BRAIN ACTIVATION CHANGES DURING rsfMRI FOLLOWING BRIEF MINDFULNESS EXERCISE: AN fMRI STUDY

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by

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LIST OF SYMBOLS

H_0,	Null hypothesis
H_1,	Alternative hypothesis
δ	Effect size
α	Alpha-value
$\mu_{\mathcal{D}}$	Means between the experimental and control condition
0	Mean difference under the null hypothesis
σ	Variability in the mean difference
E	Experimental condition
C	Control condition
F	F-statistics
t	t-statistics
σ_W	Intrasubject variability (within-scan)
σ_B	Subject-to-subject variability
N	Population size
n	Sample size
%	Percentage
T	Total ranks
U	Mann Whittney U-test
Z	z-score
kE	Cluster level
r_s	Spearman's Rho
p	p-value

LIST OF ABBREVIATIONS

AAL	Automated Anatomical Labelling
ACC	Anterior cingulate cortices
ACT	Acceptance and Commitment Therapy
AD	Alzheimer’s disease
ANOVA	Analysis of Variance
ART	Artefact Detection Tools
BA	Brodmann’s areas
BOLD	Blood-oxygenation-level-dependent
CEN/ECN	Central executive network/Executive Central Network
COVID-19	Coronavirus 2019
CSF	Cerebrospinal fluid
CT	Computed Tomography
DAN	Dorsal Attention Networks
DBT	Dialectical Behavior Therapy
DLPFC	Dorsolateral prefrontal cortex
DMN	Default mode network
DTI	Diffusion tensor imaging
EEG	Electroencephalography
EHI	Edinburgh Handedness Inventory
EPI	Echo-planar Imaging
FC	Functional connectivity
FFMQ	Five Facets Mindfulness Questionnaire
FFX	*Fixed-effect* Analysis
fMRI	functional Magnetic Resonance Imaging
GCP	Good Clinical Practice
GLM	General linear model
GM	Grey matter
ICH	International Conference on Harmonization
IPC	Inferior parietal cortex
IQ	Intelligence quotient
JEPeM-USM	Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia

LORETA	Low-resolution brain electromagnetic tomography
MAAS	Mindfulness Attention and Awareness Scale
MBCT	Mindfulness-Based Cognitive Therapy
MBSR	Mindfulness-Based Stress Reduction
MEG	Magnetoencephalography
MMAAS	Malay Mindfulness Attention and Awareness Scale
MNI	Montreal Neurological Institute
MPC	Mean phase coherence
mPFC	Medial prefrontal cortex
NIRS	Near Infrared Spectroscopy
NOV	Number of voxels
PANAS-X	Positive and Negative Affect Schedule- Expanded Form
PAR-Q	Physical Activity Readiness Questionnaire
PCC	Posterior cingulate cortices
PCU	Precuneus
PET	Positron Emission Tomography
PIS & CF	Patient or Participant Information Sheet and Consent Form
rsfMRI	resting-state functional Magnetic Resonance Imaging
SD	standard deviation
sMRI	structural Magnetic Resonance Imaging
SN	Salience network
SOPs	Standard Operating Procedures
SPM 12	Statistical Parametric Mapping 12
SPSS	Statistical Package for Social Sciences
STG	superior temporal gyrus
TE	echo time
TMS	Transcranial Magnetic Stimulation
TNPs	Task-positive networks
VAN	repetition time
VARETA	Ventral attention networks
WHO	World Health Organization
WM	White matter

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PERUBAHAN PENGAKTIFAN OTAK SEMASA rsfMRI BERIKUTAN LATIHAN KESEDARAN RINGKAS: KAJIAN fMRI

ABSTRAK

Pengenalan: Kesedaran melibatkan pengawalan tahap perhatian kepada deria rasa dan memupukkan penerimaan terhadap pemikiran. Dalam penyelidikan ini, penyelidik berminat untuk meneroka perubahan aktiviti otak pada keadaan rehat pengimejan resonans magnet kefungsian (rsfMRI).

Objektif: Tujuan penyelidikan ini adalah untuk merakamkan perubahan aktiviti otak ketika rsfMRI sebelum dan selepas latihan ringkas kesedaran dan buku audio. Selain itu, untuk juga menentukan hubungan antara ciri kesedaran peserta dengan perubahan dalam pengaktifan otak selepas latihan ringkas kesedaran dan buku audio.

Metodologi: Enam peserta, umur dalam lingkungan 20 hingga 32 tahun (M= 23.33; SD= 4.309) telah direkrut melalui iklan di Universiti Sains Malaysia. Reka bentuk kajian ini adalah reka bentuk kuasi-eksperimen. Alat neuroteknologi pengimejan resonans magnetik berfungsi (fMRI) digunakan untuk mengenal pasti bahagian pengaktifan otak. Bilangan subjek yang sama dibahagikan kepada kumpulan buku audio ringkas (kawalan) dan kumpulan kesedaran ringkas (eksperimen). Selepas proses saringan, set soal selidik yang terdiri daripada demografi, Physical Activity Readiness Questionnaire (PAR-Q), Edinburgh Handedness Inventory-Short Version (EHI), Malay Mindfulness Awareness and Attention Scales (MMAAS) and Positive and Negative Affect Schedule - Expanded Form (PANAS-X) telah diisi.

Hasil Kajian: Bagi MMAAS, peserta dalam kumpulan buku audio ringkas menunjukkan ciri kesedaran yang lebih tinggi berbanding kumpulan kesedaran ringkas. Dalam kumpulan kawalan, pengaktifan otak yang lebih tinggi diperhatikan dalam girus sudut kanan dan kiri, precuneus kanan, girus temporal tengah kiri dan girus frontal tengah kiri. Dalam latihan kesedaran ringkas, peningkatan pengaktifan ditemui pada precuneus kiri, girus frontal superior kanan dan kiri, girus temporal tengah kanan dan girus frontal medial superior kiri. Tiada korelasi yang ketara bagi MMAAS dan kebergantungan isyarat resonans magnet kepada aras kepekatan oksigen darah (BOLD), iaitu peratus perubahan isyarat diperhatikan dalam kumpulan buku audio, dan, korelasi yang ketara dalam girus sudut kanan dan antikorelasi dalam gyrus temporal tengah kanan dilihat dalam kumpulan kesedaran.

Kesimpulan: Penemuan ini mencadangkan bahawa saiz sampel yang lebih besar diperlukan untuk meningkatkan margin ralat. Kumpulan latihan kesedaran ringkas menunjukkan pengaktifan yang ketara dalam girus sudut kanan dan dalam girus temporal tengah kanan memfokuskan dalam Rangkaian Mod Lalai (DMN) berdasarkan analisis kumpulan *fixed-effect* (FFX). Ini membuka jalan untuk menggabungkan rangkaian keadaan rehat yang lain kepada DMN dalam penyelidikan masa depan untuk meneroka dengan lebih baik pengaktifan otak asas yang tepat dalam DMN dalam kajian kesedaran.

Kata kunci: Latihan kesedaran, DMN, rsfMRI, isyarat BOLD, MMAAS, peserta sihat

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ABSTRACT

Introduction: Mindfulness is a practice involved in the volitional shifting of attention from the present moment to sensations. In the current study, the researcher is interested in performing rsfMRI on healthy participants to explore brain activation changes.

Objectives: The study aims to measure the changes in brain activation during rsfMRI before and after the brief mindfulness exercise and brief audiobook listening. Besides, to also determine the relationship between participants' mindfulness traits with the changes in brain activation after the brief mindfulness exercise and brief audiobook listening.

Methodology: Six healthy participants, age ranged from 20 to 32 years old (M= 23.33; SD= 4.309) were recruited through advertisement at Universiti Sains Malaysia. The research design of this study is quasi-experimental design. Functional magnetic resonance imaging (fMRI) neurotechnology tool is used to identify brain activations. An equal number of subjects were divided into the brief audiobook group (control) and brief mindfulness group (experimental). Upon screening process, a set of questionnaires consisting of the demographics, Physical Activity Readiness Questionnaire (PAR-Q), Edinburgh Handedness Inventory-Short Version (EHI), Malay Mindfulness Awareness and Attention Scales (MMAAS) and Positive and Negative Affect Schedule - Expanded Form (PANAS-X) were used.

Results: For MMAAS, participants in the brief audiobook group showed higher mindfulness traits compared to the brief mindfulness group. In the control group, higher activated brain activations were observed in the right and left angular gyrus, right precuneus, left middle temporal gyrus and left middle frontal gyrus. In a brief mindfulness exercise, increased activations were found in the left precuneus, right and left superior frontal gyrus, right middle temporal gyrus and left superior medial frontal gyrus. No significant correlation between MMAAS and blood oxygen level-dependent (BOLD) signals, which is the percent signal change is observed in the audiobook group, and, a significant correlation in the right angular gyrus and anticorrelation in the right middle temporal gyrus were seen in the mindfulness group.

Conclusion: These findings suggest that a larger sample size is needed to increase the margin of error. The brief mindfulness group showed significant activations in the right angular gyrus and right middle temporal gyrus focusing on the default mode network (DMN) based on group *fixed-effect* analysis (FFX). This paves the way to conjoint other resting state networks into DMN in future research to better explore the brain activations changes in DMN in mindfulness studies.

Keywords: Mindfulness, DMN, rsfMRI, BOLD signals, MMAAS, healthy participants

CHAPTER 1

INTRODUCTION

The default mode network (DMN) is an anatomical group comprising distinctive regions located within the brain; they produce synchronous patterns of activation under visualization of functional magnetic resonance imaging (fMRI) (Gusnard and Raichle, 2001; Oliveira-Silva et al., 2023; Raichle, M. et al., 2001; Simon and Engstrom, 2015). The DMN activity in healthy individuals does not associate with goal-dependent task-positive networks (TNPs) (Fox et al., 2005; Kelly et al., 2008). A wide range of psychological disorders is correlated with abnormal activity of DMN, for instance, antagonistic activation in TPN activity or connectivity alterations between different regions of DMN (Bastos-Leite et al., 2014; Camchong et al., 2009; Garrity et al., 2007; Liao et al., 2010; Pomarol-Clotet et al., 2008; Sun et al., 2023; Zhao et al., 2007). The DMN has been employed as a diagnostic biomarker to measure the severity of symptoms based on abnormalities (Simon and Engstrom, 2015). Thus, it is also suitable to be utilized as a metric to evaluate post-treatment response. For example, patients with schizophrenia produce high posterior DMN connectivity and activity and after receiving medication, their DMN activity presented a healthy functioning network (Ford et al., 2016; Hilland et al., 2022; Tregellas et al., 2011). In this study, the DMN activity patterns are analyzed using fMRI to study the effectiveness of mindfulness practice.

Mindfulness is termed as an experience of awareness in the present moment without being judgmental of the present moment (Xiao et al., 2019). Over the sustained mindfulness practise, there may have positive effects on the well-being of individuals. For example, in improving emotional regulation (Oliveira-Silva et al., 2023), mindfulness meditation can serve as an effective approach (Tang et al., 2016).

In the early stages, specifically, in mindfulness meditation, the emotional monitoring system related to executive functions and regulation of attention can be enhanced (Nakamura et al., 2021; Teper and Inzlicht, 2012). Probably reduced DMN activity would be observed to the attenuation of the mind-wandering process (Bozhilova et al., 2018).

Mindfulness is interpreted as the volitional shifting of attention directing to the present-moment attention, sensations and cultivating acceptance from mind-wandering. Many studies aiming to foster mindfulness practices have been developed in recent years (Guendelman et al., 2022; Parkinson et al., 2019). The practices of mindfulness had shown to produce positive effects on mental and physical health, reduction of stress levels (Brown et al., 2007; Gotink et al., 2016; Nakamura et al., 2021), regulation of emotions (Brown et al., 2007; Farb et al., 2012; Guendelman et al., 2022), self-esteem (Bajaj et al., 2016) and a decrease in depressive and anxiety symptoms (Chiesa et al., 2015; Gamaiunova et al., 2022). Dispositional mindfulness or trait mindfulness is the tendency to be attentive and to maintain attention at the present moment experiences without judgement in daily life. Trait mindfulness acts as the most relevant personality trait for meditation-based interventions. Individuals with high trait mindfulness tend to experience a frequent state of mindfulness (Brown and Ryan, 2006; Gamaiunova et al., 2022; Thompson and Waltz, 2007).

Before mindfulness meditation, data from subjects have been obtained through questionnaires about self-reflectivity of mindfulness: Malay version of Mindfulness Attention and Awareness-Scale (MMAAS). This will be the preliminary evaluation of mindfulness in an individual based on their acknowledgement and comprehension.

1.1 Problem Statement & Study Rationale

Various resting-state networks have been classified in the brain by diversified researchers known as functional connectivity, in which different cognitive abilities and clinical conditions are correlated with the range of associated activity in various regions of the brain (Broyd et al., 2009; Damoiseaux et al., 2006; Damoiseaux and Greicius, 2009; Raichle et al., 2001; Rosazza and Minati, 2011; Sun et al., 2023; van den Heuvel and Hulshoff Pol, 2010). The three most studied networks of functional connectivity are the default mode network (DMN), salience network (SN) and central executive network (CEN)(Michon et al., 2022); they are correlated with cognitive, emotional and attentional processes associated with both state and trait mindfulness (Bilevicius et al., 2018; Hasenkamp and Barsalou, 2012; Taylor et al., 2012). In a systemic review study by Syan et al. (2018), plenty of research is based on clinical populations and a few consist of healthy study samples as in the researcher's research interest. Besides, the duration of mindfulness in methodology, although short-term ranges from a few days to a few weeks (Serrat et al., 2022; Yang et al., 2019), but rarely in a day (within 24-hours) to even for a few minutes (less than an hour) experimental period has been conducted. Besides, the experimented group in other studies is based on meditation groups versus non-meditative groups. Therefore, the researcher is interested in conducting this study within 15-minute of brief mindfulness as in a brief audiobook exercise acting as an active control group. This study is conducted to further explore the brain activation changes during rsfMRI, either reduced or increased changes upon brief mindfulness exercise. In a study by Shaurya Prakash, De Leon, Klatt, Malarkey & Patterson (2012), they found that there is an association between mindfulness disposition with greater DMN connectivity in the dorsal posterior cingulate cortex (PCC) and the precuneus upon fMRI and the administration of the MAAS questionnaires without mindfulness activity. The study explored the associations between DMN integrity and mindfulness disposition trait levels of mindfulness disposition termed as an ability in the present moment to exert emotional and attentional control bringing awareness to immediate experiences. Therefore, in this study, researcher want to contribute to science knowledge by exploring the healthy sample group within a 15-minute brief period of mindfulness exercise.

1.2 Operational Definition

Default mode network (DMN): A network of interactions of the brain regions which is active when an individual is unfocused on the outer world and is measurable by the fMRI technique (Voelcker-Rehage et al., 2016).

Functional magnetic resonance imaging (fMRI): fMRI is a non-invasive technique measuring the blood-oxygenation-level-dependent (BOLD) signals endogenous contrast and allocating spatiotemporal patterns of brain activation regions in response to external stimulation (Blache and Maloney, 2017).

Mindfulness: Mindfulness is a practice in terms of volitional shifting of attention to the present moment attention to sensations and cultivating acceptance from mind-wandering (King et al., 2016).

Resting-state network: Resting-state networks are spontaneous brain activity defined by their functional connectivity in terms of metastability and synchrony by within-network cohesion and between-network integration involving salient network, default mode network and central executive network in internally guided and higher higher-order mental functions (Lee and Frangou, 2017).

1.3 Research Questions

a) Is there a difference in DMN activations between the brief mindfulness exercise group and the brief audiobook group?

Is there any relationship between the MMAAS scores and DMN in the brief mindfulness exercise and the brief audiobook?

1.4 Objectives and Hypotheses

General: To measure the changes in brain activation during rsfMRI before and after the mindfulness exercise and the brief audiobook.

Specific:

a) To measure and compare the brain activations in DMN after the brief mindfulness exercise and the brief audiobook

b) To determine the relationship between participants' mindfulness traits in MMAAS with the BOLD signals in DMN after the brief audio mindfulness exercise and the brief audiobook.

Hypothesis

H_0: There is no difference in brain activations in DMN after the brief mindfulness exercise and the brief audiobook.

H_1: There is a difference in brain activations in DMN after the brief mindfulness exercise and the brief audiobook.

H_0: There is no relationship between participants' mindfulness trait in MMAAS with the BOLD signals in DMN after the brief audio mindfulness exercise and the brief audiobook.

H_1: There is a relationship between participants' mindfulness trait in MMAAS with the BOLD signals in DMN after the brief audio mindfulness exercise and the brief audiobook.

1.5 Conceptual Framework

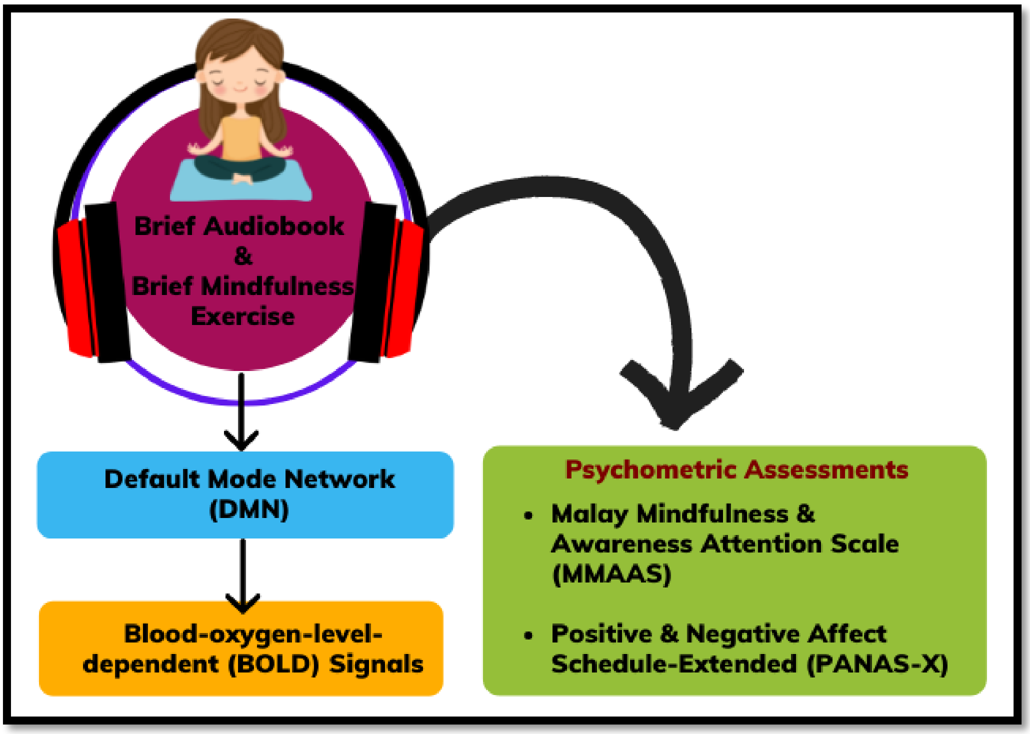

Figure 1: Conceptual framework of the changes in brain activation in DMN

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Brain activation is commonly quantified based on the regional blood flow using fMRI and those quantifications are visualized into the blood-oxygen-level-dependent (BOLD) signal. The brain in a resting state has become the foundation to measure specific tasks. During the activation of this baseline, the synchronic conduct of anatomic regions is monitored and identified as a task-specific deactivation network, also known as DMN (Gusnard and Raichle, 2001; Raichle et al., 2001). These task-specific deactivations of the DMN also yielded readings of consistent activation during the resting state. 60-80% of the brain's energy consumption contributes to the persistent low-frequency fluctuation in the resting state (Ma et al., 2022; Raichle and Mintun, 2006; Shulman et al., 2004) and initially, their significance was unaccounted for importance even though observations were recorded by most. The DMN receives the most extensive academic attention as the first of variously identified resting-state functional networks.

The DMN comprises specific nodes such as the medial prefrontal cortex (mPFC), anterior and posterior cingulate cortices (ACC & PCC), respectively, precuneus (PCU), inferior parietal cortex (IPC) and lateral temporal cortex (Raichle et al., 2001; Raichle and Snyder, 2007). Intensive fluctuations are exerted during functional tasks from the functional integration of these primary nodes. The vigor of the DMN has been proven in terms of functions (Gusnard and Raichle, 2001; Harrison et al., 2008; Raichle et al., 2001) and structure (Greicius et al., 2008; Raichle and Mintun, 2006; Shulman et al., 2004). There is an association between network activation and specific mentation of autobiographical memory, self-reflection (Sheline et al., 2009), prediction of possible future, mind-wandering (Mason et al., 2017) and processing thoughts and different perspectives (Buckner et al., 2008; Raichle, et al., 2001; Raichle and Snyder, 2007) On the Insert tab, the galleries include items that are designed

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2.1.1 The Foundation of Mindfulness

In psychiatry, practices of mindfulness and different techniques have been commonly adopted from Buddhism as forms of therapeutic mediation (Kirmayer, 2015). The practice of mindfulness that originated from Buddhism has been incorporated into Western therapeutic interventions for reducing stress, and anxiety (van der Velden et al., 2022), increasing the regulation of emotions and reducing possible symptoms of mental health disorders (Cavanagh et al., 2013; Farb et al., 2012; Parkinson et al., 2019; Tabak et al., 2015; Teasdale et al., 1995). Symptoms of various mental health disorders such as depression (Chiesa et al., 2011; Sun et al., 2023; van der Velden et al., 2022), bipolar disorder (Ives-Deliperi et al., 2013), anxiety disorders (Cavanagh et al., 2013; Müller et al., 2021; van der Velden et al., 2022), chronic disorders of dysphoria (Farb et al., 2012), obsessive compulsive disorders (Riquelme-Marín et al., 2022), chronic emotional pain (O’Connor et al., 2022) and borderline personality disorder (O’Connell and Dowling, 2013) have been reduced from therapeutic integration of mindfulness (Parkinson et al., 2019).

In general, there is a high interest in perceiving the foundation of mindfulness within clinical and non-clinical populations with perpetuating benefits. Psychological traits, cultivation of mindfulness, a state of consciousness or psychological process are commonly described by the word mindfulness (Keng et al., 2011). Based on the most renowned cited definitions, mindfulness is the concentration of the mind through "paying attention in a particular way: on purpose, in the present moment and nonjudgmentally" (Kabat-Zinn, 1994). Other researchers provided almost similar descriptions of mindfulness; mindfulness is the nonjudgmental observation of the current process of internal and external stimuli as one experiences them (Baer, 2003). There is an exclusive emphasis on the attentional perspectives of mindfulness (Brown and Ryan, 2003), but most studies tend to fluctuate towards the model of Bishop et al. (2004). There are two components of mindfulness proposed by Bishop et al. (2004): self-regulation of attention and adoption of a specific state upon an individual's experiences. In simpler terms, self-regulation of attention is a process of non-intricate observation in a state of acknowledging one's sensations, thoughts or emotions from moment to moment. Anchoring one's attention upon the current occurrence and purposely diverting attention between different perspectives upon what is occurring are required in this process. Attitudes of curiosity, open-mindedness and acceptance are correlated with inclination to experience (Cardaciotto et al., 2008; Oliveira-Silva et al., 2023).

The efficacy of interventions utilizing mindfulness in treating an extensive range of conditions is evident through the provision of systematic reviews and meta-analyses of the clinical experiment (Chiesa and Serretti, 2011; Hunot et al., 2014; Keng et al., 2011; O'Connor et al., 2022; Sedlmeier et al., 2012). Ahead of mental health treatment, mindfulness practices have been incorporated into various daily life activities of education, business, sports and other areas. In this aspect, mindfulness meditation is utilized to enrich cognitive functions (Müller et al., 2021), stress regulation, performance (Müller et al., 2021; Oguntuase and Sun, 2022) and prosperity (Chiesa et al., 2011; Zenner et al., 2014). Mindfulness-based psychological interventions arose from meditative techniques partially comprised of Buddhism, but there are various forms of meditation within Buddhism inclusive of other traditions (Goleman, 1977).

2.1.2 Mindfulness Practice in Devout Indoctrinations

One of the basic forms of meditation is vipassana (Goldstein, 1976). One is taught to focus their attention on breathing while using their mental will to observe every sensation, thought, or emotion passing through them (Goldstein, 1976). Clinical applications utilize mindfulness as a nonjudgmental observation deriving from vipassana meditation although the technique may integrate various practices. Jon Kaabat-Zinn (1982) developed mindfulness-based stress reduction (MBSR) at the Stress Reduction Clinic of the Massachusetts Medical Center in Worcester Massachusetts, deriving from Zen, Theravada Buddhism and Hatha yoga inclusive of Vietnamese Mahayana and Tibetan Buddhism. Buddhist roots and teachings of meditation are incorporated into MBSR to build a form of intervention that is comprehensible and adequate in every medical setting (Kabat-Zinn, 2011). Despite the intervention being introduced to treat chronic pain, the method holds less emphasis on the reduction of symptoms and is rather prominent in cultivating the patient’s attitude toward their disorder.

The application of mindfulness practice is evident through indoctrinations of Hinduism, Buddhism, Islam and Christianity, including the Middle Ages and modern era. Thus, mindfulness has become a vocation of clinical psychology through the human experience to resolve issues with intrinsic worth.

2.2 Modern Technologies of Mindfulness Interventions

The utility of mindfulness meditation in the psychiatric field was initiated when Jon Kabat Zinn studied possible treatments for patients with chronic pains using mindfulness meditation (Kabat-Zinn, 1982); the technique is now famously considered as Mindfulness-Based Stress Reduction (MBSR). Different interventions utilizing principles of mindfulness have also been established for treatments of a wide range of mental health disorders and chronic pain-inducing illnesses, such as Mindfulness-Based Cognitive Therapy (MBCT) (Hitchcock et al., 2022; Musa et al., 2020; Segal et al., 2002), Dialectical Behavior Therapy (DBT) (Flynn et al., 2021; Linehan, 1993; O'Sullivan et al., 2017) and Acceptance and Commitment Therapy (ACT) (Hayes et al., 1999; Huang et al., 2021; Knight and Samuel, 2022).

2.2.1 Mindfulness-based Stress Reduction (MBSR)

MBSR is a group-oriented intervention system that was established to treat patients with chronic pain (Kabat-Zinn, 1982, 1990). Intensive exercise of mindfulness meditation is provided by the program to assist individuals in perceiving their psychophysical conditions with acceptance and open-mindedness. The program comprises 8 to 10 weeks of courses requiring a group of 30 partakers to meet for instructions on mindfulness meditation in the span of two to two and a half hours per week (Kabat-Zinn, 1990). Additionally, the program also offers encouragement to participants to practice in home mindfulness meditation and join intensive mindfulness meditation refuge. The outcome of the meditation training ensures the participants cultivate acceptance and reduce judgment toward their experience and escape the habitual and dysfunctional forms of thinking and behaviour.

Various studies discovered that MBSR brings an impact on improving psychological functioning in different aspects. MBSR is known to reduce chronic anxiety disorders (Anderson et al., 2007; Guendelman et al., 2022; Shapiro et al., 1998), depressive disorders (Anderson et al., 2007; Grossman et al., 2010; Koszycki et al., 2007; Sephton et al., 2007; Shapiro et al., 1998; Speca et al., 2000), anger management issues (Anderson et al., 2007), rumination and possible delusion (Anderson et al., 2007; Jain et al., 2007). MBSR has shown an association with brain changes reflecting upon positive emotional states with fluctuations in activations of the left frontal, indicating dispositional and state positive effects (Guendelman et al., 2022; Janssen et al., 2018).

2.3 Resting-state Networks

Different qualities of trait mindfulness can be associated with the functional connectivity of resting-state networks within the brain (Parkinson et al., 2019). During an attentive breathing task, high activity is evident in the temporoparietal junction, superior parietal lobule and dorsolateral prefrontal cortex (DLPFC) for subjects scoring higher in measurements of trait mindfulness in comparison to those who scored lower (Dickenson et al., 2012). These regions of the brain are responsible for orientation and maintenance of attention; findings corroborating cognitive psychology studies proved there is an association between mindfulness and superior attentional capabilities (Quaglia et al., 2015; Quan et al., 2018). A comparison study was conducted between levels of trait mindfulness to activation of neural patterns during the affect labelling task and the results presented a reduction of amygdala response, widespread activation of the prefrontal cortex (PFC) and increased activity in the medial PFC (mPFC) are correlated with mindfulness (Creswell et al., 2007). Based on the scholars' interpretation, suggestions were drawn that higher trait mindfulness is associated with cortical regulation of limbic responses during affect labelling. The tendency to observe as a component of trait mindfulness has also been presented to estimate neural region activation when a subject is acknowledging their emotions. In a study where subjects were exposed to stimuli of positive and negative audio emotional vignettes, those with higher engagement in mindful observation induced large activation of the dorsomedial PFC (DMPFC) region than those with lower scores (Frewen et al., 2010). This proposed that mindfulness with involvement of the internal emotional reflection process requires the activation of DMPFC. A neuroimaging technique has been employed in a study to analyze the neural foundation of a trait which is known as the resting-state fMRI (rsfMRI) (Raichle, 2015). Although the subject will be conducting no task, impulsive neuronal activity through the brain persists. Prominently, the neuronal activity does not occur in a random pattern and relatively, the disparate structural regions of the brain show the correlation in which authors proposed they conjoined as a network (Damoiseaux and Greicius, 2009; Raichle, M. et al., 2001).

The DMN activity in healthy individuals does not associate with goal-dependent task-positive networks (TNPs) (Fox et al., 2005; Kelly et al., 2008). A wide range of psychological disorders is correlated with abnormal activity of DMN such as antagonistic activation during TPN activity or alterations of connectivity between different regions of the DMN (Bastos-Leite et al., 2014; Camchong et al., 2009; Garrity et al., 2007; Liao et al., 2010; Pomarol-Clotet et al., 2008; Zhao et al., 2007). These associations have led to the rising use of DMN analysis to understand mental health disorders (Whitfield-Gabrieli and Ford, 2012). The utility of the DMN is the most renowned alongside the study of Alzheimer's disease (AD) due to the overlapping regions between neuron loss and plaque deposition and the DMN (Broyd et al., 2009). The declination in metabolism and physiological disruptions induced by the plaque leads to a reduction in DMN activity and connectivity in patients with AD (Greicius et al., 2004). The DMN has been employed as a diagnostic biomarker to measure the severity of symptoms based on their abnormalities (Simon and Engstrom, 2015). Thus, it is also suitable to be utilized as a metric to evaluate post-treatment response. Patients with schizophrenia produce high posterior DMN connectivity and activity and after receiving medication, their DMN activity presented a healthy functioning network (Tregellas et al., 2011). Based on Figure 1, this study may also incorporate the DMN as a biomarker to specifically evaluate the post-treatment effects of mindfulness meditation. If the DMN activation pattern shows to be normal, then the results will prove that mindfulness meditation is effective as a treatment for clinical illness.

The DMN consists of nodes identified in the precuneus, posterior cingulate cortex, MPFC, lateral anterior temporal lobe and posterior parietal lobe. During the state of mind-wandering and self-reflection (e.g., flashbacks of the past or imagination of the future), there is an elevated activity in this network (Andrews-Hanna, 2011). Certain functions of this network oppose mindfulness. Insula and anterior cingulate gyrus are components of the SN; they contribute to the orientation of one's attention to external and internal occurrence according to sensory and limbic responses while facilitating functions between other networks (Bonnelle et al., 2012; Bressler and Menon, 2010; Seeley et al., 2007). Essential constituents of mindfulness are required by the SN to commence the functions such as the attentive focus of the moment and bodily self-acknowledgement. The CEN comprises nodes within the DLPFC, the ACC/DMPHC and the posterior parietal cortex. These regions are responsible for executing attentional regulation, language, memory and visual processes (Bressler and Menon, 2010; Rosazza and Minati, 2011). Mindfulness practice requires attentional control and thus, the CEN is associated with mindfulness.

Additionally, there are two other resting-state networks with less recognition by mindfulness scholars: the dorsal and ventral attention networks (DAN & VAN, respectively). Both are networks of frontoparietal regions that function during the orientation of sensory responses (Fox et al., 2006). Lateral PFC, posterior inferior parietal cortex and intraparietal cortex are components of the DAN. The DAN has direct involvement with voluntary orientation and maintenance of attention upon a location (Corbetta et al., 2008). It is classified as an objective-induced attentional network utilizing internal purposes or expectations to focus on sensory stimuli (Corbetta et al., 2008). The functions of DAN are directly correlated with mindfulness because mindfulness practice requires persistent attention. The VAN consists of nodes within the temporoparietal junction, anterior cingulate cortex (ACC) and anterior insula. The VAN is also an attentional network involving the recognition of significant surrounding information; nevertheless, this network depends on stimulus and serves to detect unexpected information (Corbetta et al., 2008). In comparison to the SN, the VAN is not dependent upon introspections to coordinate attention toward information in the surrounding. The central function of the VAN is linked to mindfulness requiring attention to the external surrounding.

Due to the absence of difficulty in signal acquisition and the ease of proficiency in recognizing the functional areas in various clinical populations, the rsfMRI technique captured the advantages over other techniques of fMRI. For instance, in the clinical population of paediatrics, low intelligence quotient (IQ), coma and unconscious or minimally conscious state patients (Soddu et al., 2011). Upon the contribution of study findings by Biswal and colleagues, rsfMRI was introduced in the clinical setting. The study showed that the signals in the resting-state are consistent fluctuations of low-frequency ranging from 0.01 to 0.08 Hz (Biswal, 2012; Raichle and Mintun, 2006). During the state of relaxation or resting, the human brain is in an operative condition. Discarded signals in task fMRI studies are accounted for as they are fluctuating spontaneously and are enclosed in the brain cortical network system (Fox and Greicius, 2010). To evaluate and analyse the brain functional areas, task-based fMRI is used. Participants in task-based studies will be instructed to execute specific tasks (Michon et al., 2022) related to sensory function, attention, memory, vision, language and motor task (Fox and Greicius, 2010; Kesavadas, 2013). The differences between rsfMRI and task-based fMRI techniques have been observed, although the BOLD contrast is the basic foundation behind both techniques applied (Fox and Greicius, 2010; Ma et al., 2022). Table 1 shows the contrast between task-based fMRI and rs-fMRI (Smitha et al., 2017).

Table 1: The contrast between task-based fMRI and rs-fMRI. Adapted from Smitha et al. (2017)

Rs-fMRI		**Task-based fMRI**
Paediatrics, low intelligence quotient (IQ), coma & unconscious/minimally conscious state	***Subjects' Conditions***	Cooperation is essential

Different due to task absence to avoid the task-related confusions & uncertainties by task-based fMRI	***Sessions (Repeated/Different)***	Repeated to assess the disease prognosis/treatment effect resulting in familiarity with the task affecting the output adversely
Acquired used to analyse one/more functions	***Function Analysis***	Separate tasks are required to analyse in terms of motor & language function
No need for more trials	***Result Interpretation***	A large number of trials required
Improved SNR as it takes the overall spontaneous low-frequency fluctuations	***SNR (signal to noise ratio)***	Low SNR due to discarding of the signal as noise
Discarded signals as noise in task fMRI are taken as signals in rs-fMRI as they are the low-frequency spontaneous fluctuations in the BOLD signals	***Signals***	During a task-related activity is very small compared to the noise (80% of the BOLD modulations are discarded as noise)
Resting-state brain activity is far more significant than task-related activity	***Brain Overall Activity***	During the task-based activity, the focus is only on a very small fraction of the brain's overall activity
60%–80% consumed	***Brain Energy***	Task-related increase in neuronal metabolism is <5%
In the absence of any explicit task/an input	***Analyses of the Spontaneous Modulations in the BOLD Signals***	In the presence of a particular activity (finger-tapping, eye-blinking, naming, memorizing)

2.3.1 Resting-state Structural Connectivity and Trait Mindfulness

A structural diffusion tensor imaging (DTI) study (Boekel and Hsieh, 2018) of the relationship between structural white matter density and trait mindfulness has shown a positive correlation in the corona radiata, external and internal capsule. The population group tested was middle-aged to older adults, therefore, reflecting trait mindfulness might hinder age-related neurocognitive decrease, maybe by forestalling age-related microlesions explicitly in cortico-subcortical white matter tracts. Zhuang and colleagues (2017) used both Mindfulness Attention and Awareness Scale (MAAS) and Five Facets Mindfulness Questionnaire (FFMQ) scores to measure trait mindfulness, which both scores correlated with different brain alterations. The facets of nonjudging and describing in FFMQ showed an association in the structural characteristics. Nonjudging facet related with an increased volume of the superior prefrontal cortex, whereas describing facet correlated with an increased volume of the left superior prefrontal cortex, right dorsolateral prefrontal cortex and the inferior parietal lobule. High scoring in the facets of nonjudging and describing has been explained to show an enhancement in emotional regulation and attention control. For MAAS scores, it was shown an increased volume of grey matter in the right precuneus, surrounding the posterior cingulate cortex. A higher level of awareness was interpreted with an increased volume of grey matter in the right precuneus.

2.3.2 Resting-state Functional Connectivity and Trait Mindfulness

According to the study by Bilevicius et al. (2018), within-network connectivity of the DMN was reduced, moderated by decreased connectivity between the left superior temporal gyrus and left medial frontal gyrus. A reduced level of mind-wandering was related to weaker connectivity within the DMN. This finding was bolstered by the correlation of FFMQ scores with reduced left inferior temporal gyrus, right superior temporal gyrus and bilateral medial temporal gyri activity (Parkinson et al., 2019). MAAS scores have been reported to be associated with increased functional connectivity between the anterior cingulate cortex and the insula, portrayed by a higher awareness of physical sensations. The elements of DMN, precuneus and cuneus, have been stated to have reduced functional connectivity with the CEN and SN (Bilevicius et al., 2018). Besides, another study by Lim et al. (2018) reviewed reduced functional connectivity between DMN and DAN, and, between DMN and SN. The authors hypothesized that task-ready states have higher involvement of DAN and SN networks, whereas the idling state has a weaker within-network functional connectivity of DMN to explain higher awareness and attention in high trait mindfulness individuals. Bolstered by Bilevicius et al. (2018), to aid in the detection of mind-wandering, it was proposed to have greater separation of the brain networks. However, Lim et al. (2018)'s study reported an inconsistent result of increased functional connectivity within DMN correlating with trait mindfulness.

2.4 Neuroimaging Techniques as Modalities

In the past 20 years, neuroimaging utility has risen from the advancement of computing technology, providing an in-depth comprehension of the mechanisms of the brain, inclusive of detecting causes of impairments. Neuroimaging defines a wide range of methods, technologies and non-invasive methods to produce structural and functional data of neural mechanisms. These include electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and near-infrared spectroscopy (NIRS); this procures functional information such as neural activity and cognitive functions. Others are inclusive computed tomography (CT), structural MRI (sMRI) and diffusion tensor imaging (DTI), yielding structural or anatomical information about the brain. There are additional methods to provide stimulation such as transcranial magnetic stimulation (TMS) and localizing source issues of EEG also including variable resolution electromagnetic tomography (VARETA), and low-resolution brain electromagnetic tomography (LORETA) (Tulay et al., 2018).

A neurodynamic study of EEG functional connectivity (FC) (Berkovich-Ohana et al., 2013) has been carried out to investigate the advantages of exploring DMN and the induced mindfulness meditation EEG-FC effect. The result depicted identified DMN activity as, during the resting-state transition to a time-production task, there is a reduction in overall inter-hemispheric gamma mean phase coherence (MPC). Induced mindfulness meditation increased in alpha MPC but decreased in traits in EEG-FC. Besides, in a systematic review of neurophysiology of EEG oscillations studies based on mindfulness (Lomas et al., 2015). It has been summarised that most commonly related to mindfulness are enhanced theta and alpha power in both clinical and healthy populations, with the comparison of eye-closed resting-state. In terms of delta, beta and gamma, no consistent patterns were observed. A state of relaxed alertness signifies the elevated theta and alpha.

In this study, the researcher is interested in performing rsfMRI on healthy participants based on a systemic review (Syan et al., 2018), most studies have been conducted in the clinical population but rarely in the normal population sample (Bandt et al., 2019; Eyler et al., 2019; Lee et al., 2018; Soehner et al., 2019). Besides, the duration of mindfulness was long-term and short-term up to a few hours (Lemmers-Jansen et al., 2019; Zeidan et al., 2019; Zeidan and Vago, 2016) or a few days (Taren et al., 2017), weeks (Chumachenko et al., 2021; Desbordes et al., 2012; Jain et al., 2019; Korponay et al., 2019; Kral et al., 2018) or even months (Sevinc et al., 2018; Weiss et al., 2020), but not yet in 1 to 15-minute period of mindfulness exercise, which makes this study beneficial.

CHAPTER 3

METHODOLOGY

3.1 Introduction

This study has been approved by Human Research Ethics Committee Universiti Sains Malaysia (JEPeM-USM) and assigned with a study protocol code of USM/JEPeM/21060419 (refer to Appendix J). JEPeM-USM complies with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

3.1.1 Research Design

Quasi-experimental design was used in this research to test out the procedure to see whether is there a difference in the BOLD signals in DMN before and after the brief mindfulness exercise and the brief audiobook. Besides, to determine whether is there a relationship between participants' mindfulness traits with the BOLD signals in DMN after the brief audio mindfulness exercise and brief audiobook. Participants have been given the Malay version of MAAS questionnaires (Zainal et al., 2015) to be completed (refer to Appendix E). The duration of data collection has been obtained over a short period, approximately one month. Two groups of participants have been randomly assigned to the audiobook book group acting as an active control group and the audio mindfulness group as the experimental group that has been experimented with in this study using fMRI.

3.1.2 Study Area

This research has been conducted at Universiti Sains Malaysia (USM), Health Campus at Kubang Kerian, Kelantan. Volunteering young adults who have been recruited through advertisement (Refer to Appendix A) have been approached and given a short briefing regarding the researcher's study and how is the data collected. Subjects have completed MMAAS and participated in the fMRI study upon briefing. Data has been collected in the MRI Suite, Department of Radiology, Hospital University Sains Malaysia, Kelantan.

3.1.3 Study Population

The study population is 8 Malaysian healthy young adults in the age range of 18 to 34 years old (Franssen et al., 2020) at Kelantan with a self-reported no chronic illness, history of trauma or fainting, neuropsychiatric illness, psychiatric illness, neurological disorders, hearing or visual impairments and no prior experience or exposure to mindfulness exercises.

3.1.4 Subject Criteria

Table 2 outlines the inclusion and exclusion criteria of participants included in this study.

Table 2. The inclusion and exclusion criteria of participants

Subject Criteria		
Inclusion	I.	Young adults
	II.	Age 18 to 34 years old (Franssen et al., 2020)
	III.	Able to read and write in Bahasa Malaysia and English
	IV.	Healthy
	V.	Malaysian
	VI.	Right-handed (Veale, 2013)

Exclusion	I.	Hearing and visual impairment based on self-report
	II.	Tattooed body
	III.	Inner piercings
	IV.	Diagnosed with psychiatric, chronic, neuropsychiatric and neurological illnesses
	V.	Metal implantation
	VI.	Pregnant
	VII.	Claustrophobic
	VIII.	History of head trauma or fainting
	IX.	Using sleeping aids or medications
	X.	Prior experience or exposure to mindfulness exercises

3.1.5 Sampling Technique and Subject Recruitment

Purposive sampling has been used in this study as the researcher made judgements when subjects are being selected. Subjects have been recruited voluntarily and required to present themselves at USM Health Campus in terms of advertisement (Refer to Appendix A). To answer the research goals, subjects must fulfil the inclusion and exclusion criteria (Creswell and Plano Clark, 2011) as in Table 2. Subjects had been given an incentive of RM50 each upon participation. Informed consent had been given to ensure the privacy and confidentiality of the participants. The handedness of the subjects was measured by the short version of the Edinburgh Handedness Inventory (EHI) (Refer to Appendix D) (Veale, 2013). Besides, the Physical Activity Readiness Questionnaire (PAR-Q) (refer to Appendix C)(Thomas et al., 1992) was required to be completed to ensure participants are healthy. Participant's demographic survey form (refer to Appendix B), MMAAS (Refer to Appendix E) and pre-Positive and Negative Affect Schedule-Expanded Form (PANAS-X) (refer to Appendix H)(Watson and Clark, 1994) questionnaires were completed by participants upon participation. Next, subjects were brought to be experimented with in the fMRI machine to obtain data. No task is given as the researcher will be only focusing on the resting-state brain activity of the subjects. Post-PANAS-X were given to participants to be completed for about 10 minutes. Since the population is self-reported, the researcher will not be conducting any confirmation assessment.

3.1.6 Sample Size Estimation

Power in statistics can be defined as the probability of rejecting H_0, which is the null hypothesis when false (Dorey, 2011). The major factors influencing power conducting experiments in behavioural sciences are the effect size (mean differences of control and experimental condition, and difference variability across subjects), the alpha value used (probability of rejecting H_0 when true) and the sample size (experimented subject number)(Desmond and Glover, 2002). The most prone to manipulation by researchers, out of these three factors, is the sample size (Desmond and Glover, 2002). Experimental design can impact the effect size, given differences in interest are out of the control of researchers. Increasing alpha, α can increase power when H_0 is false. If H_0 happens to be true, rejecting it poses an increased risk whereby it is reviewed as an intolerable outcome (Desmond and Glover, 2002). Power can be increased when the sample size is increased as the mean standard error decrease by $\sqrt{N}$ (Desmond and Glover, 2002). When the sample size is larger, there is a higher probability to reject H_0 when false. According to the formula below in terms of power calculation (Kraemer and Thiemann, 1987), of within-subject experiment depending on the effect size,