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Issue: *Advances in Meditation Research: Neuroscience and Clinical Applications***Meditation and neurodegenerative diseases**

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Neurodegenerative diseases pose a significant problem for the healthcare system, doctors, and patients. With an aging population, more and more individuals are developing neurodegenerative diseases and there are few treatment options at the present time. Meditation techniques present an interesting potential adjuvant treatment for patients with neurodegenerative diseases and have the advantage of being inexpensive, and easy to teach and perform. There is increasing research evidence to support the application of meditation techniques to help improve cognition and memory in patients with neurodegenerative diseases. This review discusses the current data on meditation, memory, and attention, and the potential applications of meditation techniques in patients with neurodegenerative diseases.

Keywords: meditation; neurodegenerative disease; cognition; memory; mindfulness

Introduction

Meditation has been an integral part of many spiritual and healing traditions for over 5000 years. It has become increasingly popular in many countries and there has been a continual growth of research into the potential benefits of meditation for reducing stress and anxiety, and improving physical health and well-being. More recently researchers have started to examine the potential cognitive benefits of various meditation practices and the impact of meditation on the brain. The current research suggests that even short periods of meditation can change brain structure and function and lead to improvements in cognitive function. Preliminary evidence indicates that meditation training can specifically enhance memory as well as protect memory capacity from deteriorating during periods of high stress. All of these findings may be particularly relevant in the context of neurodegenerative diseases for which meditation might provide a useful adjunctive therapy. In this review, we discuss recent findings on the relationship between meditation, and attention and memory, and relate these findings to neurodegenerative diseases.

Brief overview of neurodegenerative diseases

There are several broad categories of neurodegenerative diseases, each having unique pathophysiological findings and damage to specific brain structures or systems. Different neurodegenerative disorders tend to have specific neuroimaging findings that contribute to their diagnosis. The most common neurodegenerative disease is Alzheimer's disease (AD), for which the diagnostic criteria were defined by the Working Group of the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) in 1984.¹ The clinical criteria for the diagnosis of AD require clinical evidence of progressive, chronic cognitive deficits in middle-aged and elderly patients with no identifiable underlying cause. The pathophysiological findings include amyloid plaques and neurofibrillary tangles of hyperphosphorylated tau proteins in paired helices. Unfortunately, while it is possible to make an accurate diagnosis of dementia in most patients with severe disease, it is very difficult to differentiate between AD and

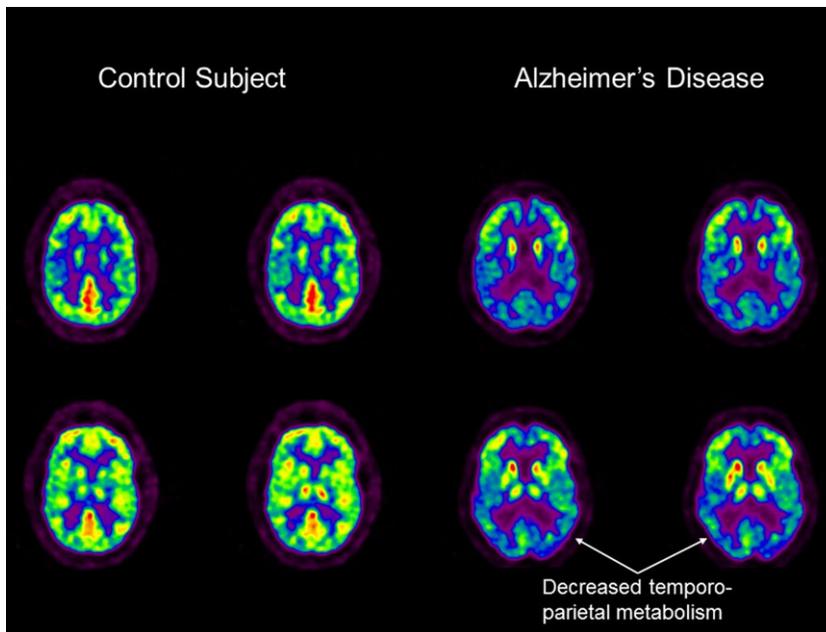


Figure 1. [^{18}F]Fluorodeoxyglucose positron emission tomography scans of a healthy control and a patient with Alzheimer's disease. The scans show relatively uniform and symmetric metabolism throughout the brain of the control subject and moderately decreased metabolism in the temporoparietal regions (arrows) of the brain in the Alzheimer's patient.

other dementing disorders in patients with mild disease.^{2,3} A variety of approaches have been used to aid in the diagnosis of AD, including specific clinical assessments such as the mini-mental status examination, levels of pathological molecules (i.e., tau protein) in the cerebrospinal fluid, and the use of imaging studies such as magnetic resonance imaging (MRI) to assess for volumetric changes.⁴

In addition, it is believed that functional imaging studies using positron emission tomography (PET) or single-photon emission computed tomography (SPECT) might help in making the diagnosis of AD and elucidating the mechanisms underlying the disorder. Since 1980, a large number of studies have used PET in the assessment of patients with AD. Most studies have shown that patients with AD have decreased whole-brain glucose metabolism and blood flow, with the bilateral parietal and temporal lobes particularly affected.^{5–7} This parietal hypometabolism (Fig. 1) is often referred to as representing the typical pattern of AD and may be particularly pronounced in patients younger than 65 years.⁸ More recent studies have focused on the pathophysiology of Alzheimer's disease itself with the development of imaging tracers that target the amyloid plaque.⁹

Frontotemporal lobar dementia (FTLD) is a clinical syndrome caused by the degeneration and ultimate atrophy of the frontal and anterior temporal lobes of the brain, often unilaterally. In 1892, Arnold Pick performed histological analyses of the brains of patients who had developed this pattern of atrophy. He identified swollen neurons that had inclusions of protein, later found to be randomly arranged filaments of tau protein, and these inclusions were dubbed "Pick bodies." As molecular neurobiological techniques have progressed, what was initially termed *Pick's disease* has since been discovered to be a spectrum of conditions in which particular proteins in particular brain locations tend to be misfolded and lead to degeneration. Behavioral variant frontotemporal lobar dementia (bvFTLD) is characterized primarily by behavioral disinhibition and impaired executive function; while the frontal lobes appear to be the primary site where neurodegeneration begins, the process is not always confined to this area. While about half of these bvFTLD patients end up having inclusions of the tau protein in the degenerating neurons, the other half have inclusions of transactivation response (TAR) DNA-binding protein of 43 kDa (TDP-43). In agrammatic or nonfluent primary progressive aphasia, expressive

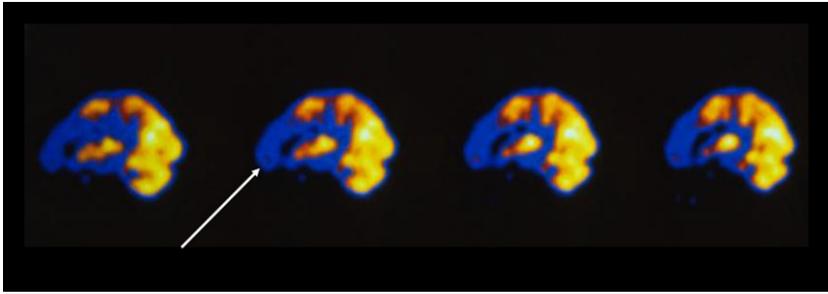


Figure 2. [^{18}F]Fluorodeoxyglucose positron emission tomography scans in the sagittal view of a patient with Pick's disease. The scans show severely decreased metabolism in the frontal cortex (arrow) compared to the metabolism in the other cortical structures.

language declines, while memory and other cognitive functions are initially spared; inclusion bodies include either tau or TDP-43, invariably in the dominant inferior frontal gyrus, sometimes extending to the precentral gyrus or frontal operculum. In semantic dementia, speech production is normal yet comprehension of meaning, or the semantics, of speech becomes progressively disturbed. TDP-43 inclusions are found in one or both of the anterior temporal lobes. Although each of the variants of the FTL spectrum initially manifest as symptoms arising from neurodegeneration in one particular brain area, inevitably the disease advances; hence a variant that initially involved only the anterior temporal lobe will spread to the ipsilateral frontal lobe, or vice versa. The most common finding in PET images is hypometabolism in the frontal and anterior temporal lobes bilaterally,^{10,11} which is consistent with the findings on histopathologic examination (Fig. 2).

Another prominent group of neurodegenerative diseases include movement disorders, of which the most common is Parkinson disease (PD), caused by loss of the pigmented neurons in the substantia nigra and the locus coeruleus and is characterized by the triad of bradykinesia, tremor, and rigidity. PD is considered an α -synucleinopathy because this protein accumulates in Lewy body inclusions in the degenerating neurons. The loss of pigmented neurons is associated with decreased production and storage of dopamine, and nigrostriatal system dysfunction. It is believed that initially there is an up-regulation of dopamine receptors^{12,13} followed by a downregulation that occurs as the disease progresses. Eventually, PD can lead to dementia in 20–30% of the patients. PET imaging studies in PD have

primarily focused on the dopaminergic system with [^{18}F]fluorodopa to evaluate presynaptic dopaminergic function, and have shown marked reductions in nigrostriatal dopaminergic projections as well as reduced basal ganglia activity (Fig. 3).^{14–16}

As delineated below, each of the neurodegenerative diseases can affect memory and attention, and there is evidence that certain medications, currently available for the different disorders, help preserve brain function, and consequently, memory, attention, and cognition. Such medications include acetylcholinesterase inhibitors, glutamate regulators, antioxidants/anti-inflammatory supplements, and experimental approaches such as vaccines and immunological modulation to help manage and treat dementia. Movement disorders are currently treated primarily with dopaminergic medications and deep brain stimulation procedures. However, there are no clear treatment options that eliminate the underlying pathophysiology of these diseases.

Given the limitations and potential side effects of medications for neurodegenerative diseases, it would seem reasonable to explore other non-pharmacological approaches to help manage these diseases. Meditation appears to be able to enhance memory and attention, and it would seem that meditation practices could potentially be an excellent adjunct treatment. The hope would be that meditation practices can help support the brain's functions and allow an individual to maintain brain function for as long as possible as the neurodegenerative disease progresses. The following sections review the data on meditation in memory and attention, as well as its potential applications in neurodegenerative diseases.

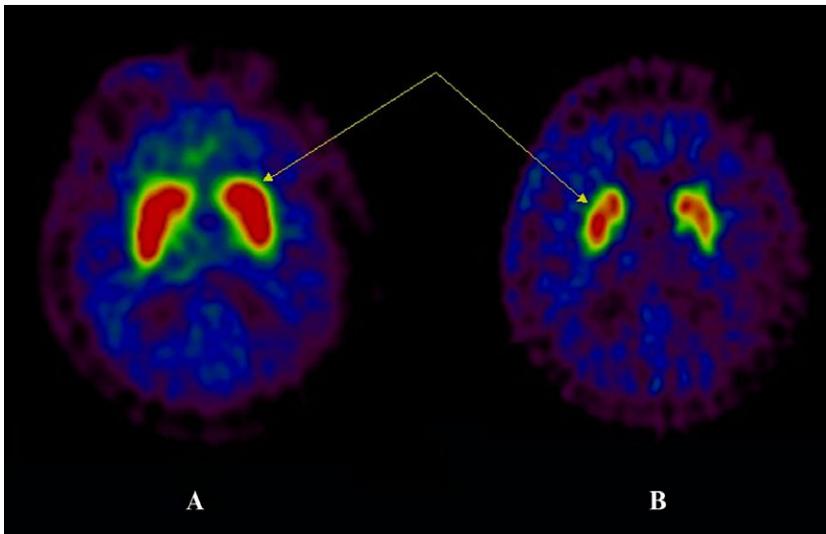


Figure 3. [^{18}F]Fluorodopa scans of a control subject and a Parkinson disease patient. The scans show strong uptake in the basal ganglia of the control subject (A) and minimal uptake in the basal ganglia of the Parkinson disease patient (B). This reflects abnormal dopaminergic function in the Parkinson disease patient since the fluorodopa is a precursor of dopamine.

Brief overview of meditation practices

The term *meditation* refers to a wide range of practices arising out of different religious, spiritual, and secular traditions. Depending on the tradition, meditation may be a way to establish a sense of calm and serenity; reduce stress and alleviate depression; reduce anxieties and deal with panic disorders; improve health; or deal with chronic illness. Meditation may also allow cultivation of greater self-awareness and a spiritual path, a way to be in touch with peak spiritual experiences. This divergence in forms and understandings of meditation corresponds to studies of meditation, with different meditation practices showing different outcomes. Given the variety of meditation practices and traditions, an all-encompassing definition of meditation is not possible. However, it is helpful for the scientific study of meditation to have some basic way to categorize the different types of meditation. In general, most forms of meditation involve the regulation of attention or emotion. Recently, meditation practices have been divided into two broad categories—focused attention and open awareness meditation.¹⁷ A brief discussion of attention will be helpful in elaborating this broad categorization of meditation.

The most consistent theoretical model of attention processing suggests that it consists of three distinct networks: alerting (also referred to as vig-

ilance or sustained attention), orienting (selective attention or concentration), and conflict monitoring (executive attention).^{18–20} Alerting is involved in achieving and maintaining an attentive state; orienting is involved in selectively focusing on a subset of space or available information; and conflict monitoring is involved in the management of goal-directed behavior, target and error detection, conflict resolution, and the inhibition of automatic responses. These three networks are behaviorally and neurally distinct and dissociable.^{21–23} In addition to these different components of attention, attention switching refers to an ability to change attentive focus in a flexible manner.^{24,25}

Neuroimaging studies of attention have generally shown activation in three different neural networks using specific spatial cuing and flanker tasks that require an individual to focus attention in relation to various supporting or distracting stimuli. While attention “sources” have been identified in frontal and parietal subregions for all the different attention networks, “sites” have been localized to considerably different subregions across these networks. Alerting primarily activates the prefrontal cortex (PFC), the premotor cortex, intraparietal sulcus, the locus coeruleus, and thalamic regions.²⁶ Orienting activates cortical areas, including the dorsolateral PFC, medial PFC, and anterior and posterior cingulate cortex, and specific subregions of

the parietal cortex.^{27–29} Collectively, engagement of attention for relevant stimuli, disengagement of attention from task-irrelevant stimuli, and movement of attention are described as the “shift” operation. It has been suggested that distinct subregions of the parietal cortex (including the superior parietal lobule, the temporal parietal junction, and the intraparietal sulcus) are involved in the engagement of attention that varies under different perceptual load conditions,²⁷ the disengagement of attention,³⁰ and covert and overt movement of attention.³¹ Having briefly discussed the attention networks and their neural correlates, we can now return to the discussion of meditation.

Given this description of attention, meditative practices have been categorized into the two general styles mentioned above depending on how the meditator deploys his/her attention.^{32–34} If attention is focused on a single object, whether the object is abstract (such as an imagined picture or a feeling) or concrete (such as a mantra, the breath, a body sensation, or an external object), then the style is categorized as focused attention meditation or concentration practice.³⁵ To sustain this focus, the practitioner has to constantly monitor and regulate the quality of attention toward that object. When attention wanders, the practitioner is to notice that without judgment, let go of whatever engaged his/her attention, and return to the object of focus.

Thus, focused attention is thought to not only train one’s ability to sustain attention, but also to develop three other regulative attentional skills, including the monitoring faculty that allows one to remain vigilant to distraction while maintaining the intended focus; the ability to disengage from a distracting object without further involvement (attention switching); and the ability to promptly redirect focus to the chosen object (selective attention).³² Slagter *et al.*³⁶ highlight the parallels between the processes involved in focused attention meditation and the recent neuroscientific conceptualizations of attention. The ability to focus and sustain attention on an intended object or task requires skills involved in the focus of attention and detecting distraction, disengaging attention from the source of distraction, and (re)-directing and engaging attention to the intended object.¹⁹

The second general category of meditation is open monitoring meditation, sometimes referred to as mindfulness meditation, where the meditator

maintains an open awareness of whatever arises in the field of attention (whether it is a sound, a body sensation, or a thought) moment by moment, and without judgment. Open monitoring meditation involves nonreactively monitoring the content of experience, without focusing on any explicit object.³⁵ The distinction between focused attention (concentration practice) and open awareness (mindfulness practice) is used and commonly accepted within the meditation literature and teaching practices. However, it is important to note that they are neither exclusive nor exhaustive in describing meditation practices. For example, mindfulness meditation training usually starts with training in focused attention to build concentration, progressing eventually to open awareness meditation practices. Even during a particular open meditation practice, the practitioner usually starts by calming the mind and reducing distractions with focused attention. The practitioner then gradually reduces focus on a single object and opens up the field of awareness to all objects.

In mindfulness or open monitoring meditation, the monitoring faculty of attention is emphasized. Open monitoring meditation is thought to enhance nonreactive, meta-cognitive monitoring, as well as increase awareness of automatic cognitive and emotional interpretations of sensory, perceptual, and endogenous stimuli, thereby enhancing cognitive flexibility and reappraisal.^{37–39}

Meditation and attention

Neurocognitive studies have shown that meditation may improve attention and cognitive function.^{25,32,35} Specifically, meditation practice and increased mindfulness appear to be related to improved attentional functions and cognitive flexibility.^{40–43} Several studies have compared long-term meditators with matched controls and observed significantly better performance in tasks involving sustained attention in meditators. For example, Pagnoni and Cekic⁴⁴ used a rapid visual presentation task to investigate age-related effects of meditation practice in meditators and nonmeditators. While the control subjects displayed the expected decrease in attentional performance with age, no such decrease was found in meditators. A more recent study by the same group observed a significant group difference in the functional magnetic resonance imaging (fMRI) signal from

the ventral posteromedial cortex in experienced Zen practitioners compared to controls that was significantly correlated with performance on a rapid visual information processing test for sustained attention.⁴⁵ The authors argued that their findings reflected a dynamic tension between mind wandering, meta-awareness, and directed attention among individuals, which may relate to specific clinical conditions affecting these parameters. Valentine and Sweet⁴⁶ found that meditation practitioners scored significantly higher on a test of sustained attention (Wilkin's counting test) than nonmeditators. Furthermore, the authors found that long-term meditators (more than 24 months of meditation experience) scored significantly higher than short-term meditators (less than 24 months), suggesting a training effect that might be useful, particularly when applied in patients with neurodegenerative diseases.

In another study by Jha *et al.*⁴² expert meditators that participated in a one-month intensive Vipassana meditation retreat were compared with novices with no prior meditation practice assigned to either an eight-week mindfulness-based stress reduction (MBSR) course (a standardized and secular form of mindfulness training) or to a waiting list. (Vipassana meditation is Buddhist insight meditation in which mindfulness is a key element.) The study found a significant reduction of response time scores as measured by the attentional network task (ANT) in the intensive retreat group compared with novices. Interestingly, study results also showed that those in the MBSR group had significant improvements on selective attention compared with the one-month intensive retreat and control group, as measured with the ANT. This may reflect an enhancement in the ability to exclude unwanted stimuli following early stages of MBSR practice in novice meditators but not in expert meditators who were more concerned with training their open monitoring faculty.

Other studies show higher levels of selective attention in long-term meditators compared with controls.^{47,48} Chan and Woollacott⁴¹ compared the effects of meditation practice on the Stroop (measures executive network) and Global-Local Letters (measures orientation network) tasks. They found that meditation practice was associated with increased efficiency of the executive attentional network, although it did not have an effect on the orienting network. In addition, Moore and Malinowski⁴³ compared meditators to

a meditation-naïve control group on performance of tasks that measure cognitive flexibility and the speed of processing visual information. They found that meditators outperformed nonmeditators on all measures and this performance was positively correlated with participants' self-reported scores on mindfulness measures.

In a longitudinal study comparing individuals randomly assigned to a meditation retreat group or a waiting list control, three months of focused awareness meditation practice (5 h/day) was found to improve sustained visual attention.⁴⁹ Compared to the control group, meditation retreat participants showed enhanced perceptual discrimination and vigilance on a sustained visual attention task. Notably, the enhancements in sustained attention ability were still observed three months after the end of the retreat, demonstrating enduring changes in sustained attention.

Collectively, these findings suggest that even brief periods of meditation training, such as in an eight-week MBSR program or other short intensive training programs, can improve memory, attention, and cognitive function. However, studies suggest that the beneficial effects of meditation are moderated by intensity and length of training. And as mentioned above, significantly higher attentional abilities have been found in long-term meditators compared to matched controls on different domains of attention. A significant positive relationship was observed between the amount of meditation experience and enhanced cognitive abilities and brain structural changes.⁴⁴ Furthermore, meditation appears to protect the brain from age-related cognitive decline.⁵⁰

Meditation and memory

Although there have been fewer studies investigating the effects of meditation practices on memory, these studies suggest that there are meditation-related improvements in working memory (along with sustained attention) measures in novice meditators who underwent meditation training compared to nonmeditators.^{51,52} Chambers *et al.*³⁸ examined the impact of participation in a 10-day Vipassana (mindfulness) meditation retreat on novice meditators' working memory capacity, measured by response time on a novel attention task that required participants to attend and update information between two categories, and by five self-reported measures of cognitive processes and affect. They found

that meditation training increased mindfulness, enhanced working memory capacity, and reduced switch costs in the attention task. In addition, mindfulness training reduced anxiety, negative affect, and depression. Zeidan *et al.*⁵³ studied the effects of a four-day mindfulness retreat in novice meditators and found a significant improvement in working memory capacity as measured by the digit span backward and forward of the Wechsler Adult Intelligence Scale.

Another study by Jha *et al.* examined the protective effects of mindfulness-based mental fitness training, modeled on MBSR training, on working memory capacity and mood states in military service members preparing for deployment.⁵¹ This is a period of intense stress, which can lead to decreases in cognitive function and increases in emotional disturbances.⁵⁴ Working memory capacity was assessed by the operation span (Ospan) task, on which scores showed a trend in improvement in the mindfulness training group with high practice, whereas they deteriorated over time in the control group and in the meditation group with low practice. Study results also suggest that improvements in working memory capacity may mitigate negative affect such as stress or anxiety.⁵¹

Newberg *et al.* studied the effects of meditation on memory in a group of older subjects with memory problems ranging from age-associated memory loss, mild cognitive impairment, and early Alzheimer's disease.⁵⁵ An 8-week (12 min/day) practice of Kirtan Kriya (KK, a form of mantra meditation) led to improvements on neuropsychological tests of verbal fluency and logical memory, and on trails B, in the meditation group compared to controls. These improvements in cognitive function were correlated with changes in the brain that will be discussed more fully below. The findings from this preliminary study are noteworthy because it is one of the few studies to look at the effects of meditation in an elderly population with age-related cognitive decline, mild cognitive impairment, and early Alzheimer's disease. The results suggested that improved memory and changes in cerebral blood flow (CBF) were associated with meditation practice.

It is also possible that other factors, such as stress reduction, increased positive emotions, or decreased negative emotions, may contribute to the memory-promoting effects of meditation. For example, a follow-up analysis showed that the Kirtan Kriya

meditation technique also helped improve psychological status in these patients based on results from the Profile of Mood Scale (POMS).⁵⁶ Compared to controls, those who participated in the meditation training program experienced notable improvements in mood, anxiety, tension, and fatigue. Interestingly, in the KK group, there were several significant correlations observed between the change in baseline CBF ratios and the change in results for the POMS scores. Specifically, areas such as the amygdala and caudate correlated with depression scores while the PFC, inferior frontal lobe, parietal region, and cingulate cortex correlated with feelings of tension. The findings regarding psychological status may ultimately bear directly on the effects of meditation on memory. Studies show that stress and negative emotions may have an adverse effect on learning and memory.^{57,58} Thus, part of the mechanism by which meditation may improve memory may be related to a reduction in stress and negative emotions.

Neuroimaging studies of meditation

The results of neuroimaging (PET, SPECT, and fMRI) studies indicate a number of changes that support the proposed mechanism by which meditation may help with memory and cognition. For example, in a study by Herzog *et al.* that used [¹⁸F]fluorodeoxyglucose (FDG) PET to measure regional glucose metabolism in subjects undergoing yoga meditative relaxation,⁵⁹ a significant increase in the frontal:occipital ratio of cerebral metabolism was found in the meditators. Specifically, there was only a mild increase in the frontal lobe, but marked decreases in metabolism in the occipital and superior parietal lobes. Other studies utilizing fMRI in subjects performing a similar yoga relaxation technique designed to bring about the "relaxation response" demonstrate relative increases in cerebral blood flow in the frontal lobes as well as in the limbic system.^{60,61} These results are beginning to suggest a specific pattern of brain activity associated with different types of meditation practices.

A SPECT imaging study of Tibetan Buddhist meditation demonstrated the presence of a number of complex changes, including relatively increased CBF in the PFC and cingulate gyrus (Fig. 4).⁶² The regional CBF ratio in long-term meditators was higher than nonmeditators in the PFC, amygdala, thalamus, and brain stem regions. Together, the

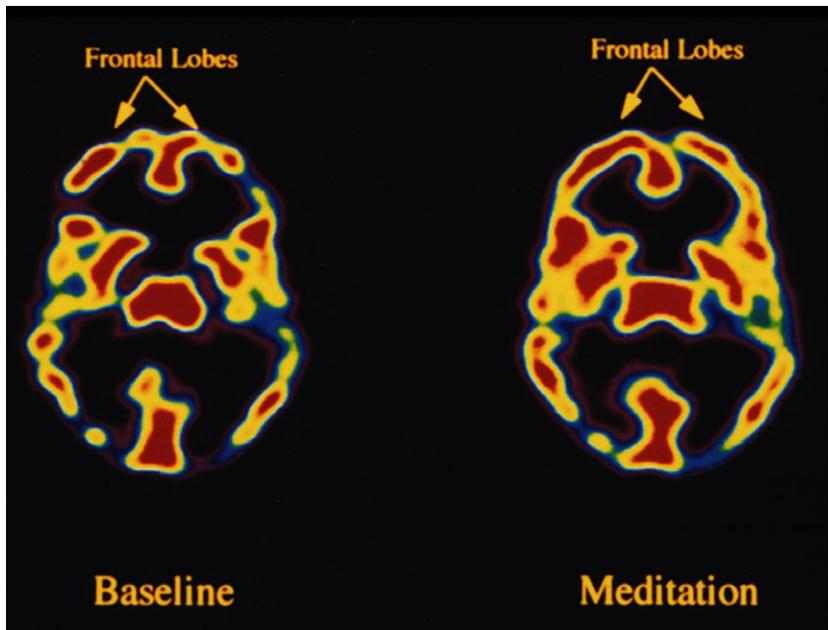


Figure 4. SPECT scans of a subject at rest and during peak meditation showing increased cerebral blood flow (arrows) during meditation.

results of these studies suggest that meditation may lead to increased activity in the structures underlying attention and memory processes.⁶³

A study by Holzel *et al.* found that Vipassana meditation activated the rostral anterior cingulate cortex (ACC) and the dorsal medial PFC in both hemispheres.⁶⁴ In addition, these investigators found that Vipassana meditation might enhance cerebral activity in brain areas related to interoception and attention, such as the PFC, the right anterior insula, and the right hippocampus.⁶⁵ These findings suggest that mindfulness meditation may enhance attentional abilities.

A study by Lazar *et al.* compared individuals with extensive training in Kundalini (mantra-based) or Vipassana meditation using fMRI. Subjects were studied during meditation and several control tasks.⁶⁶ Similar but nonoverlapping frontal and parietal cortices and subcortical structures were engaged during meditation by both groups, and these patterns differed from those observed during control tasks. The main area of common activation was the dorsal cingulate cortex. Overall, the studies suggest that there are some common, as well as distinct, patterns of brain activation across different meditation practices.

Lazar *et al.*⁶⁷ also used MRI to investigate individual differences in cerebral cortical thickness and found that brain regions associated with attention and sensory processing, including the PFC and right anterior insula, were thicker in meditators than matched controls. The differences in cortical thickness were specific to areas relevant to meditation, as the groups did not differ in mean thickness across the entire cortex. In an MRI study by Holzel *et al.*⁶⁸ changes in gray matter concentration were investigated in MBSR practitioners using voxel-based morphometry and compared with a waiting list control group. Increases in gray matter concentration were shown within the left hippocampus, and whole-brain analyses identified increases in the posterior cingulate cortex, the temporoparietal junction, and the cerebellum in the MBSR group compared with the controls. The authors concluded that eight-week mindfulness training is associated with changes in gray matter concentration in brain regions involved in learning and memory processes, emotion regulation, self-referential processing, and perspective taking. The previously described study by Pagnoni and Cecik⁴⁴ revealed the expected negative correlation of both gray matter volume and attentional performance

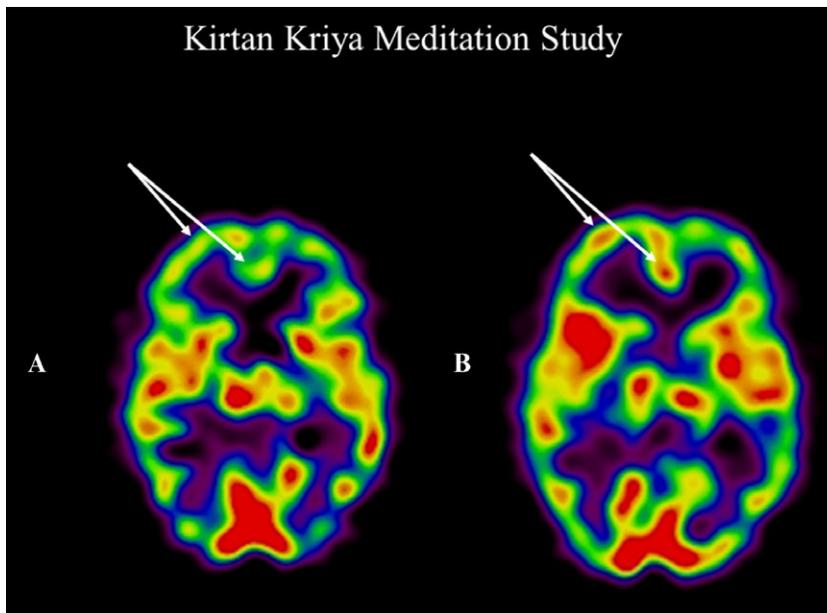


Figure 5. Resting SPECT scans of a subject in the Kirtan Kriya meditation study before (A) and after (B) eight weeks of daily meditation practice. The scans show increased perfusion at rest in the prefrontal cortex and anterior cingulate gyrus (arrows) after participating in the meditation program.

with age while meditators did not show a significant correlation of either measure with age. These authors argued that the regular practice of meditation may have a neuroprotective effect, thereby reducing the cognitive decline associated with normal aging.

Tang *et al.* have performed several studies with integrative body–mind training (IBMT), which incorporates mindfulness, body relaxation, and mental imagery, and showed that increased CBF in the right anterior cingulate, putamen, and caudate was associated with a five-day training program, implying changes in self-regulation, executive function, and reward networks.⁶⁹ This same group also found improvements in performance on the ANT and in levels of anxiety, fatigue, depression, and anger as measured by the Profile of Mood States scale.⁵² Finally, Tang *et al.* performed diffusion tensor imaging before and after IBMT training and found changes in fractional anisotropy in the corona radiata associated with the anterior cingulate, which is a central structure involved in the self-regulation network.⁷⁰

Several fMRI studies of meditation have specifically shown activation of a larger distributed network of attention-related brain regions, including frontal parietal regions, insula, thalamus, basal ganglia, and cerebellar regions. Individuals with more

meditation experience show greater activation in these regions compared to novices, suggesting a training effect. A study by Brefczynski-Lewis *et al.*⁷¹ using fMRI found that there are overlapping activation regions for expert meditators with over 10,000 h of practice and novice meditators in attention-related brain regions, including the insula, multiple thalamic nuclei, basal ganglia, frontal parietal, lateral occipital, and cerebellar regions. Despite these similarities, expert meditators showed greater activation than novice meditators in several other brain regions implicated in attentional processing, including the superior frontal sulcus and the intraparietal sulcus. In contrast, novice meditators had greater activation in regions shown to negatively correlate with performance in a sustained attention task.

A previously mentioned SPECT study by Newberg *et al.*⁵⁵ that examined changes in CBF in elderly subjects with memory problems after eight weeks of Kirtan Kriya (mantra meditation) practice found that, compared to controls, the meditation group showed significantly higher CBF in the frontal lobe regions and right superior parietal lobe (Fig. 5). Further, there was a correlation between improved cognitive function and increased CBF. The increased baseline CBF in the frontal cortex for the meditation

group is particularly interesting since these frontal lobe structures are not only important mediators of attention and executive function, but also appear to be affected in patients with various dementia disorders and mild cognitive impairment.

Together the results of these studies show that the mental training of attention and cognitive skills as cultivated through focused attention and open monitoring meditation is associated with changes in brain structure and function, as well as improved attention and memory task performance. Moreover, neuroimaging work suggests that both types of meditation not only activate brain regions during meditation, but also may produce long-lasting changes in brain and mental function that translates into tasks that are not associated with meditation.³⁹

Conclusions

In this review, we discussed the relationship between meditation and attention, and examined the literature on meditation effects on attention and working memory, and the neuroscientific literature on meditation effects on the brain. While the neuroscientific literature is difficult to parse out, with different imaging techniques and differential impact of an array of meditation practices complicating the picture, studies generally indicate that even short-term meditation training can improve various attentional networks and working memory capacity. The findings do suggest that meditation effects are moderated by length and intensity of training. Meditation appears to prevent age-related cognitive decline as well as reductions in cortical thickness. The neuroimaging studies demonstrate that not only are particular areas of the brain activated during meditation, but also that meditation practice leads to changes in brain structure and function that persist beyond the time of actual practice. Longer longitudinal studies will be necessary to determine if meditation results in long-term changes in brain structure and function. All of these findings are extremely encouraging and have many clinical implications for improving working memory capacity in those with disorders associated with working memory deficits—in preventing a decline in working memory capacity for those in high-stress professions, such as the military in active duty, as well as improving memory and cognitive function in elderly individuals with memory loss or mild cognitive impairment.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. McKhann, G., D. Drachman, M. Folstein, *et al.* 1984. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* **34**: 939–944.
2. Tierney, M.C., R.H. Gisher, A.J. Lewis, *et al.* 1988. The NINCDS-ADRDA Workgroup criteria for the clinical diagnosis of probable Alzheimer's disease: a clinical pathological study of 57 cases. *Neurology* **38**: 359–364.
3. Joachim, C.L., J.H. Morris & D.J. Selkow. 1988. Clinical diagnosed Alzheimer's disease. Autopsy results in 150 cases. *Ann. Neurol.* **24**: 50–56.
4. Gauthier, S., C. Patterson & H. Chertkow, *et al.* 2012. 4th Canadian consensus conference on the diagnosis and treatment of dementia. *Can. J. Neurol. Sci.* **39**(6 Suppl 5): S1–S8.
5. Heiss, W.D., J. Kessler, B. Szekely, *et al.* 1991. Positron emission tomography in the differential diagnosis of organic dementias. *J. Neural. Transm. Suppl.* **33**: 13–19.
6. Bonte, F.J., J. Hom, R. Tinter & M.F. Weiner. 1990. Single photon tomography in Alzheimer's disease and the dementias. *Semin. Nucl. Med.* **20**: 342–352.
7. Rapoport, S.I., B. Horowitz, C.L. Grady, *et al.* 1991. Abnormal brain glucose metabolism in Alzheimer's disease as measured by positron emission tomography. *Adv. Exp. Med. Biol.* **291**: 231–248.
8. Ichimiya, A., K. Herholz, R. Mielke, *et al.* 1994. Difference of regional cerebral metabolic pattern between presenile and senile dementia of the Alzheimer type: a factor analytic study. *J. Neurol. Sci.* **123**: 11–17.
9. Wong, D.F., P.B. Rosenberg, Y. Zhou, *et al.* 2010. In vivo imaging of amyloid deposition in Alzheimer disease using the radioligand ¹⁸F-AV-45 (Florbetapir [corrected] F 18). *J. Nucl. Med.* **51**: 913–920.
10. Salmon, E., P. Maquet, B. Sadzot, *et al.* 1998. Positron emission tomography in Alzheimer's and Pick's disease. *J. Neurol.* **235**: S1.
11. Lieberman, A.P., J.Q. Trojanowski, V.M. Le, *et al.* 1998. Cog, neuroimaging, and pathological studies in a patient with Pick's disease. *Ann. Neurol.* **43**: 259–265.
12. Marsden, C.D. 1982. Basal ganglia disease. *Lancet* **2**: 1141–1147.
13. Marsden, C.D. 1982. The mysterious motor function of the basal ganglia. *Neurology* **32**: 514–539.
14. Brooks, D.J., V. Ibanez, G.V. Sawle, *et al.* 1990. Differing patterns of striatal (18F)-dopa uptake in Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy. *Ann. Neurol.* **28**: 547–555.
15. Martin, W.R. 1989. Parkinson's disease: positron emission tomographic studies. *Semin. Neurol.* **9**: 345–350.
16. Nahmias, C., E.S. Garnett, G. Firnau, *et al.* 1985. Striatal dopamine distribution in Parkinsonian patients during life. *J. Neurol. Sci.* **69**: 223–230.

17. Lutz, A., H.A. Slagter, J.D. Dunne & R.J. Davidson. 2008. Attention regulation and monitoring in meditation. *Trends Cogn. Sci.* **12**: 163–169.
18. McDowd, J.M. 2007. An overview of attention: behavior and brain. *J. Neurol. Phys. Ther.* **12**: 117–125.
19. Posner, M.I. & S.E. Petersen. 1990. The attention system of the human brain. *Ann. Rev. Neurosci.* **13**: 25–42.
20. Posner, M.I. & M.K. Rothbart. 2007. Research on attention networks as a model for the integration of psychological science. *Ann. Rev. Psychol.* **58**: 1–23.
21. Fan, J., B. McCandliss, T. Sommer, *et al.* 2002. Testing the efficiency and independence of attention networks. *J. Cogn. Neurosci.* **14**: 340–347.
22. Fan, J., B.D. McCandliss, J. Fossella, *et al.* 2005. The activation of attentional networks. *NeuroImage* **26**: 471–479.
23. Fan, J., J. Byrne, M.S. Worden, *et al.* 2007. The relation of brain oscillations to attentional networks. *J. Neurosci.* **27**: 6197–6206.
24. Mirsky, A.F., B.J. Anthony, C.C. Duncan, *et al.* 1991. Analysis of the elements of attention: a neuropsychological approach. *Neuropsychol. Rev.* **2**: 109–145.
25. Chiesa, A., R. Calati & A. Serretti. 2011. Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. *Clin. Psychol. Rev.* **31**: 449–464.
26. Coull, J.T., C.D. Frith, R.J. Dolan, *et al.* 1997. The neural correlates of the noradrenergic modulation of human attention, arousal and learning. *Euro. J. Neurosci.* **9**: 589–598.
27. Corbetta, M., G.L. Shulman, F.M. Miezin & S.E. Petersen. 1995. Superior parietal cortex activation during spatial attention shifts and visual feature conjunction. *Science* **270**: 802–805.
28. Astafiev, S.V., G.L. Shulman, C.M. Stanley, *et al.* 2003. Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. *J. Neurosci.* **23**: 4689–4699.
29. Vandenberghe, R., D.R. Gitelma, T.B. Parrish & M.M. Mesulam. 2001. Functional specificity of superior parietal mediation of spatial shifting. *NeuroImage* **14**: 661–673.
30. Posner, M.I., J.A. Walker, F.A. Friedrich & R.D. Rafal. 1987. How do the parietal lobes direct covert attention? *Neuropsychologia* **25**: 135–145.
31. Yantis, S., J. Schwarzbach, J.T. Serences, *et al.* 2005. Transient neural activity in human parietal cortex during spatial attention shifts. *Nat. Neurosci.* **5**: 995–1002.
32. Lutz, A., H.A. Slagter, J.D. Dunne & R.J. Davidson. 2008. Attention regulation and monitoring in meditation. *Trends Cogn. Sci.* **12**: 163–169.
33. Cahn, B.R. & J. Polich. 2006. Meditation states and traits: EEG, ERP, and neuroimaging studies. *Psychol. Bull.* **132**: 180–211.
34. Fell, J., N. Axmacher & S. Haupt. 2010. From alpha to gamma: electrophysiological correlates of meditation-related states of consciousness. *Med. Hypotheses* **75**: 218–224.
35. Lutz, A., J.D. Dunne & R.J. Davidson. 2007. “Meditation and the neuroscience of consciousness: an introduction.” In *Cambridge Handbook of Consciousness*. P. Zelazo, M. Moscovitch & E. Thomspon, Eds.: 499–554. New York: Cambridge University Press.
36. Slagter, H.A., A. Lutz, L.L. Greischar, *et al.* 2007. Mental training affects distribution of limited brain resources. *PLoS Biol.* **5**: 1228–1235.
37. Bishop, S.R., M. Lau & S. Shapiro. 2004. Mindfulness: a proposed operational definition. *Clin. Psychol.* **11**: 230–241.
38. Chambers, R., B.C.Y. Lo & N.B. Allen. 2008. The impact of intensive mindfulness training on attentional control, cognitive style and affect. *Cogn. Ther. Res.* **32**: 303–322.
39. Slagter, H.A., R.J. Davidson & A. Lutz. 2011. Mental training as a tool in the neuroscientific study of brain and cognitive plasticity. *Front. Hum. Neurosci.* **5**: 17.
40. Carter, O.L., D.E. Presti, C. Callistemon, *et al.* 2005. Meditation alters perceptual rivalry in Tibetan Buddhist monks. *Curr. Biol.* **15**: R412–R413.
41. Chan, D. & M. Woollacott. 2007. Effects of level of meditation experience on attentional focus: is the efficiency of executive or orientation networks improved? *J. Altern. Complement. Med.* **13**: 651–657.
42. Jha, A.P., J. Krompinger & M.J. Baime. 2007. Mindfulness training modifies subsystems of attention. *Cogn. Affect. Behav. Neurosci.* **7**: 109–119.
43. Moore, A. & P. Malinowski. 2009. Meditation, mindfulness and cognitive flexibility. *Conscious Cogn.* **18**: 176–186.
44. Pagnoni, G. & M. Cekic. 2007. Age effects on gray matter volume and attentional performance in Zen meditation. *Neurobiol. Aging* **28**: 1623–1627.
45. Pagnoni, G. 2012. Dynamical properties of BOLD activity from the ventral posteromedial cortex associated with meditation and attentional skills. *J. Neurosci.* **32**: 5242–5249.
46. Valentine, E.R. & P.L.G. Sweet. 1999. Meditation and attention: a comparison of the effects of concentrative versus mindfulness meditation on sustained attention. *Ment. Health Relig. Culture* **2**: 59–70.
47. Hodgins, H.S. & K.C. Adair. 2010. Attentional processes and meditation. *Conscious Cogn.* **19**: 872–878.
48. Van den Hurk, P.A., F. Girommi & S.C. Gielen, *et al.* 2010. Greater efficiency in attentional processing related to mindfulness meditation. *Quart. J. Exp. Psychol.* **44**: 405–415.
49. McLean, K.A., E. Ferrer & S.R. Aichele, *et al.* 2010. Intensive meditation training improves perceptual discrimination and sustained attention. *Psychol. Sci.* **21**: 829–839.
50. Van Leeuwen, S., N.G. Muller & L. Melloni. 2010. Age effects on attentional blink performance in meditation. *Conscious Cogn.* **18**: 593–599.
51. Jha, A.P., E.A. Stanley, A. Kiyonaga, *et al.* 2010. Examining the protective effects of mindfulness training on working memory capacity and affective experience. *Emotion* **10**: 54–64.
52. Tang, Y.-Y., Y. Ma & J. Wang, *et al.* 2007. Short-term meditation training improves attention and self-regulation. *Proc. Natl. Acad. Sci.* **104**: 17152–17156.
53. Zeidan, F., S.K. Johnson & B.J. Diamond, *et al.* 2010. Mindfulness meditation improves cognition: evidence of brief mental training. *Conscious Cogn.* **19**: 597–605.
54. Stanley, E.A. & A.P. Jha. 2009. Mind fitness: improving operational effectiveness and building warrior resilience. *Joint Force Quart.* **55**: 145–151.
55. Newberg, A.B., N. Wintering, D.S. Khalsa, *et al.* 2010. Meditation effects on cognitive function and cerebral blood

- flow in subjects with memory loss: a preliminary study. *J. Alzheimers. Dis.* **20**: 517–526.
56. Moss, A.S., N. Wintering, H. Roggenkamp, *et al.* 2012. Effects of an eight week meditation program on mood and anxiety in patients with memory loss. *J. Comp. Alt. Med.* **18**: 48–53.
 57. Schwabe, L. & O.T. Wolf. 2012. Stress modulates the engagement of multiple memory systems in classification learning. *J. Neurosci.* **32**: 11042–11049.
 58. Osaka, M., K. Yanoi, T. Minamoto & N. Osaka. 2013. When do negative and positive emotions modulate working memory performance? *Sci. Rep.* **3**: 1375.
 59. Herzog, H., V.R. Lele, T. Kuwert, *et al.* 1990–1991. Changed pattern of regional glucose metabolism during yoga meditative relaxation. *Neuropsychobiol* **23**: 182–187.
 60. Lazar, S.W., G. Bush & R.L. Gollub, *et al.* 2000. Functional brain mapping of the relaxation response and meditation. *Neuroreport* **11**: 1581–1585.
 61. Lou, H.C., T.W. Kjaer, L. Friberg, *et al.* 1999. A 15O-H₂O PET study of meditation and the resting state of normal consciousness. *Hum. Brain Mapp.* **7**: 98–105.
 62. Newberg, A.B., A. Alavi & M. Baime, *et al.* 2001. The measurement of regional cerebral blood flow during the complex cognitive task of meditation: a preliminary SPECT study. *Psychiatr. Res.* **106**: 113–122.
 63. Frith, C.D., K. Friston & P.F. Liddle, *et al.* 1991. Willed action and the prefrontal cortex in man: a study with PET. *Proc. R. Soc. Lond.* **244**: 241–246.
 64. Holzel, B.K., U. Ott, H. Hempel, *et al.* 2007. Differential engagement of anterior cingulate and adjacent medial frontal cortex in adept meditators and non-meditators. *Neurosci. Lett.* **421**: 16–21.
 65. Holzel, B.K., U. Ott, T. Gard, *et al.* 2008. Investigation of mindfulness meditation practitioners with voxel-based morphometry. *Soc. Cogn. Affect. Neurosci.* **3**: 55–61.
 66. Lazar, S.W., G. Bush, R.L. Gollub, *et al.* 2003. Functional brain imaging of mindfulness and mantra-based meditation. Paper presented at the meeting of the Society for Neuroscience. New Orleans, LA.
 67. Lazar, S.W., C.E. Kerr & R.H. Wasserman, *et al.* 2005. Meditation experience is associated with increased cortical thickness. *Neuroreport* **16**: 1893–1897.
 68. Hölzel, B.K., J. Carmody, M. Vangel, *et al.* 2011. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatr. Res.* **191**: 36–43.
 69. Tang, Y.-Y., Y. Ma & Y. Fan, *et al.* 2009. Central and autonomic nervous system interaction is altered by short-term meditation. *Proc. Natl. Acad. Sci.* **106**: 8865–8870.
 70. Tang, Y.-Y., Q. Lu & X. Geng, *et al.* 2010. Short-term meditation induces white matter changes in the anterior cingulate. *Proc. Natl. Acad. Sci.* **107**: 15649–15652.
 71. Brefczynski-Lewis, J.A., A. Lutz, H.S. Schaefer, *et al.* 2007. Neural correlates of attention expertise in long-term meditation practitioners. *Proc. Natl. Acad. Sci. USA* **104**: 11483–11488.