स्वामी विवेकानन्द योग अनुसंधान संस्थान

Swami Vivekananda Yoga Anusandhāna Samsthāna

(Declared as Deemed-to-be University under Section 3 of the UGC Act, 1956)

Eknath Bhavan, # 19, Gavipuram Circle, Kempegowda Nagar, Bangalore - 560 019

Ph: 080 - 2661 2669, Telefax: 080 - 2660 8645

E-mail: svyasa@svyasa.org Website: www.svyasa.org

Certificate

This is to Certify that the Doctoral Committee confirms that this is an authentic approved copy of the thesis titled **"Prefrontal Oxygenation Changes Associated with Working Memory Following Yoga Practice in Type 2 Diabetes Mellitus Patients" submitted by Chidananda Kaligal bearing Registration No. PhD/Res/01/Jan17.**

The Viva-voce examination was conducted on **Friday, 08th September 2023** through online google meet with session link: meet.google.com/mpz-fgdi-jbn

The committee recommends the award of the PhD Degree.

Dr. K. K. Deepak
National Reviewer & Examiner
Professor , Centre for Biomedical Engineering,
(CBME), IIT, Delhi

Prof. Jongsoon Seo
International Reviewer & Examiner
Professor, Head, Department of Yoga Studies
and Meditation, Wonkwang Digital University,
Korea.

Dr. Deepeshwar Singh
Guide & Associate Professor
Department of Yoga,
Babasaheb Bhimrao Ambedkar University,
Lucknow

Prof. Ramesh Mavathur
Dean of Academics
S-VYASA, Bengaluru

Prof. Sony Kumari
Controller of Examinations
S-VYASA, Bengaluru

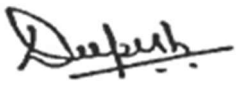
Prof. S. Siva Shankar Sai
Registrar
S-VYASA, Bengaluru

Dr. B. R. Ramakrishna
Vice-Chancellor
S-VYASA, Bengaluru

C E R T I F I C A T E

This is to certify that **Mr. Chidananda Kaligal** who has been given Ph.D. registration with effect from January 2017 by Swami Vivekananda Yoga Anusandhana Samsthana (S-VYASA), deemed to be University, under the division of yoga and life sciences has completed the required 'training' in acquiring the relevant background knowledge and has completed the required 'course of research' to submit this thesis entitled **PREFRONTAL OXYGENATION CHANGES ASSOCIATED WITH WORKING MEMORY FOLLOWING YOGA PRACTICE IN TYPE 2 DIABETES MELLITUS PATIENTS** as per the regulations of the university.

I also declare that the subject matter of the thesis entitled **"PREFRONTAL OXYGENATION CHANGES ASSOCIATED WITH WORKING MEMORY FOLLOWING YOGA PRACTICE IN TYPE 2 DIABETES MELLITUS PATIENTS"** has not previously formed the basis of the award of any degree, diploma, associate ship, fellowship, or similar titles.



Signature of Guide

Dr. Deepeshwar Singh,
Associate Professor,
Department of Yoga,
Babasaheb Bhimrao Ambedkar University, Lucknow.

D E C L A R A T I O N

I, hereby declare that this study was conducted by me at Swami Vivekananda Yoga Anusandhana Samsthana (S-VYASA), deemed to be University, Bangalore, under the guidance of **Dr. Deepeshwar Singh**, Associate Professor, Department of Yoga, Babasaheb Bhimrao Ambedkar University, Lucknow.

I also declare that the subject matter of my thesis entitled "**PREFRONTAL OXYGENATION CHANGES ASSOCIATED WITH WORKING MEMORY FOLLOWING YOGA PRACTICE IN TYPE 2 DIABETES MELLITUS PATIENTS"** has not previously formed the basis of the award of any degree, diploma, associate ship, fellowship, or similar titles.

Date: 08th September 2023 **Chidananda Kaligal**

Place: Bangalore **(Reg No. PhD/Res/01/Jan17)**

A C K N O W L E D G E M E N T

I would like to take this opportunity to express my deep gratitude to all the individuals and institutions whose unwavering support, guidance, and encouragement have been instrumental in the completion of my Ph.D. program.

I am immensely grateful to my supervisor, **Dr. Deepeshwar Singh**, for his exceptional mentorship, valuable insights, and endless patience throughout this research journey. I would also like to acknowledge his valuable contributions and guidance.

This research would not have been possible without the generous financial support from the **Ministry of AYUSH, Govt. of India**. Their investment in my work allowed me to dedicate my time and resources to advancing knowledge in this field.

I would like to acknowledge **S-VYASA** for providing an enriching academic environment and access to resources essential for my research. I am grateful to **Guruji Dr. H. R. Nagendra**, Chancellor, S-VYASA University, **Dr. R. Nagaratna**, Chief Medical Director, Arogyadhama, and **Dr. N.K. Manjunath**, Director, Anvesana Research facility, for instilling the research mindset and promoting research in the field of yoga. Also, thank the **faculty and staff of S-VYASA** for their assistance and support extended to me in the successful completion of my Ph.D. program.

My special thanks to **Dr. Subramanya Pailoor**, Associate Professor, Central University of Kerala, for his guidance, support, and valuable suggestions.

I extend my thanks to all the participants who volunteered for this study for their time and effort, without whom this study would not have been possible.

I would like to thank my fellow Ph.D. students, seniors, and friends for the camaraderie, stimulating discussions, and the sense of community that enriched my academic experience.

To my family, who have been my pillars of strength, and my constant source of inspiration, I owe an immeasurable debt of gratitude. Your love and support sustained me through the highs and lows of this challenging endeavor.

I would like to express my heartfelt gratitude to the countless unnamed individuals who, directly or indirectly, contributed to my academic growth and this thesis. Your collective efforts have not gone unnoticed or unappreciated.

Finally, I surrender to the Divine, and without its blessings, this work would not have been possible.

Thank you all for being a part of this incredible journey.

Date: 08th September 2023

Place: Bangalore **Chidananda Kaligal**

STANDARD INTERNATIONAL TRANSLITERATION CODE USED TO TRANSLITERATE SANSKRIT WORDS

a	=	अ	**ṅa**	=	ङ	**pa**	=	प
ā	=	आ	**ca**	=	च	**pha**	=	फ
i	=	इ	**cha**	=	छ	**ba**	=	ब
ī	=	ई	**ja**	=	ज	**bha**	=	भ
u	=	उ	**jha**	=	झ	**ma**	=	म
ū	=	ऊ	**ñ**	=	ञ	**ya**	=	य
ṛ	=	ऋ	**ṭa**	=	ट	**ra**	=	र
ṝ	=	ॠ	**ṭha**	=	ठ	**la**	=	ल
e	=	ए	**ḍa**	=	ड	**va**	=	व
ai	=	ऐ	**ḍha**	=	ढ	**śa**	=	श
o	=	ओ	**ṇa**	=	ण	**ṣa**	=	ष
au	=	औ	**ta**	=	त	**sa**	=	स
ṁ	=	अं	**tha**	=	थ	**ha**	=	ह
ḥ	=	अः	**da**	=	द	**kṣa**	=	क्ष
ka	=	क	**dha**	=	ध	**tra**	=	त्र
kha	=	ख	**na**	=	न	**jña**	=	ज्ञ
ga	=	ग						
gha	=	घ						

ABBREVIATIONS

AD	Alzheimer’s Disease
ACE-R	Addenbrooke's Cognitive Examination - Revised battery
AGE	Advanced glycation end products
ANOVA	Analysis of Variance
ANS	Autonomic Nervous System
AR-IRLS	Autoregressive iteratively reweighted least squares
BA	Brodmann Area
BBB	Blood Brain Barrier
BDNF	Brain Derived Neurotrophic factor
BMB	Baduanjin mind-body
BMI	Body mass index
BOLD	Blood oxygen level dependent
CBF	Cerebral blood flow
CI	Confidence Interval
CO	Cardiac output
DeoxyHb	Deoxyhemoglobin
dlPFC	Dorsolateral prefrontal cortex
dmPFC	Dorsomedial prefrontal cortex
DPF	Differential pathlength factor
DSST	Digit symbol substitution test
DST	Digit symbol test
DWRT	Delayed word recall test
ECG	Electrocardiogram
EEG	Electroencephalogram
FBG	Fasting Blood Glucose
FBS	Fasting Blood Sugar
fMRI	Functional Magnetic Resonance Imaging
fNIRS	Functional Near Infrared Spectroscopy
GABA	Gamma aminobutyric acid

GLM	General linear model
HbA1c	Glycated Hemoglobin
HDL	High-density lipoprotein
HF	High Frequency
HPA	Hypothalamic-pituitary-adrenal
HR	Heart Rate
HRV	Heart Rate Variability
KY	Kundalini yoga
LDL	Low density lipoprotein
LF	Low Frequency
MAP	Mean arterial pressure
MAAS	Mindful Attention Awareness Scale
MCI	Mild Cognitive Impairment
MET	Memory enhancement training
MFG	Middle frontal gyrus
MI	Myoinositol
MMSE	Mini-mental state examination
MoCA	Montreal cognitive assessment
NAA	N-acetyl aspartate
NASH	Non-alcoholic steatohepatitis
OFC	Orbitofrontal cortex
OxyHb	Oxyhemoglobin
PET	Positron Emission Tomography
PFC	Prefrontal cortex
PGIMS	Punit Govil intelligence memory scale
PNS	Parasympathetic nervous system
PPBG	Post Prandial Blood Glucose
PPG	Post Prandial Blood Glucose
RCT	Randomized Controlled Trial
RMSSD	Square Root of the Mean Squared Difference between adjacent RR intervals
ROI	Region of interest
RR	Respiratory Rate

RRS	Rumination Response Scale
SCL90-R	Symptom checklist 90-Revised
SDNN	Standard Deviation of normal-to-normal interval
SFG	Superior frontal gyrus
SNS	Sympathetic nervous system
ST	Sternberg test
SV	Stroke volume
TCD	Transcranial Doppler Ultrasonography
T2DM	Type 2 diabetes mellitus
VD	Vascular dementia
VFT	Verbal fluency test
vlPFC	Ventrolateral PFC
vmPFC	Ventromedial PFC
WAIS	Wechsler Adult Intelligence ScaleF
WFT	Word fluency test
WM	Working memory
WML	White matter lesion
WMS	Wechsler Memory Scale
WMT	Word memory test

ABSTRACT

BACKGROUND

In recent years, cognitive impairments and dementia (including Alzheimer's disease) have been recognized as common complications and comorbidities of Type1 diabetes (T1DM) and Type2 diabetes mellitus (T2DM). It is estimated that 7% of people aged 60–64 are affected by mild cognitive impairment (MCI) and that 25% may develop cognitive impairment as they get older. It has been found that the risk of converting mild cognitive impairment to dementia is 1.53 times higher in individuals with diabetes. Diabetes-related complications, such as glucose and insulin imbalances, microvascular and macrovascular complications significantly predispose patients to the progression of MCI and dementia. Additionally, several risk factors for cognitive dysfunction in diabetes were identified, such as hypertension, dyslipidemia, depression, age, duration of diabetes, genetic factors and educational level of patients. Brain imaging studies show that T2DM is associated with both degenerative and vascular brain damage, which is likely to contribute to abnormalities in brain functional and structural connectivity leading to cognitive dysfunction. It has been found that, even at an early stage of cognitive decline, there was a clear abnormality in cerebral hemodynamics and oxygenation parameters. Working memory, a cognitive ability that enables one to actively maintain and manipulate information and forms an essential part of the human memory system, is implicated along with other cognitive functions such as attention, executive function, verbal memory and information processing speed. Besides medications, non-pharmacological approaches such as physical exercise, yoga, computer-based training, nutrition, brain stimulation, sleep, and music are gaining importance in treating cognitive deficits. Yoga has been one such non-pharmacological approach gaining popularity as a form of complementary and alternative medicine worldwide and its therapeutic benefits are being explored in various clinical conditions.

AIMS AND OBJECTIVES

The study investigated the effect of yoga practice on oxygenation changes in the prefrontal cortex (PFC) associated with working memory in T2DM participants. The study also examined the effects of yoga practice on heart rate variability and psychological conditions (rumination

and preservative thinking). The objectives of the study were to assess the effect of 12-week yoga practice in T2DM participants on

- Oxygenation in the PFC region during resting and while performing a working memory task
- Working memory performance – accuracy and reaction time
- Resting-state heart rate variability
- Psychological conditions, namely rumination and perseverative thinking

METHODS

Participants: Participants were, both male and female, with ages ranging from 35 to 65 years, diagnosed with type 2 diabetes mellitus based on established criteria including medical history, medication use, glucose levels and undergoing conventional treatment.

Design: This study was a randomized controlled trial (RCT). The participants were randomized into two groups, the yoga and waitlist control groups.

Assessments: The pre- (day 1), mid- (6 weeks) and post-intervention (12 weeks) assessments included measurement of PFC oxygenation while performing working memory tasks (n-back) using functional near-infrared spectroscopy. The Accuracy and Reaction time of working memory performance were assessed. Heart rate variability parameters such as mean heart rate (HR), Square Root of the Mean Squared Difference between adjacent RR intervals (RMSSD), Standard Deviation of normal-to-normal interval (SDNN), Low-frequency component (LF), High-frequency component (HF) and LF/HF ratio were assessed. The psychological conditions, namely rumination and perseverative thinking were assessed using the Rumination Response Scale (RRS) and Perseverative Thinking Questionnaire (PTQ).

Intervention: Participants in the yoga group engaged in twelve weeks of yoga practice. Waitlist control group members were instructed not to engage in any form of exercise such as running, jogging, swimming, or lifting weights during the study period. The waitlist control group received yoga practice for four weeks upon completion of the trial.

RESULTS

Following a 12-week intervention, the yoga group showed improved performance in working memory [accuracy (geometric mean difference of 3.15%, 95% CI [2.33,3.96], p = 0.001) and

reaction time (mean difference of -100.8 milliseconds,95% CI [-166.6, -35.1], p=0.002] in the high task load (2-back) associated with higher oxygenation in dorsolateral PFC (β coefficient mean difference of 95.6, 95% CI [0.23,191], p=0.049) and ventrolateral PFC (β coefficient mean difference of 53.4, 95% CI [7.8,98.9], p=0.018) regions. Higher oxygenation in dorsolateral PFC during the 2-back task was positively correlated with accuracy ($r(23)= 0.65$, $p<0.001$) and negatively correlated with reaction time ($r(23)= -0.47$,$p=0.017$).

The yoga group showed improved autonomic functions with a decreased mean HR, decreased LF component and increased HF component values. Decreased mean HR at post-intervention compared to pre- and mid-intervention with a mean difference of -7.0, 95% CI [-9.5, -4.4], $p < 0.001$ and -6.1, 95% CI [-10.1, -2.2], $p = 0.002$ respectively. Decreased LF value at post-intervention compared to pre- and mid-intervention with a mean difference of -10.7, 95% CI [-21.0, -0.3], $p = 0.041$ and -10.6, 95% CI [-20.5, -0.6], $p = 0.034$ respectively. Increased HF value at post-intervention compared to pre- and mid-intervention with a mean difference of 10.7, 95% CI [0.23, 21.1], $p = 0.043$ and 11.3, 95% CI [1.1, 21.5], $p = 0.03$ respectively.

The yoga group showed reduced rumination following the yoga intervention with a decrease in RRS score at post-intervention compared to pre-intervention, with a mean difference of -4.72, 95% CI [-8.5, -1.0], $p = 0.011$. The decrease in rumination scores (at post-intervention) was positively correlated with the improvement in reaction time (at post-intervention) compared to pre-intervention, $r (25) = 0.65$, $p < 0.001$.

CONCLUSION

The findings suggest that yoga practice may improve working memory performance associated with higher PFC oxygenation in patients with T2DM. Also, yoga may prevent the onset of a depressive condition by reducing rumination symptoms and influence positively on cognitive functions. Yoga practice may be an effective adjunct approach for enhancing cognitive functions in clinical populations.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES