Meditate Don't Medicate: How Medical Imaging Evidence Supports the Role of Meditation in the Treatment of Depression

Abstract:

Introduction

Depression is a debilitating psychiatric disorder that affects a large proportion of the population. The current treatment for depression involves anti-depressant medication which is associated with side effects and a heightened risk of relapse.

Methods

A systematic literature review was performed to determine the value of medical imaging studies in measuring the impact of meditation on depression.

Results

Medical imaging studies have successfully demonstrated that meditation may counteract or prevent the physiological cause of depression by decreasing amygdala activity and increasing grey matter volume and activity of the hippocampus, prefrontal cortex and other brain regions associated with attention and emotional self-regulation. Recent advances in functional imaging have enabled visualisation of neural plasticity within the brain. This has shown that for meditators, practice-induced alterations could be due to micro-anatomical processes that may represent an increased functional capacity within the brain regions activated. These changes within brain physiology in association with the skills gained during meditation such as self-regulation, mental processing of negative information and relaxation techniques could potentially lead to a permanent cure for depression and thus prevent relapse.

Conclusions

The results of this review suggest that medical imaging has a valuable role to play in evidencing the physiological changes within the brain caused by meditation that counteract those that cause depression. These studies indicate that meditation is a viable alternative to medication for clinical treatment of patients with depression. More rigorous longitudinal imaging studies are proposed to enhance understanding of the neural pathways and mechanisms of meditation.

Keywords

Depression, Diffusion Tensor Imaging, Magnetic Resonance Imaging, Meditation

Introduction:

For thousands of years, many religions have encouraged believers to use the ancient spiritual practice of meditation to improve concentration, calm the mind and promote inner peace and well-being. Science on the other hand, values above all else the investigation of truths where results are based on discoveries and evidentiary proofs that can be replicated by peers experimentally. This literature review attempts to marry these 2 paradigms to determine the value of medical imaging in measuring the impact of meditation on depression.

Depression is a medical illness that affects how an individual feels, thinks and acts. It is a condition that causes a persistent feeling of sadness and loss of interest and is one of the most prevalent and debilitating psychiatric disorders.[1] In 2008, the Australian Bureau of Statistics reported that depression affected one million Australians and further stated that one in seven people will have depression at some point in their lives.[2] Beyond Blue, an Australian organisation documented that depression-associated disability cost the Australian economy $14.9 billion annually and over $600 million each year for the cost of treatment.[3]

Long-standing evidence links depression with changes in the levels or activity of certain chemicals or areas within the brain. In particular a reduction of available monoamine neurotransmitters including serotonin (5-HT), norepinephrine (NE) and dopamine (DA) induces depression.[4,5] From these findings, clinicians have resorted to treating depression with medication such as selective serotonin reuptake inhibitors (SSRIs).

The pharmacological treatments for depression are often accompanied by side effects including nausea, agitation, dizziness, drowsiness, weight fluctuations and headaches.[6,7] Medications for depression commonly suppress the reuptake of serotonin and/or noradrenaline in the synaptic cleft between nerves.[7] In particular this enhances neurotransmission in key structures such as the amygdala and the hippocampus; areas where reductions in serotonin and noradrenaline play a central role in the pathogenesis of depression. Medications that improve depressive symptoms also promote neurogenesis in the hippocampus and reverse depression related atrophy however they also replace the function of the pre-frontal cortex (PFC) leading to atrophy. The fact that adult hippocampal neurogenesis is impaired by stress and facilitated by antidepressant medication suggests that neurogenesis may play a critical role in the pathogenesis of depression.[6] Chronic depression and other syndromes that are characterised by high levels of glucocorticoids (such as anxiety disorders) are associated with hippocampal volume loss that is proportionate to the duration of illness, independent of age.[8] Unfortunately antidepressant medication is symptom-

suppressive rather than curative due to the loss of PFC function and thus used indefinitely to prevent relapse. There is no published evidence to suggest that antidepressants reduce further risk of depressive episodes once treatment is terminated which suggests that causal mechanisms of depression are unchanged. This leaves patients with an elevated risk for subsequent episodes of depression.[9] Thus alternative treatments such as meditation have recently been investigated to treat depression.

Meditation is an ancient spiritual practice used to gain insight and to transform consciousness. This has been done through introspectively observing one's own emotions as well as focusing attention on the here and now. It aims to still the fluctuations of the mind through cognitive function and improve concentration, mental clarity and help discriminate emotions.[10,11] Meditation is an increasingly popular treatment for individuals with depression.[12] Although there are many different types of meditation, each form aims for inner peace and to still the fluctuations of the mind. Most of the recent clinical therapeutic interventions utilise Mindfulness Meditation, which originated in India as part of Theravada and Mahayana Buddhist meditation practices.

Developments in neuroimaging technologies such as structural magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), as well as functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and single photon emission computed tomography (SPECT) have enabled investigation of the biology and neuroscience of meditation. While functional studies have identified areas of the brain that become activated during the act of meditation, structural studies have been able to demonstrate areas of the brain which have responded with neurogenesis and neuroplasticity. Although there are many regions of the brain that are potentially affected by meditation practices, the scope of this literature review will only address those regions involved in the structural and functional changes seen in people with depression. The review aimed to determine the role of medical imaging in measuring the efficacy of meditation for the treatment of depression.

Methods

A literature search was undertaken in 2014 within Scopus, Web of Science, ScienceDirect and Pub Med for relevant English language publications from 2000 onwards when functional imaging started to become more widespread. Table 1 summarises the search strategy. Other journal articles were located from citation lists. A 2-stage screening approach was utilised to select and categorise appropriate evidence. Initially abstract review was performed to ensure the inclusion criteria were met and to exclude published "abstracts only", letters and comments, case reports

and animal studies. Following this, a full-text article screening was performed to ensure relevance of content. For inclusion articles must have reported outcomes measured by medical imaging procedures related to treatment of depression with a meditation-based intervention. There were no limitations on study design, although publications that were clearly derived from an identical patient dataset were excluded. Critical review and scoring of the resulting selected articles was performed independently by 2 researchers to reduce observer bias. A structured approach to critical review was utilised based on the SIGN critical appraisal checklists[13]. Subsequent thematic analysis identified key themes arising within the selected evidence. Ethical approval was not required given that no primary research was conducted.

Results

A total of 51 studies were located vai the search strategy; the screening and critical appraisal process resulted in 12 structural and functional studies being passed for analysis. Table 2 summarises the characteristics of the included studies. The evidence clearly identifies the structures within the brain that consistently exhibit increased grey matter volume and density in meditators. Although the types of meditation used varied across the studies the results from all studies were consistent irrespective of meditation style. The responding structures are found within the limbic system, and include PFC, amygdala and hippocampus. Since patients with depression are found to have neurotransmitter degradation or decreased reuptake of serotonin, noradrenaline and dopamine within these structures, the review findings drawn from appraisal of all the included studies have been structured around them.

Discussion

Pre-Frontal Cortex

One of the major functions of the PFC is executive cognitive function, and as part of this it moderates the activity of the amygdala. Thus, when the PFC is dysfunctional and the normal suppressive activity is absent or reduced, the amygdala becomes hyperactive, leading to depressive symptoms.[6] One of the ways antidepressants reduce depressive symptoms is by imitating the PFC function, and thus suppressing an overactive amygdala. A pioneering 2005 study used MRI to compare cortical thickness between meditators and a randomly selected and matched cohort of non-meditators.[14] When the images of the two groups were compared, it was found that particular areas of the brain, including the PFC, in long term meditators were thicker than in non-meditators. Functional imaging studies using PET, SPECT and fMRI confirm this increase of cortical thickness is consistent with repeat activations of these structures. Several functional studies further demonstrated functional activations of the PFC, right insula or left temporal gyrus.[15-19] This is consistent with suggestions that meditation could promote neural plasticity in regions that

are routinely engaged during the meditative practice.[14] SPECT studies detected an increased regional cerebral blood flow during meditation of eight Tibetan Buddhists with greater than 15 years' experience compared to controls.[17,19] Other functional studies also consistently demonstrated activation of the PFC in meditators.[10,15,16,18]

Right Amygdala

Studies involving pre and post functional neuroimaging studies of depressed patients treated with SSRIs have shown a possible inhibition of the amygdala and other limbic regions.[20] A 2004 fMRI study found that symptom decreases due to SSRI medication caused functional decrease in amygdala activity.[21] Desbordes' 2012 study monitored longitudinal effects of meditation on the amygdala by using fMRI, where participants were imaged while being presented photographs of people in a variety of settings. The photographs were designed to elicit a range of positive, negative and neutral emotional responses from the participants.[22] FMRI images were taken three weeks before the eight-week mindfulness program commenced and again three weeks after the intervention. Meditators and non-meditators did not show any significant difference before the intervention. The authors found that mindfulness training reduced right amygdala response to emotional stimuli even while participants were not meditating indicating a change in brain function in a non-meditative state. This suggests that meditation can improve emotional stability and response to stress with enduring beneficial changes in brain function, in particular those areas concerned with emotional processing. Holzel conducted a study on participants who complained of high levels of stress during the previous month.[23] MRI was used to image participants 1 week before an 8-week mindfulness-based stress reduction (MBSR) intervention and then 2 weeks after. The authors found a significant reduction in stress levels as measured on the Perceived Stress Scale and a significant statistical decrease in right amygdala grey matter density ($p = 0.042$).

Hippocampus

The hippocampus is responsible for emotional memory and sensory function, modulates amygdala activity and is involved with attention and emotional processes; studies have linked hippocampal volume loss with depression through MRI.[8] Alterations of neural networks involving the hippocampus have been associated with impaired emotional processes, memory and executive functions in major depression.[24] An interesting MR imaging study in 2009 compared 22 long-term practitioners of different meditation traditions with a control group of 22 people who were matched for gender age and duration of education.[25] It should be acknowledged that additional factors such as prior stress levels, socio-economic and employment were not considered in this study. Their results were consistent with the findings of an earlier matched comparison study on the effects of mindfulness meditation on brain structure.[26] A region of interest (ROI) analysis demonstrated

statistically significant increases in density of the right hippocampus ($p = 0.027$) and right insula ($p = 0.022$) when comparing meditators to non-meditators. The same authors' 2011 follow up study found an increase in grey matter of the hippocampus.[27] The findings of this study are consistent with Lazar's earlier work as it further demonstrated an increase in the grey matter density of the hippocampus suggesting its activation during meditation.[14,16,18]

A 2009 longitudinal study investigated 16 meditation-naive participants as they underwent an 8-week MBSR course.[23] Participants were scanned prior to commencing the course and again upon completion. The data confirmed increased size, thickness and density of grey matter in the left hippocampus and left inferior temporal lobe. The improvement in Perceived Stress Scale scores after the eight-week program correlated with decreased grey matter concentration within the amygdala. The changes were similar to those seen following the administration of an antidepressant for the treatment of depression. These longitudinal studies may provide some evidence to reject the hypothesis that people who undertake meditation have a predisposed neural configuration. Interestingly, an earlier longitudinal study found that over a 3-year period, depressed patients who were treated with antidepressants showed increased hippocampal volumes (normalised) with positive effects on emotion.[28] Thus, increased activity of the hippocampus as a result of meditation may assist in treating patients with depression and provide a more permanent solution to treating this illness. Subsequently, functional studies demonstrating the relationships and connections of these structures should be further analysed in separate studies using DTI in conjunction with fMRI.

Other Structures

The newest medical imaging modality utilised to investigate the effects of meditation is DTI. A 2012 study investigated the white matter fibre characteristics in a well-matched sample of long-term meditators and controls.[29] The results showed increased structural connectivity in meditators compared to controls throughout the entire brain. Studies that support these findings showed meditation-induced changes only a month after training.[27] These correlations suggest that the effects are a result of meditation rather than a pre-disposed brain network that draws individuals to meditative practice. Although investigations involving DTI are still in their infancy, they do provide a useful context for considering how meditation practices may influence regional cerebral macro and microstructure. More importantly, the establishment of connections within the brain structures provides some evidence of the effects of meditation, which support a clinical role for treating depression.

Limitations of the Evidence Base

Some variation in findings reflects potential limitations arising from inconsistencies in methods. These include poor methodological rigour such as the variability in meditation tradition in combination with other interventions and the small sample sizes common to alternative therapy studies. A brief summary of these methodological issues is presented in Table 2; these frustrate attempts at detailed meta-analysis and future studies should utilise larger cohorts and stronger control to increase confidence. Longitudinal assessment studies tracking meditators from initial practice to expert would help identify the correlates of brain function with specific forms of meditation. The time spent meditating and levels of experience may have affected the results as it is possible that more experienced meditators have already undergone the physiological changes in brain neuroplasticity as a result of meditative practice.

Another limitation for these studies may include the medical imaging modalities used. For example, the noisy physical environment of an fMRI scanner may have affected the individual's ability to relax and attain the required subconscious state. This could have altered the results for studies that used fMRI scans where the sample was imaged during meditation.[10] Other limitations based on imaging methods apply to PET and SPECT studies which demonstrate decreased spatial resolution when compared to MRI as a result of the image acquisition techniques.[30]

Conclusion

All the studies within this review demonstrated a clear role for medical imaging in measuring the benefits of mindfulness meditation for promoting key physiological changes in structure and function of the human brain. Moreover, these studies confirm that the resulting decreased grey matter of the amygdala and increased grey matter of the hippocampus and prefrontal cortex can counteract the dysfunction of these structures in depressed patients.

Meditation is free from side effects, is highly cost effective and once learned, can be practiced independently at no cost to the patient, while helping to minimise relapse. From the physiological evidence provided by medical imaging, it can be proposed that meditation could be clinically applied to patients suffering from depression. Longitudinal functional medical imaging studies demonstrate that the meditation induced structural changes in brain physiology result from repeat activations. This literature review does provide good evidence for continued use of medical imaging techniques to measure neuroplasticity within the brain arising from meditation.

The findings further suggest that techniques such as correcting maladaptive thinking and emotional processing in meditation induce permanent structural changes and thus may reduce relapse. This is a promising finding as current antidepressant medication has negative side effects and is recommended for indefinite use to prevent relapse. Future medical imaging studies should include larger sample sizes, longitudinal studies and limit the form of meditation practice undertaken by the sample. It is recommended that these aim to identify the most appropriate meditation tradition to best treat the brain physiology within depressed patients and map the stages at which change occur.

The demonstrated structural and functional changes in areas of the brain associated with both stress and the onset of depression evidenced by a range of medical imaging modalities support the use of meditation in helping treat depression and prevent relapse. This, combined with self-perceived reductions in stress felt by meditators, upholds the validity of meditation as a modality for improved health and for the treatment and prevention of depression.

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Table 1: Search terms

Population	Intervention	Comparison	Outcome
Depression	Meditation Mindfulness	(not searched but must have a control group)	Medical imaging Neuro imaging fMRI SPECT

Table 2: Included study characteristics

Paper	Design	Cohort	Style	Timing	Imaging	Measure	Critical appraisal
Lazar et al. (2005)	CC	15 C 20 M	MF	9.1 +/- 7.1 years	MRI	Cortical thickness	"Acceptable" Small sample size
Newberg et al. (2001)	CC	9 C 8 M	TIB	>15 years; 1hr daily 5 days /week	SPECT	ROI Analysis	"Acceptable" Small sample size Unclear matching control
Engstrom et al. (2010)	CC	0 C 8 M	SM	<2 years	fMRI	ROI Analysis	"Acceptable" Small sample size No controls Experience of meditators
Newberg et al. (2010)	CC	14 C 12 M	VAR	>15 years; 30–60 mins daily	SPECT	ROI Analysis	"Acceptable" Small sample size Previous study cohort Varied styles
Desbordes et al. (2012)	RCT	12 C 12 M 12 CBC	MF CBC	8 weeks; 140 mins daily	fMRI	ROI Analysis	"Acceptable" Imbalance of male : female ratio
Holzel et al. (2009)	LONG	0 C 27 M	MF	8 weeks	MRI	ROI Analysis	"Good" Some poor control
Luders et al. (2009)	CC	30 C 3 M	VAR	5-46 years	MRI	Functional Anisotropy	"Good"
Holzel et al. (2011)	RCT	17 C 16 M	MF	8 weeks; 27 mins daily	MRI	ROI Analysis	"Good"
Holzel et al. (2008)	CC	20 C 20 M	MF	8.6 years (2 hours daily)	MRI	Voxel Based Morphometry	"Good"
Luders et al. (2012)	CC	30 C 30 M	VAR	5–46 years	MRI + DTI	Point Wise Thickness	"Acceptable" Some age-related changes

Key:
C = number in the control cohort
CBC = Cognitive Based Compassion
CC = Case control
DTI = Diffusion Tensor Imaging
fMRI – Functional Magnetic Resonance Imaging
LONG = Longitudinal Study
M = number in the meditation cohort
MF = Mindfulness
MRI = Magnetic Resonance Imaging
RCT = Randomised Controlled Trial
ROI = Region of Interest
SM = Silent Mantra
SPECT = Single Positron Emission Computed Tomography
TIB = Tibetan Buddhist
VAR = Various