Meditation Effects on Cognitive Function and Cerebral Blood Flow In Subjects with Memory Loss: A Preliminary Study

Andrew B. Newberg[a,b,*], Nancy Wintering[a,b], Dharma S. Khalsa[b,c], Hannah Roggenkamp[a] and Mark R. Waldman[b]

[a]*Division of Nuclear Medicine, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA*
[b]*Center for Spirituality and the Mind, University of Pennsylvania, Philadelphia, PA, USA*
[c]*Alzheimer Research and Prevention Foundation, Tucson, AZ, USA*

Abstract. This preliminary study determined if subjects with memory loss problems demonstrate changes in memory and cerebral blood flow (CBF) after a simple 8-week meditation program. Fourteen subjects with memory problems had an IV inserted and were injected with 250MBq of Tc-99m ECD while listening to a neutral stimulus CD. They then underwent a pre-program baseline SPECT scan. Then subjects were guided through their first meditation session with a CD, during which they received an injection of 925MBq ECD, and underwent a pre-program meditation scan. Subjects completed an 8-week meditation program and underwent the same scanning protocol resulting in a post-program baseline and meditation scan. A region of interest (ROI) template obtained counts in each ROI normalized to whole brain to provide a CBF ratio. Baseline and meditation scans and neuropsychological testing were compared before and after the program. The meditation program resulted in significant increases ($p < 0.05$) in baseline CBF ratios in the prefrontal, superior frontal, and superior parietal cortices. Scores on neuropsychological tests of verbal fluency, Trails B, and logical memory showed improvements after training. This preliminary study evaluated whether an 8-week meditation program resulted in improvements in neuropsychological function and differences in CBF in subjects with memory loss. While the findings are encouraging, there are a number of limitations that can be addressed in future studies with more participants and more detailed analyses.

Keywords: Cerebral blood flow, cognitive impairment, meditation, memory, single photon emission computed tomography

INTRODUCTION

The number of older Americans continues to grow and with it the number who are thought to suffer from cognitive impairment and Alzheimer's disease (AD). Among people aged 65, 2–3% show signs of AD, while 25–50% of people aged 85 have symptoms of AD [1].

An even greater number have some of the pathological hallmarks of the disease without the characteristic symptoms. Until now, there have been few treatment options for patients with early cognitive impairment. Several medications and vaccine trials are underway. However, a non-pharmacological approach without side effects and without interfering with medications would be very useful and cost effective in the management of such patients without interfering with any medical interventions. Initial studies have suggested that specific cognitive practice programs will help improve memory [2,3]. Meditation has long been touted as a potential technique for improving memory and lowering levels of stress, depression, and anxiety. This

study was designed to explore the effects of a very specific form of meditation in patients with cognitive impairment and to track potential changes with functional brain imaging using single photon emission computed tomography (SPECT).

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

This is the first study to investigate potential improvements in cognition in subjects with actual memory loss.

Studies utilizing positron emission tomography (PET), SPECT, and functional magnetic resonance imaging (fMRI) have all demonstrated specific changes in cortical and sub-cortical structures when subjects were actively meditating [4–7]. There is a growing, although still relatively limited, number of studies that have evaluated the long-term effects of meditation practices. Specifically, these studies showed increased activity in expert meditators in the frontoparietal regions, cerebellar, temporal, parahippocampal, and posterior occipital cortex during meditation. These areas have also been implicated in a variety of memory tasks utilizing fMRI [8]. Other studies have compared experienced meditators to non-meditators with regard to brain structure and function [9]. For example, a study by Lazar and colleagues using structural MRI demonstrated that long-term meditators, practicing for approximately 1 hour a day, had thicker prefrontal cortexes than non-meditators [10]. Additionally, Lutz and collaborators using electroencephalography (EEG) showed that expert meditators were able to induce changes in their brain activity during meditation [11]. However, these studies did not determine if the findings were the result of the meditation practices since these studies were not longitudinal. Thus, one possibility is that the individuals had brains that were fundamentally different which predisposed them to such practices. A second possibility is that the individual affected their brain over the

course of their practice. Fewer studies have actually tried to evaluate the longitudinal effects of meditation over time. Davidson et al. showed that there were significant changes over time in the brain's EEG when individuals engaged in a daily 1 hour mindfulness based meditation practice [12]. Moreover, no previous studies have investigated the effect of meditation in patients with actual cognitive decline or AD. From the perspective of improving memory using meditation, it is imperative to longitudinally study subjects before and after a meditation training program to determine if there are long term effects of such a program.

Therefore, the primary purpose of this study was to investigate a particular type of meditation practice called Kirtan Kriya (KK), in patients who presented with memory problems, before and after an 8-week program. KK meditation is a simple technique that involves the repetition of four sounds – SA TA NA MA. While the person vocalizes these sounds, they sequentially touch their thumb to their index finger, middle finger, fourth finger, and then fifth finger. This is performed out loud for 2 minutes, in a whisper for 2 minutes, in silence for 4 minutes, followed by in a whisper for 2 more minutes and finally out loud for the final 2 minutes. The total time is 12 minutes. Since this is a simple and quick practice, it has the potential to be a very practical and low cost measure to help improve memory. This also distinguishes this practice from a number of other meditation practices that require extended class sessions and long meditation practices that may not be practical in an older population. This was the purpose for the present study which was to evaluate the effects of performing daily KK meditation for 8 weeks on brain function and cognition and measure changes in cerebral blood flow (CBF) utilizing SPECT imaging.

We hypothesized that several structures would be particularly affected by the KK meditation program. Specifically, attention focusing practices such as meditation have activated the attentional network in the brain which includes frontal lobe structures as well as the anterior cingulate cortex [13,14]. We also hypothesized that structures such as the amygdala and thalamus would be affected since these structures have shown changes in other studies of the long term effects of meditation and are also part of the network of structures involved in the default network [15,16]. We have previously found changes in the temporal lobe associated with verbal meditation practices and changes in the parietal lobe associated with altered spatial perceptions during meditation [6].
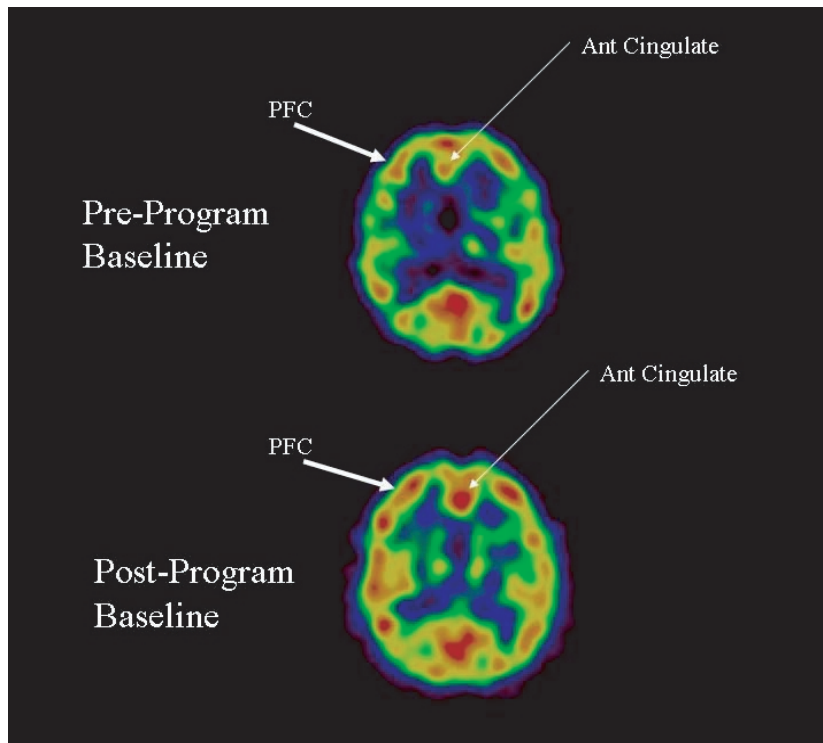
Fig. 1. This figure shows transaxial slices of SPECT scans (with CBF represented as red > yellow > green > blue) in the pre-program baseline state and the post-program baseline state. The post-program baseline state shows that there is relatively increased activity in the right prefrontal cortex (thick arrows) and anterior cingulate cortex (thin arrows) after the training program.

METHODS

Subjects and imaging acquisition

Fifteen subjects were recruited from local neurology clinics, local medical groups, and hospital based advertisements, who presented complaining of memory problems ranging from mild age-associated memory impairment ($n = 7$), to mild cognitive impairment (MCI) ($n = 5$), to moderate impairment with a diagnosis of AD ($n = 3$). The Mini-Mental Status Examination scores (MMSE) ranged from 16–30. There were 6 men and 9 women with ages ranging from 52–77 years with a mean age of 64 ± 8 years. The patients with AD were diagnosed on the basis of criteria established by the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria [17]. The MCI patients were diagnosed based upon criteria reported in Grundman et al. [18] which includes memory complaint, abnormal memory based

upon performance on the Logical Memory II subtest of the Wechsler Memory Scale Revised, normal general cognitive function, no impairment in activities of daily living, and not sufficiently impaired to meet the NINCDS/ADRDA criteria for AD. The remaining subjects were considered to have age-associated memory impairment and were otherwise normal controls who perceived their memory to be impaired. Each subject had no significant experience with meditation or yoga. Subjects were studied on their first KK training day and then again after an 8-week self-directed training program. We excluded the data from the single AD patient with a MMSE of 16 due to her inability to adequately perform the meditation.

On the first day of the study, after obtaining informed consent (approved by the human subjects Institutional Review Board with the study protocol), a room was set up in the hospital to function as a meditation room. Approximately 20 minutes prior to the baseline scan, an intravenous canula (IV) was placed in one arm so that all injections could be performed without touching or disturbing the subject. The subjects reported minimal

discomfort from the IV that resolved prior to initiating the remainder of the study. For the baseline scan, the subject was instructed to rest in the room with their eyes closed and listen to a general informational CD about the effects of meditation practices for approximately 12 minutes. This CD was neutral in its content. However, we would suggest that having content on the CD that discusses meditation rather than a completely neutral topic is appropriate to exclude any possible expectation effect that might have resulted from both conditions. The subject was injected through the IV with 250 MBq of ^{99m}Tc-Bicisate (Bristol-Myers Squibb Medical Imaging, N. Billerica, MA), prepared as specified by the manufacturer. The subject continued to listen to the CD for another 5 minutes while the tracer uptake occurred in the brain. Approximately 15 minutes following the injection, the subjects underwent SPECT scanning for 30 minutes. This scan was labeled the "pre-program baseline" scan.

Projection images were obtained at three-degree angle intervals on a 128 × 128 matrix (pixel size 3.56 mm × 3.56 mm) over 360 by rotating each head 120 . These SPECT images were reconstructed in the transaxial, coronal, and sagittal planes using filtered backprojection, followed by a low pass filter and 1st order Chang attenuation correction (attenuation coefficient 0.11 cm^{-1}. The reconstructed slice thickness was 4 mm with a spatial resolution of 8–10 mm.

Following this pre-program baseline scan, the subject returned to the room for their first meditation session. Subjects initially viewed a 10 minute video with one of the investigators (DSK) showing how to perform the Kirtan Kriya meditation. This video reviewed the phrases, the sounds, and demonstrated the manner of performing the meditation. It was explained to subjects to focus on the sounds and finger movements. Subjects were not asked to do anything more than perform the task. Thus, there were no additional instructions regarding the state of mind that they should be in, any preparatory exercises, or any mindfulness exercises. At the end of the video, the principal investigator answered any questions and then observed the subjects doing the meditation to make sure that it was done correctly. Subjects were instructed that they would perform the meditation while listening to a meditation CD that guided them through the entire practice. The CD contains an individual performing the meditation practice in its intended manner with some background music to aid in the rhythm of the meditation. The subjects were then asked to perform the meditation for 12 minutes the first time during which they would receive a second

injection of approximately 925 MBq of ^{99m}Tc-Bicisate though the IV while he/she continued to meditate for approximately another five minutes. The subject was then scanned for 30 minutes using the same imaging parameters as for the baseline study. This scan was labeled the "pre-program meditation" scan.

Subjects were discharged home with the meditation CD so that they could practice it at home. They were instructed to perform the practice every day for 8 weeks. Subjects completed a log to record when they performed the meditation practice and their subjective experience of the practice and its effects. We contacted them at 4 weeks to remind them to continue practicing daily and to enquire as to their performance of the meditation. We also directly interviewed subjects upon completion of the program to review their progress. Upon completion of the 8-week meditation training program, subjects returned to the University of Pennsylvania Nuclear Medicine Department to undergo a second imaging day essentially identical to the first. They received a "post-program baseline" scan in which they were injected with ^{99m}Tc-Bicisate while listening again to an informational CD. After the baseline scan, the subjects then performed the meditation for the final time during which they were injected with ^{99m}Tc-Bicisate and underwent a "post-program meditation" scan. We maintained the same order in the pre- and post-program imaging studies so that the effect of doing the meditation would not interfere with the baseline scans.

Although this was an open label study to assess effect as well as feasibility, we also recruited a small comparison group in which the KK meditation was replaced with a "music listening" task. Five subjects, two having MCI and three having age-associated memory impairment (all women with a mean age of 65 ± 10 years and a range from 56 to 79 and mean MMSE of 29 ± 1), were asked to simply listen to two Mozart violin concertos each day for approximately 12 minutes, the same amount of time required for the KK meditation. The subjects were asked to focus their attention on the music and to record their progress in a log book. Subjects underwent the same SPECT imaging procedures as the KK group with listening to the music replacing listening and performing KK meditation. The music group listened to the same neutral content CD to produce the same comparison state. A group listening to music for the same amount of time might provide an adequate comparison for the KK meditation program since subjects would undergo similar types of programs with the exception of not doing the active part of the meditation.

Table 1
Baseline characteristics of the KK and Music comparison groups

Baseline characteristics	KK group	Music group	p
Age	64.0 ± 8.0	65.0 ± 9.9	N.S.
MMSE	28.1 ± 0.7	29.0 ± 1.0	N.S.
Category Fluency (Animals)	21.1 ± 7.9	21.5 ± 5.0	N.S.
Trails A	30.5 ± 12.2	37.0 ± 11.7	N.S.
Trails B	105.5 ± 52.8	132.5 ± 58.6	N.S.
Digit Symbols	63.7 ± 25.3	67.6 ± 21.7	N.S.
Logical Memory Delayed	10.6 ± 5.2	12.3 ± 6.5	N.S.
POMS	52.2 ± 12.9	47.5 ± 17.2	N.S.

Since the music group received an intervention (i.e., the music), we felt that the results would help reduce effects related to placebo and practice effects related to repeated performance of the neuropsychological tests. Furthermore, since some studies have suggested that music might also improve cognition and mood, this comparison group might actually be more stringent in terms of helping to observe an effect specifically from the KK meditation.

Subjects in both groups were also evaluated on the first imaging day with a brief neuropsychological test battery (see Table 1) that was adapted from the battery currently used by our Memory Disorders Clinic at the University of Pennsylvania and comprised of a Category Fluency task in which subjects named as many animals as possible in a 60 second time period, the Wechsler Adult Intelligence Scale (WAIS) Digit Symbol Substitution Test, a Logical Memory task, and Trails A and B. These tests also were selected based upon other studies in which neuropsychological tests were used to evaluate changes in cognition associated with mental task interventions [19,20]. These same tests were repeated on the 8-week follow up session.

Image analysis and statistics

The images of the pre- and post-program baseline and meditation scans were reconstructed and resliced, using an oblique reformatting program, according to the anterior-posterior commissure line so that the final two sets were aligned for analysis. A previously validated template methodology consisting of regions of interest (ROI) corresponding to the major cortical and subcortical structures was placed over the baseline scan [21]. For the purposes of this study, we examined the CBF as measured in only a selected number of ROIs which was hypothesis driven. The ROIs examined included the inferior frontal, superior frontal, dorsolateral prefrontal, orbitofrontal, inferior temporal, superior temporal, inferior parietal, superior parietal,

and sensorimotor areas, as well as the precuneus, thalamus, amygdala, and cingulate gyrus since these are areas that have been found to be previously affected during meditation tasks and also because these structures subserve a number of cognitive processes. The location for each ROI was determined based upon MRI anatomy such that they could then be placed directly on functional SPECT scans [20]. Furthermore, each ROI fits within each specified region which helps to ensure proper placement and to avoid problems with partial voluming. The ROIs were placed on the initial scan and then copied directly onto all subsequent scans. This was possible because the images were already resliced into the same planes as described above. The count values for the baseline and meditation scans were obtained by determining the number of counts in each ROI on the meditation scan and normalizing those counts to the whole brain activity. This provides a CBF ratio for each ROI compared to the whole brain. Since two SPECT scans were performed on the same day, the second scan had the decay corrected counts from the first scan subtracted out prior to analysis. We have previously validated this technique and show that there is a high test-retest correlation with less than 6% variability [22].

A percentage change between the meditation and baseline scans (for both the pre- and post-program sessions) was calculated using the equation:

$$\%\text{Change} = \frac{(\text{Meditation} - \text{Baseline})}{(\text{Baseline})} \times 100$$

Scan results were statistically evaluated using paired t-tests comparing the pre- and post-program baseline scans, and also the change in activation between the baseline and meditation scans for both the pre- and post-program condition. Similarly, neuropsychological test scores were compared using paired t-tests. We corrected the CBF data analysis for multiple comparisons using the False Discovery Rate method [23]. A limited number of Pearson correlations between changes

Table 2

Comparison of the pre and post training program baseline scans revealing changes in CBF in the following structures (values are presented as mean ROI/whole brain ratios)

Structure	Pre baseline	Post baseline	p
KK Group			
R Inferior Frontal	1.12 ± 0.10	1.19 ± 0.09	0.002
R Superior Frontal	1.12 ± 0.09	1.16 ± 0.08	0.007
R Superior Parietal	1.12 ± 0.07	1.18 ± 0.06	0.007
R DLPFC	1.10 ± 0.15	1.20 ± 0.15	0.007
R Sensorimotor	1.12 ± 0.08	1.18 ± 0.10	0.008
R Posterior Cingulate	1.36 ± 0.16	1.28 ± 0.17	0.02
R Orbitofrontal	0.86 ± 0.24	1.00 ± 0.13	0.03
R Anterior Cingulate	1.15 ± 0.19	1.21 ± 0.13	0.05
L Superior Frontal	1.11 ± 0.08	1.15 ± 0.10	0.006
L Thalamus	1.26 ± 0.09	1.18 ± 0.13	0.03
L Superior Parietal	1.12 ± 0.05	1.16 ± 0.09	0.02
L Medial Frontal	1.17 ± 0.11	1.22 ± 0.11	0.05
Music Group			
R Amygdala	0.86 ± 0.04	0.95 ± 0.06	0.004
R Precuneus	1.23 ± 0.02	1.11 ± 0.07	0.02

Still significant when corrected for multiple comparisons.

Table 3

Change in activation between pre and post meditation (or music listening) scans (given as mean percentage change between the baseline and meditation states)

Structure	Pre-activation	Post activation	p
Kirtan Kriya			
R DLPFC	+0.9	−6.3	0.001
R Superior Temporal	+0.3	−5.7	0.005
R Sensorimotor	+2.4	−4.6	0.026
R Precuneus	−0.8	−5.8	0.042
R Inferior Frontal	−0.7	−6.3	0.049
L Thalamus	−0.2	+8.1	0.023
L Amygdala	−2.1	−10.0	0.026
Music			
R Thalamus	+4.6	−7.3	0.03
R Precuneus	−5.6	+7.5	0.03

Still significant when corrected for multiple comparisons.

in neuropsychological test scores and changes in the pre and post-baseline CBF were compared for selected regions that were significant in the above analysis and known to be related to such parameters. Thus, we compared prefrontal cortex and thalamic activity to tests of cognition and executive function such as the Trails B, Digit Span Test, and the WAIS Digit Symbol Substitution Test.

RESULTS

There were a number of significant changes in the pre program baseline and the post program baseline scans in the KK group (see Table 2). In particular, structures in the frontal lobe regions and right superior parietal lobe had significantly higher baseline CBF after the 8-week training program (even after correction for multiple comparisons). These findings were in contrast to the baseline CBF values observed in the music comparison group. The structures that had higher baseline CBF values after the 8-week music program were in the amygdala and precuneus rather than the frontal lobes (see Table 2). However, with the small sample size, these changes were not significant after correction for multiple comparisons.

We also compared how much the different structures were activated (or deactivated) during the performance of the meditation (or listening to music) both pre and post training program (see Table 3). In the KK group, individuals mildly activated their prefrontal cortex in the first meditation scan, but had significantly decreased activity in the prefrontal cortex during meditation after the training program. The music group showed no significant differences in brain activation after correction for multiple comparisons.

When neuropsychological test scores were compared between the pre and post training program sessions, there were a several improvements observed in the KK group (see Table 4). The KK group did significantly better than the music group in Category Fluency – Animals ($p < 0.05$). However, several of the other neuropsychological tests demonstrated similar improvements between the KK and music groups even though the changes observed in the music group were not significant.

In the KK group, there was a significant Pearson correlation between CBF in the right prefrontal cortex versus the Trails B task ($R = −0.61, p = 0.02$) which was also significant after correction for multiple comparisons. There was a trend in the Pearson correlations between the left thalamus versus the Trails B task ($R = −0.62, p = 0.02$), and the left thalamus versus the Digit Span Test ($R = 0.56, p = 0.03$), but these were not significant after correction for multiple comparisons. No significant correlations were observed in the music group.

Finally, it should be noted that the log books and exit interviews with the subjects revealed that the subjects in general found the meditation practice enjoyable and beneficial. The subjects were able to perform the practice a mean of 75% of the days that they were in the study. Most subjects reported that they subjectively perceived that their cognitive function was improved after the 8-week program.

Table 4
Neuropsychological test score means (±SD) pre and post meditation training program

NP Test	Pre	Post	% Change	p
KK Group				
MMSE	28.1 ± 0.7	27.6 ± 1.6	−2%	0.13
Category Fluency*	21.1 ± 7.9	24.0 ± 6.3	+14%	0.006†
Trails A (seconds)	30.5 ± 12.2	33.6 ± 20.5	−10%	0.18
Trails B (seconds)	105.5 ± 52.8	84.6 ± 50.6	+20%	0.05
WAIS Symbol Substitution Test**	63.7 ± 25.3	67.6 ± 21.7	+6%	0.05
Logical Memory Delayed***	10.6 ± 5.2	12.4 ± 6.5	+17%	0.05
Music Group				
MMSE	29.0 ± 1.0	29.0 ± 0.82	0%	0.25
Category Fluency*	21.5 ± 4.2	20.8 ± 6.2	+3%	0.43
Trails A (seconds)	37.0 ± 11.8	35.0 ± 17.5	+5%	0.30
Trails B (seconds)	132.5 ± 58.7	100.3 ± 58.6	+24%	0.19
WAIS Symbol Substitution Test**	62.8 ± 7.5	67.3 ± 13.4	+7%	0.30
Logical Memory Delayed***	12.2 ± 7.9	16.5 ± 3.7	+35%	0.11

†Still significant after correction for multiple comparisons.
*Number of animals named in 60 seconds.
**Number of correct answers in 120 seconds.
***Number of correct details of a recalled story out of 25.

DISCUSSION

The purpose of this pilot study was to determine for the first time if a mind/body medical practice could improve cognition in subjects with memory loss. In this case a brief, simple, and low cost meditation practice called Kirtan Kriya performed for only 12 minutes daily over an 8-week period of time revealed positive results in both functional neuroimaging changes as well as an improvement in cognitive function in people with memory loss, including those with age-associated memory impairment and MCI.

Thus, this study was unique in attempting to measure the longitudinal effects of meditation using functional brain imaging with SPECT in an older population than previously studied, especially those patients already suffering from memory loss. It is important to note that the subjects in general found the meditation practice enjoyable and beneficial. The subjects were compliant, performing the practice a mean of 75% (range from 41% to 100%) of the days that they were in the study, and indicating that they were able to perform the practice successfully. However, the one AD patient with an MMSE of 16 had great difficulty performing the meditation and when she returned for the 8-week follow up, was unable to perform the meditation properly. While her data were excluded from the analysis, it also raised an important issue that once subjects become too impaired, meditation may not be possible. For the remaining subjects, there was no clear relationship between those with varying degrees of cognitive impairment, although these subjects were in a much

narrower range with MMSE scores from 24 to 30. Most subjects indicated that they perceived that their cognitive function was improved after the 8-week program. Furthermore, the results of the imaging and neuropsychological testing revealed that subjects did experience significant changes during the 8-week training period.

In the study presented here, there were several significant changes in baseline CBF associated with the 12 minute daily KK meditation training program. For example, there were significant increases in CBF in the frontal cortex that aid in attention and executive function. This finding is particularly significant 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 as well as MCI [24–26].

It is interesting that the changes in baseline and activated states of the brain were in very different structures in the KK group compared to the music group. This, of course, is consistent with the fact that the two groups were doing different types of tasks. The activated states, in particular, were quite different with the KK group showing significantly decreased CBF in the prefrontal cortex during meditation after the training program. While the findings in the music group were not significant after multiple comparisons, the regions that were significant before correction, namely the amygdala and the thalamus, have also been observed to be affected in research studies evaluating listening to music on the brain [27–29].

It is a particularly interesting finding that the areas activated by music (such as the limbic and posterior

structures) are different from those involved in the KK meditation (namely the frontal cortex and superior parietal lobe). The initial hypotheses regarding KK meditation is that it should have had its primary impact on the frontal cortex. It is also interesting to note that the frontal lobes, superior parietal lobes, and posterior cingulate are also part of the brain's default network and have been observed to be substantially different in patients with memory deficits associated with normal aging, MCI, and AD [30,31]. This suggests the possibility that the KK practice has an effect on this default network over time.

There were also improvements in cognitive function in the KK group as revealed by neuropsychological testing. These changes were significant in verbal fluency, although the KK group did not achieve results that were statistically better than the music group in the other neuropsychological tests. The KK group did show trends in improvement in several other tests including the Trails B, WAIS Symbol Substitution Test, and Logical Memory Delayed task.

As this is a pilot study, there are many limitations that need to be considered and that will need to be addressed before being able to definitely state that meditation practices provide a cognitive benefit in older individuals. For example, it could be argued that the music group was also performing a "meditation-type" task and thus, might not have been as appropriate a control group as possible. In fact, several studies have observed a beneficial effect of listening to music on cognitive function and our data show improvements although they were not significant, possibly because of the small sample size. Emery and colleagues showed that exercise plus music resulted in improved verbal fluency compared to exercise alone [32]. Another study showed the music therapy resulted in improvements in verbal fluency in dementia patients [33]. Thus, it is possible that this music listening group might be considered an active intervention group as well, in which case both KK meditation and music resulted in improvements in cognitive function in these patients, but appeared to be associated with different physiological correlates.

It should be noted that determining the appropriate control comparison group for meditation practices is always a challenge since it is difficult to select a particular intervention (i.e., solving puzzles, doing spatial tasks, reading, etc.) that would not have some component of improving cognitive function. Furthermore, doing a simple test-retest group would not represent any intervention and thus might also not sufficiently control for

a placebo effect or a practice effect. It should also be stressed that a major limitation of this preliminary study is the size of the music comparison group and future studies evaluating music as well as other types of meditation might be useful in determining the most effective types of interventions. Thus, larger trials are necessary to determine whether music itself has a beneficial effect on cognition, as well as recruiting intervention groups of more similar sizes. In particular, it will be important to have more uniform groups, such as studying only patients with MCI, to help evaluate specific changes in both brain function and neuropsychological status.

While it was also interesting to find a correlation between the change in prefrontal cortex CBF and improvement in the Trails B test, the pilot nature of this study limits any definitive statement about such a relationship. While such findings at least support the notion that the physiological changes associated with meditation may be related to improvements in cognition, larger studies will be necessary to confirm such correlations.

As a pilot study, the data do provide important information regarding general effect sizes and the standard deviation for CBF changes and neuropsychological test changes associated with a meditation practice that might have implications for powering future studies. Of course, an important issue would be what the primary outcome measure would be for future studies – imaging or neuropsychological outcomes. That the baseline brain activity, particularly in the frontal cortex, was increased after eight weeks of meditation practice supports the hypothesis that meditation may affect brain function over longer periods of time. Of course, it is also known that cognitive decline with aging or with MCI is slower than that for AD patients. Thus, the current study does not address whether meditation will actually have long term benefits for slowing that decline with either normal aging or MCI. On the other hand, these findings provide a hypothetical basis for future studies exploring the effects of meditation techniques on memory and cerebral activity by indicating which brain structures are likely involved and also provided information regarding the effect size and variability of specific measures.

We also recognize that the use of complementary and alternative medicine techniques in the management of aging and dementia is still controversial. There have been few large scale studies and most data, including the current study, must be viewed as preliminary. However, we also hope that the results of studies such as this one will help to foster a greater interest within the

medical community to explore such techniques. Even if techniques such as meditation prove to have only a small value, their low cost and ease of use may make them a beneficial adjunct to the pharmacological arsenal currently being explored. Thus, we hope that future studies with a larger population size, different comparison groups, and a larger battery of neuropsychological tests, would be able to advance the findings from this initial study.

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