemoglobin. Deoxyhemoglobin has a paramagnetic property, which distorts the near magnetic field, captured by MR and transformed into an image. Through fMRI exams, it is possible to measure changes that occur during meditation (meditation state), usually with the volunteer meditating inside the MRI equipment, as well as lasting changes (meditation trait) present in long-term meditators in which brain function of meditators during rest or other tasks non-related to meditation are analyzed with fMRI. In this regard, Cahn and Polish (15) suggest neurobiological differences in both the state and trait of meditators but, due to methodological issues, there are difficulties in assessing both meditation state and trait effects. Moreover, Nash and Newberg (1) categorized diverse meditation methods and found different frameworks which may induce different outcomes. In a meta-analysis, Fox *et al.* (64) analyzed fMRI meditation studies and found brain activation in four common meditation techniques (focused attention, mantra recitation, open monitoring, and compassion/loving-kindness). In this systematic review with meta-analysis the volunteers meditation average experience time was from a few hours to more than 45 years of meditation practice. Brain regions reportedly activated include insula, pre/supplementary motor cortices, dorsal anterior cingulate cortex, and frontopolar cortex. According to these authors, although some similarities were found, divergence is more common. Therefore, it is difficult to find a common denominator among the various meditation techniques. Also, as seen before, different levels of expertise cause different alterations in brain areas (65).

One of the pioneering fMRI studies was Lazar *et al.* in 2000 (66)(Tables 1-2). They performed two analyses in five Kundalini practitioners. The volunteers were told to meditate (mantra) during the exam and were compared with a control epoch. Authors observed increasing activity during meditation in putamen, midbrain, pregenual, anterior cingulate cortex and hippocampal/parahippocampal formation. When comparing steady-state meditation (the last 2 min of meditation periods) with meditation induction (the first 2 min of meditation periods), the authors describe activation in prefrontal, parietal and temporal cortices, precentral and postcentral gyri, and hippocampal/parahippocampal formation. Although the sample was small and there was no control group, Lazar and colleagues opened new reads for the study of brain changes promoted by meditation.

As seen in Kabat-Zinn (2), Bishop *et al.(3)*, Cardoso *et al.* (5), attention is an important task required during meditation. Furthermore, prefrontal lobe areas are associated with attention and other executive functions (67). Thereby, the activation of some areas in the prefrontal lobe of people during meditation is expected. It was what Davanger and colleagues (68) found in meditators. Authors compared Acem meditation (a mantra-based meditation) in advanced male practitioners with meditation-like concentrative tasks and relaxation as a control task. In order to discriminate neuronal activation of relaxed focus of attention from those activated due to language (meditation sound), meditators performed three control tasks: pseudo word repetition, word sequence generation and relaxation. Results pointed to significant activation during meditation task in the left superior temporal gyrus, left precentral gyrus when compared to waiting intervals. However, when compared to waiting intervals, the control task exhibited bilateral temporal lobe activation in the auditory cortex (verbal activity), bilateral cluster extending in the medial frontal and inferior frontal gyri (relaxation task), bilateral frontal lobe/anterior cingulum and bilateral parietal lobe (word sequence generation). To differentiate areas activated by meditation from those areas related to control tasks, continuous meditation was contrasted with the three control tasks. Davanger and colleagues detected an activated area during meditation in the left inferior frontal gyrus when compared to the three controls tasks, and in the left superior temporal gyrus when meditation was compared to the word sequence generation task. Interestingly, the authors showed that meditation has specific patterns of brain activation that distinguish it from concentrative or relaxation tasks. Regarding focused attention network, Doll *et al.* (69) demonstrated activation in the superior and middle frontal gyrus of meditators in a focused attention-to-breathing task during an emotional stimulation. Additionally, Brefczynski-Lewis *et al* (65) showed activation in attention-related regions comparing meditation versus rest condition in a functional MRI. The activated regions included frontal parietal regions, insula, lateral occipital, thalamic nuclei, basal ganglia and cerebellar regions. In this study, Brefczynski-Lewis and team, compared expert meditators (10,000-54,000 hours of practice) to novice meditators (one week of practice). Both groups had activation of attention-related brain regions (as seen above). However, when expert meditators were divided into most hours of practice (44,000 mean hours) and least hours of practice (19,000 mean hours), the result resembled an inverted U-shape, showing less effort in novice (learning the skill), greater levels of effort in meditators with average of 19,000 h of practice and less effort in expert meditators with 44,000 average hours of practice (skill acquired).

In a non-controlled study, Guleria *et al.* (70) compared meditation versus a control task during fMRI. Meditation task yielded activation in the left medial prefrontal cortex, left inferior frontal gyrus, supplementary motor area and left precuneus. On the other hand, control task lead to activation in the left middle and superior middle temporal, left inferior parietal, and left post-central gyrus. Similarly, Engen and Singer (71) observed more positive affect and emotion regulation due to Compassion meditation training. In their study, meditators were scanned during short film clips with negative and neutral stimuli. Participants were asked to perform compassion meditation (CM) or reappraisal (condition that resembles compassion - for control task). Regarding CM versus negative stimuli, activated areas were observed in portions of left prefrontal cortex and frontal cortex, supplementary motor area, areas in parietal lobules, and temporal gyrus, portions of the anterior cingulate cortex, posterior cingulate cortex, some portions of the thalamus, hypothalamus, ventral pallidum, globus pallidus, caudate, putamen, portions of the cerebellum and right amygdala. In the contrast between CM and reappraisal, CM exhibited higher activation in the ventromedial prefrontal cortex, medial orbitofrontal cortex, gyrus rectus, portions of anterior cingulate cortex, frontopolar cortex, supplementary motor area, mid-cingulate, precuneus, bilateral superior temporal gyrus and inferior frontal gyrus/operculum, right fusiform gyrus, bilateral amygdala, hypothalamus, caudate, globus pallidus, putamen, right hippocampus and portions of the thalamus. Reappraisal, for its part, showed higher activation in portions of the middle temporal gyrus, posterior cingulate/precuneus and cerebellum, bilateral middle frontal gyrus and left inferior frontal gyrus, pre- supplementary motor area /medial superior frontal gyrus, left calcarine gyrus. Because several areas in the left hemisphere and prefrontal cortex exhibited higher activation in these studies, meditation seems to develop positive affect, positive emotions and happiness, as those feelings are associated with the left hemisphere and prefrontal cortex (72), (73).

Desbordes *et al.* (74) investigated amygdala response to emotional stimuli of meditators (in which images from the IAPS database were presented to the subjects) compared to a control group. Subjects were randomized into three groups: Mindful Attention Training (MAT), Cognitively-Based Compassion Training (CBCT) and active control intervention. The CBCT group showed negative correlation in amygdala activation to negative images and depression scores. The MAT group showed decreased BOLD signal change in the right amygdala when compared to control for all images of the IAPS. This group also exhibited significant decrease in BOLD signal in the right amygdala throughout the eight weeks of intervention in response to all images and positive valence images of the IAPS. Authors believe that this effect of meditation training on amygdala activation (emotion regulation) is due to improvement in attentional skills, an essential component of meditation. The amygdala is known to play an important role in emotions, threat and stress. Hözel *et al.* (40) found a positive correlation between stress and gray matter density of the amygdala following MBSR program. In their study, participants (all of them reporting high levels of stress) underwent eight weeks of MBSR. At the end of the 8-week stress reduction training, there were decreases in both perceived stress and gray matter density in the right amygdala. Therefore, meditation plays an important role in emotion and stress management. King *et al.* (75), reported altered default-mode network (DMN) in 16 weeks of Mindfulness-based Exposed Therapy (MBET) for combat veterans with posttraumatic stress disorder (PTSD). Authors compared two groups: MBET and active control group therapy and observed increased PCC connectivity with bilateral dorsolateral prefrontal cortex and with the dorsal anterior cingulate cortex, increased connectivity between the left amygdala and left hippocampus and dorsal anterior cingulate cortex following MBET. Regarding the active control group, increased post-posterior cingulate cortex connectivity with bilateral precuneus and left cuneus were shown. In practice, the use of meditation can be interesting in the anxiety disorders context.

Taylor *et al.* (76) investigated resting state of experienced meditators compared to a novice group. Participants were asked to observe a cross placed centrally on a screen during an fMRI. Results pointed to increased activity for beginners, between the dorso-medial prefrontal cortex and left inferior parietal lobe, right inferolateral temporal cortex and left parahippocampal gyrus. Also, beginners showed stronger correlations between left inferior parietal lobe and precuneus/posterior cingulate cortex, right parahippocampal gyrus, left inferolateral temporal cortex and left parahippocampal gyrus; precuneus/posterior cingulate cortex and left inferior parietal lobe, dorsomedial prefrontal cortex and left inferior parietal lobe, dorsomedial prefrontal cortex and ventromedial prefrontal cortex, ventromedial prefrontal cortex and right inferolateral temporal cortex. All these regions are associated with DMN. Significant correlations were shown for experienced meditators between the ventro-medial prefrontal cortex and dorso-medial prefrontal cortex, right inferolateral temporal cortex and left parahippocampal gyrus, as well as between the right inferior parietal lobe and precuneus/posterior cingulate cortex, dorsomedial prefrontal cortex and left inferior parietal lobe; right inferior parietal lobe, precuneus/posterior cingulate cortex, dorsomedial prefrontal cortex and precuneus/posterior cingulate cortex. Finally, hours of meditation correlated negatively with activation in dorsomedial prefrontal cortex – ventromedial prefrontal cortex. Because of the attention training of experienced practitioners, meditation seems to be associated with weaker activity in DMN, suggesting increased present moment awareness, since DMN is involved in cognitive elaboration of mental events such as autobiographical memory and thinking about the future. Also, sustained attention may be related to brain efficiency in meditators. Kozasa *et al.* (77) showed greater activity in the right medial frontal gyrus, middle temporal gyrus, precentral and postcentral gyri and the lentiform nucleus in non-meditators compared to meditators in an attentional and impulse control task (Stroop Word-Color Task) during fMRI. In all these cases differences in brain activity was demonstrated even outside meditation practice.

According to the definition of meditation (see the Introduction section), the "present moment" is an essential characteristic of meditation. When individuals are involved in cognitive elaboration of mental events – therefore not in the present moment – the DMN is more active. The default mode network is a group of brain regions which has a self-referential nature including the medial prefrontal cortex, the precuneus/posterior cingulate cortex, the inferior parietal lobule, the lateral temporal cortex, and the hippocampal formation. It can be considered as the baseline state of the human brain in internal modes of cognition. DMN is active when individuals are engaged in internally focused tasks such as autobiographical memory retrieval, thinking about the future, and taking perspectives of others. It can be divided into subsystems: the medial temporal lobe subsystem provides information from memories and associations that allows mental simulation while the medial prefrontal subsystem enables the construction of self-relevant mental simulations. These two subsystems converge on the posterior cingulate cortex. The default network may contribute to the use of past experiences to plan for the future and maximize the experience of not being engaged by the external world (78), (79).

DMN activity is reduced in goal-directed tasks in healthy individuals. It is an interesting candidate as a neurobiological representation of mind-wandering. Mind-wandering is considered one of the core elements of a sense of self. It is spontaneous, related to internal mental process which one can be unaware of and is difficult to control or replicate (80). It may indicate the existence of an organized, baseline default mode of brain function, suspended during non-self-referential activities (78).

According to some researchers, activity in DMN may reflect mind-wandering; activity in this network may reflect enhanced vigilance in relation to external environment or a combination of both (83). Reduced BOLD response of the DMN regions is observed during cognitive tasks (81), (82), (83). Meditation is a mental training which results in emotional regulation and attention, body awareness, and change in self-perspective (40), (84).

The subtraction of meditation from a control task condition showed decreased activity in DMN regions probably due to reduced mind-wandering, in an activation likelihood estimation (ALE) meta-analysis of meditation studies. Meditation-related negative signal changes were found in the fusiform, angular, and middle temporal gyri (right hemisphere) and in medial structures of the precuneus and the superior medial gyrus. Angular gyrus, precuneus and middle temporal gyrus belongs to the DMN. Precuneus is associated with self-referential mode and reduction in its activation during meditation is expected because this practice decreases this mode (85).

An fMRI study used a meditative condition intercalated with a lexical decision task, while comparing regular Zen practitioners and matched control subjects. Zen meditation is related to awareness with regulation of attention, bodily posture and reduced conceptual content. In that study, Zen meditators displayed a reduced duration of neural response associated with conceptual processing in DMN regions, suggesting meditation may improve the ability to regulate spontaneous mental processing (86).

Regarding focused attention meditation and DMN regions, internal and external focus of attention were compared, as well as the different phases of a meditation: mindful attention, mind-wandering and refocusing. Participants were trained for few days in two different meditation focuses: external (focused on a sound) and internal (focused on breath). After that, they performed meditation during fMRI scanning. At pseudorandom intervals, participants were asked if they had been engaged exclusively on the task or if they had been distracted. During mindful attention, DMN brain regions showed significantly less neural activation compared to mind-wandering. DMN exhibited reduced activity during meditation task. Posterior cingulate cortex showed stronger deactivation during internal attention compared to external attention (87). Similarly, in a cross-sectional study, assessing brain network during meditation, Hasenkamp and Barsalou (88) demonstrated activity in the executive network regions in meditators. Focused meditation is an activity in which attentional networks are involved. However, during meditation, moments of distraction are common. In this fMRI study, volunteers were examined during a resting state and during meditation. They were instructed to press a button every time they perceived themselves distracted. Results revealed activity in the dorsolateral prefrontal cortex during focused attention. In high practice meditators, there was also stronger activation in the right insula, left dorsolateral prefrontal cortex and the mid-cingulate gyrus as well as reduced functional connectivity between the right dorsolateral prefrontal cortex and cuneus and middle occipital gyrus. When participants were mind-wandering, activity was detected in areas related to DMN (ventromedial prefrontal cortex, bilateral posterior cingulate cortex). In this way, meditation is related to connectivity within attentional network (present moment awareness) (88).

During resting-state, long-term mindfulness meditators (MM) and control participants were scanned. MM were also examined during meditation practice. Analyses on functional connectivity within and between DMN and visual network resulted in an increase in functional connectivity between the two networks in MM compared to controls; functional connectivity within both networks were higher in the control group compared to the MM group; functional connectivity between DMN and visual network was reduced during meditation compared to resting-state and a negative correlation was found between DMN functional connectivity and meditation expertise (89). In another study, the MM group exhibited greater visual cortex responsivity and weaker negative responses in DMN areas during a visual recognition memory task. Regarding behavioral performance, MM were faster than controls. Long term meditators expressed opposite changes in the visual and DMN during rest and task. Therefore, unlike mind-wandering, meditation is a skill associated with "present moment" which recruits attentional related areas.

Few studies evaluate the DMN during an attention task. In a study comparing regular meditators and non-meditators in the Stroop Word-Color Task (SWCT), participants were instructed to name the color of single words during an MRI scan. The activity in the precuneus/posterior cingulate cortex contained information to predict the activity in the right lateral parietal cortex and the accuracy in this prediction was higher in regular meditators than in the other group. This result may be related to a stronger link between these regions and meditators. As non-meditators have more distraction during attention task, functional differences in DMN connectivity may be present during the attention task when non-meditators are compared to meditators (90).

5. CONCLUSION

The use of different structural analyses methods such as cortical thickness, voxel based morphometry, gray matter volume and fractional anisotropy in the studies hinders the comparison among them but, at the same time, expands the possibility to analyze structural brain morphometry. It is essential that future studies pay attention to the various approaches if they want their results to be comparable. The implementation of different study designs that differ in the sample size, in the experience of the subjects considered and meditation methods, makes it difficult to draw a stringent conclusion. Other variables correlated to the structural changes make it even more difficult. Therefore it is important to run replication studies to further strengthen the results detected. Functional MRI studies revealed the involvement of brain regions related to attention, inhibition, emotional experience, as well as the DMN. Nevertheless, there is undisputably strong evidence that the general regular practice of mental exercises indeed leads to changes in large scale brain networks rather than only in specific regions. However, despite similar techniques, researchers cannot control what each participant is going through during its practice, since personal experience is hard to be measured. Cross-sectional studies cannot draw conclusions about causal inferences. Therefore, longitudinal studies that can evaluate the structural and functional changes over a longer period should also be expanded. This could be done, for example, by following participants several times during months or years of meditation practice, and thus confirm a causal inference with more accuracy and reliability. This could help to evaluate which functional and structural correlates exist prior to meditation practice, and whether neurophysiological changes are directly associated with it. Finally, behavioral and well-being consequences for the participants brought about by meditation practice should be better evaluated for researchers to draw a conclusion on the effects of brain changes. It is also important to keep in mind that due to the heterogeneity of the studies it is difficult to reach a general conclusion, and that the various types of meditation may cause different structural changes. There are also uncontrolled studies, small groups, and other methodological failures which weaken the potential of the technological resources available through imaging exams to detect actual meditation effects on the brain.

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Send correspondence to: Rui Ferreira Afonso, Hospital Israelita Albert Einstein, Av. Albert Einstein, 627, 2º subsolo, Bloco A, Morumbi, Sao Paulo - SP, CEP 05652-900, Brazil, Tel 55-11-21510800, Fax: 55-11-2151-0273 E-mail: ruiafonsobr@yahoo.com.br