EFFECT OF YOGA AND MEDITATION ON NEUROPSYCHOLOGICAL FUNCTIONS AND BRAIN CONNECTIVITY NETWORKS IN MILD COGNITIVE IMPAIRMENT (MCI) & COGNITIVELY NORMAL SUBJECTS

SATYAM SCHEME

PROJECT COMPLETION REPORT

DST File No: SR/SATYAM/278/2015

Dr. Ramshekhar N Menon
Additional Professor
CBNS, Department of Neurology
Sree Chitra Tirunal Institute for Medical Sciences & Technology
Thiruvananthapuram - 695011

PROJECT COMPLETION REPORT

1. Title of the project:

Effect of Yoga and Meditation on Neuropsychological functions and Brain Connectivity Networks in Mild Cognitive Impairment (MCI) and cognitively normal subjects

2. Principal Investigator(s) and Co-Investigator(s):

Principal Investigator

Dr. Ramshekhar N Menon

Additional Professor

Cognition & Behavioral Neurology Section (CBNS)

Department of Neurology, SCTIMST, Thiruvananthapuram – 695011

Co-Investigators:

Dr. C Kesavadas

Professor

Dept of IS & IR, SCTIMST, Thiruvananthapuram

Dr. Bejoy Thomas

Additional Professor

Department: IS&IR, SCTIMST, Thiruvananthapuram

Dr. Aley Alexander

Senior Psychologist

Dept of Neurology, SCTIMST, Thiruvananthapuram

Dr. S Krishnan

Associate Professor

Department of Psychiatry, Govt. Medical College

Thiruvananthapuram

Mindfulness meditation Experts

(i) Dr. S. Krishnan, Associate Professor, Medical Officer-in-Charge of Holistic and Psychosomatic Clinic, Department of Psychiatry, Govt. Medical College, Thiruvananthapuram

(ii) Ms. Lekshmi K (Mindfulness meditation trainer) Psychologist and Counsellor, B-GHUD, Puthiyakaavu, Mavelikara

3. Implementing Institution(s) and other collaborating Institution(s):

Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram

4. Date of commencement:

06/06/2016

5. Planned date of completion:

06/06/2019

6. Actual date of completion:

06/12/2019

7. Objectives as stated in the project proposal:

i. To evaluate the neural correlates of meditation and resting state in routine practitioners of mindfulness meditation compared with normal healthy controls and subjects with MCI and prodromal AD.

ii. To study the effect of meditation & cognitive retraining (CR) and its continued practice in reinforcing cognitive abilities and betterment in quality of life in individuals with MCI and prodromal AD by validating and comparing information from established modalities – structural and functional connectivity, as well as measures of stress and resilience on neuronal plasticity and neuropsychology

8. Deviation made from original objectives if any, while implementing the project and reasons thereof:

   Nil

9. Experimental work giving full details of experimental set up, methods adopted, data collected supported by necessary table, charts, diagrams & photographs:

The project started on 06/06/2016 after approval from the Institute Ethics Committee of SCTIMST and receipt of funds from DST.

The study is designed in two phase, Phase I – Pilot Phase, featuring Mindfulness meditation practitioners and Meditation naive controls and Phase II - Comprised of patients with mild cognitive impairment who follow cognitive retarining as well as mindfulness meditation sessions. Data collection mainly highlight the data from

Neuroimaging (structural and functional MRI) and Neuropsychology test battery. Phase I of the study was performed as a pilot phase to ensure the neural benefits of mindfulness meditation also to study the fMRI setup ensure reliable data acquire. Phase II, Patient phase was the challenging part of the study, which was performed with experimental setup for neuroimaging data acquire as given below

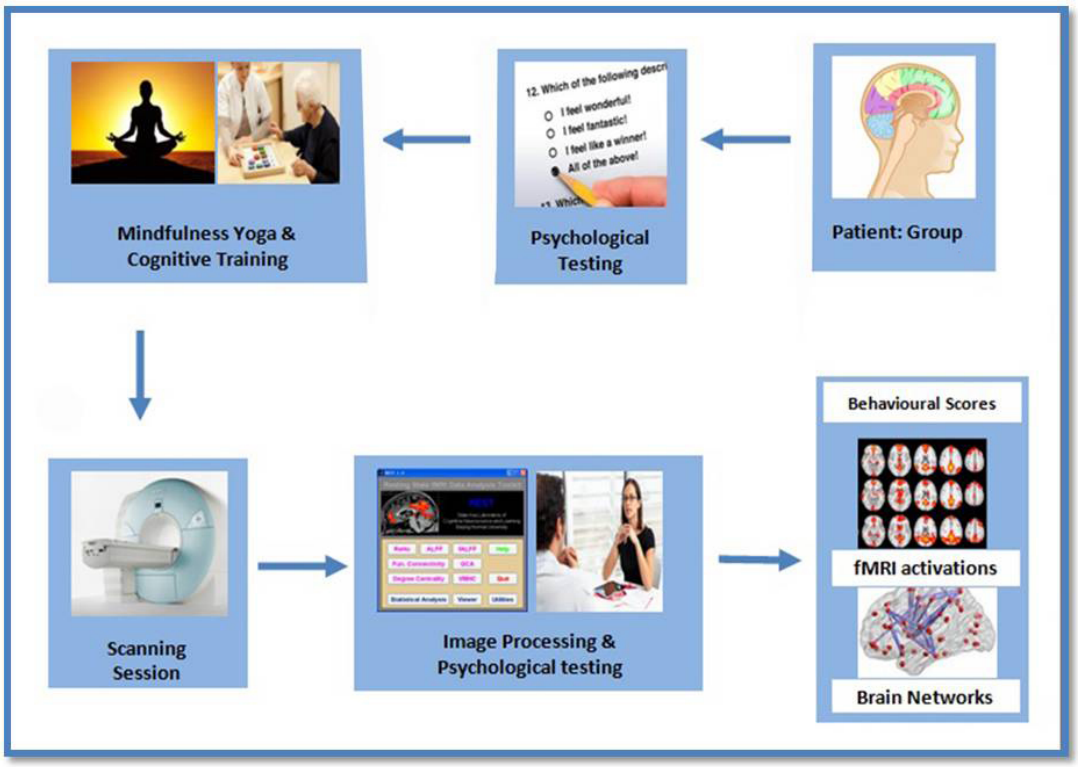


Figure: Experimental Setup

With regard to cognitive retraining of patients, we have developed a manual for cognitive retaining (Appendix: A). Details regarding the sample and the experimental setup for neuroimaging data acquire are described below.

a. PHASE I : PILOT PHASE

The subjects include 13 right-handed healthy volunteers and 13 right-handed meditation practitioners with 1 to 2 years of experience with mindfulness meditation. Handedness was ascertained using Edinburgh Handedness Inventory. The meditation practitioners were of age 36-53 years with mean age 42.42±5.9 years. Controls were of age 27-55 years with mean age 40.75±8.8 years. To assess the neuropsychological performance and to rule out depression or anxiety, standard neuropsychology test battery were administered

a.1. MEDITATION fMRI PARADIGM

The Meditation fMRI paradigm was developed as a block design paradigm with 3 blocks: Resting Phase, Relaxation Phase and Meditation Phase. We used sound of a bell in mp3 format in the paradigm to designate the start of each block of the paradigm. During resting phase the volunteer had to lie-down calm in the scanner without thinking anything in particular. During the relaxation phase, the participants are instructed to scan their body from head to toe (Mindful body awareness) and during the meditation phase, the instruction is to mindfully attend to breathe (Mindful breath awareness).

The paradigm was implemented using paradigm designing software called presentation (NeurobehaviouralSystems INC, USA). This ensured perfect synchronization of the paradigm with scanner pulses. The total duration of paradigm was 15.45 minutes (The indication bell for each phase was presented for 1.5 minutes

followed by 5 minutes for task phases). The echo-planar images were obtained and fMRI post processing was done using SPM 12.

a.2. MRI DATA ACQUISITION

The data was acquired using 3T GE MRI machine (Discovery MR750w TM) using a 32 channel head coil. Each acquisition consisted of structural MRI, Resting state fMRI and a Meditation task fMRI. The BOLD response was tracked using Gradient-echo echoplanar imaging sequence. The meditation fMRI data acquisition employed scanner parameters - TR= 2500 ms, TE=30 ms, time of inversion=500 ms, Flip angle=80°, Slice thickness=3.2 mm, No: of averages=1, No: of slices=43, imaging matrix=64×64. The Resting state fMRI followed same parameters with the Number of time points=376. For acquiring Structural images, T1 weighted sequence with following parameters were employed TR= 8.14 ms, TE=2.97 ms, time of inversion=500 ms, Flip angle=12°, Slice thickness=1 mm, No: of averages=1, No: of slices=172, imaging matrix=256×256.

a.3 Data Analysis

Analysis of data was performed in 3 disciplines (i) Resting state connectivity analysis (ii) Task based activation analysis and (iii) Task based connectivity analysis

a.3.1. Resting state connectivity analysis

To estimate the resting state brain connectivity, CONN tootbox (conn 18.b) for MATLAB R2017 (MathWorks Inc., Natick, MA, USA) was used. The fMRI data

were preprocessed using the default pipeline for volume based analysis with direct normalisation to MNI (functional realignment, structural segmentation & normalization, functional normalization, outlier detection and smoothing) .To select adequate low frequency, a band-pass filtering was used in conn toolbox with a frequency range of 0.008 to 0.09 Hz. The seed-based correlation analysis was then applied on the preprocessed data using the general linear model. Furthermore, ROI to ROI connectivity was established with default network seeds with selected regions from all over the brain, including all the resting state network nodes. By using the ROI-to-ROI results explorer of the Conn toolbox, resting state connectivity networks were extracted for all networks namely Default mode, Salience, Sensory motor, FrontoParietal, Dorsal Attention and Language network nodes were analysed through a threshold value of 0.05 with seed level FDR-correction.

a.3.2. Task based activation analysis

SPM12 (Wellcome Department of Imaging Neuroscience, London, United Kingdom), the image processing toolbox in Matlab R2017 was used to perform this analysis Imaging time series were realigned, normalised into standard space defined by a MNI (Montreal Neurological Institute template) and smoothed using a Gaussian kernel with a full width at half maximum (FWHM) of 8mm.SPM data analysis employs a mass-univariate approach based on General Linear Modelling (GLM). Here, the first level fixed analysis as well second level random effect analysis were done for 3 task phases - "REST", "RELAX" and "MEDITATE". All respective conditions (rest, relax

and meditate) were modelled for resultant hemodynamic response function (HRF) using standard parameters of SPM12. The first level fixed effect analysis, carried out with 3 conditions rest, relax and meditate generated three contrast images for individual subjects and these contrast images were then used for second-level random effects analysis. The group level HRF was modelled for the two conditions Meditate and Relax following a two sample t test for practitioners versus controls

a.3.3. Task based connectivity analysis

Task based connectivity analysis was also achieved using conn toolbox with default preprocessing steps used for resting state fMRI, here adequate frequency was selected sticking to 0.09 Hz to infinity. The seed-based correlation analysis was then applied on the preprocessed data using the general linear model. ROI to ROI connectivity was then calculated for three task conditions - "REST", "RELAX" and "MEDITATE". A two sample t test was then performed for practitioners versus controls for each of the three task conditions and corresponding connectivity networks were extracted using the ROI-to-ROI results explorer of the Conn toolbox

b. PHASE II:MIDFULNESS MEDITATION & COGNITIVE RETRAINING

b.1 COGNITIVE RETRAINING

The recruitment of patients with Mild cognitive impairement (MCI) and prodromal AD was based on the assessment of the Neurologist after ascertaining clinical and

neuropsychological performance. MRI session - Dementia protocol was also administered on patients recruited for the study. The phase II was done to study the effect of Mindfulness meditation training and Cognitive Retraining. Resting state fMRI was also performed pre and post training to assess the resting state brain network changes. The acquired image data is processed using Conn toolbox to study the effect. Mindfulness meditation training was administered by mindfulness experts following a structured 10 weeks Mindfulness practice manual. The continued practice of the same aided in reinforcing cognitive abilities as well as in improving quality of life in individuals with MCI and prodromal AD by validating information from established psychological testing modalities

10. Detailed analysis of results indicating contributions made towards increasing the state of knowledge in the subject:

Result : Phase I

i. Resting State fMRI

Resting state connectivity analysis focusing Practitioners > Controls at $p<0.05$ features difference only in analysis involving seeds from default mode network and Salience network. The network difference relayed on medial prefrontal cortex (Figure a) connected to left and right Insular cortex and left and right planum polar. Significant difference in connectivity with salience network seeds are noted in Right anterio insula and its connections with left amygdale, left parahippocampal gyrus and left fusiform cortex (Figure b). Significant connections and their respective pvalues

are listed in Table I. There were no significant differences in connectivity with analysis involving seeds from Frontoparital network, Dorsal Attention Network and Sensory motor network and language network.

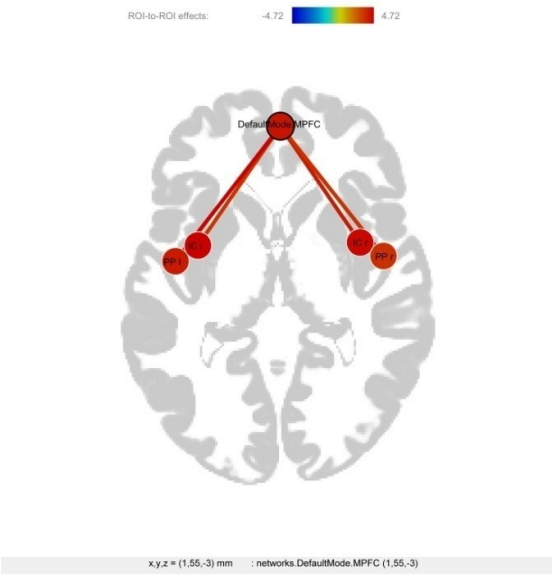


Figure a

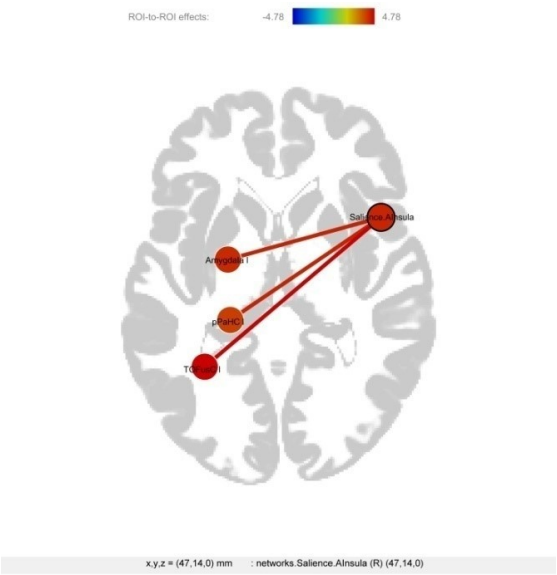


Figure b

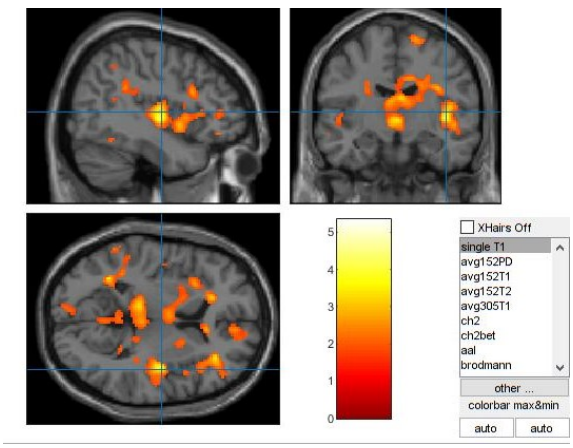
RESTING STATE ROI TO ROI CONNECTIVITY				
Seeds	**Connections**	**T Statistic**	**p-unc**	**p-FDR**
MPFC (1,55,-3) DMN	Planum Polare Left	4.72	0.0001	0.0086
	Insular Cortex Right	4.12	0.0002	0.0183
	Planum Polare Right	3.67	0.0007	0.0342
	Insular Cortex Left	3.58	0.0008	0.0342
RIGHT ANTERIOR INSULA (47,14,0)	Temporal Occipital Fusiform Cortex Left	4.78	0	0.0073
	Parahippocampal Gyrus, posterior	4.31	0.0001	0.0083

SALIENCE NETWORK	division Left Amygdala Left	 4.28	 0.0002	 0.0083

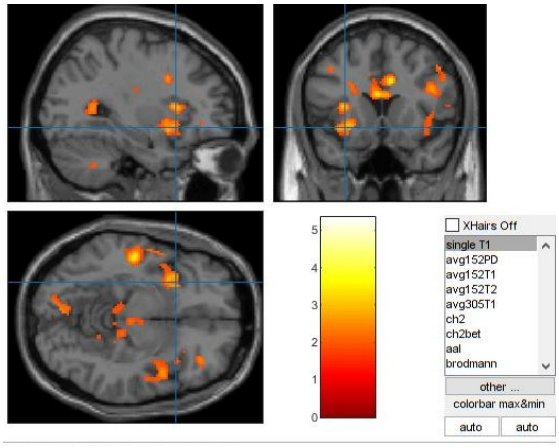
Table I

ii. Task based fMRI

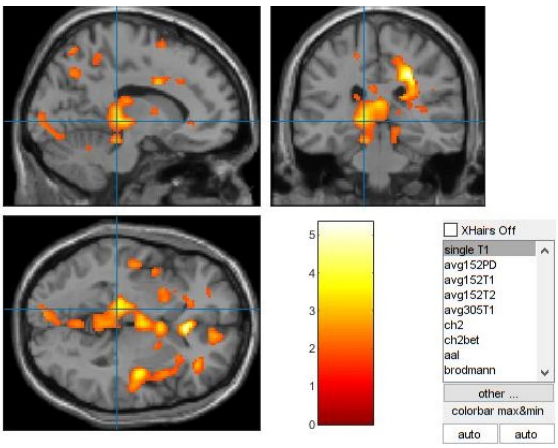
For Meditation Phase, maximal BOLD activation for contrast PRACTITIONERS > CONTOL was noted over bilateral right insula, bilateral thalamus, Anterior Cigulate, and putamen (figure i, ii, iii,iv, v, vi).



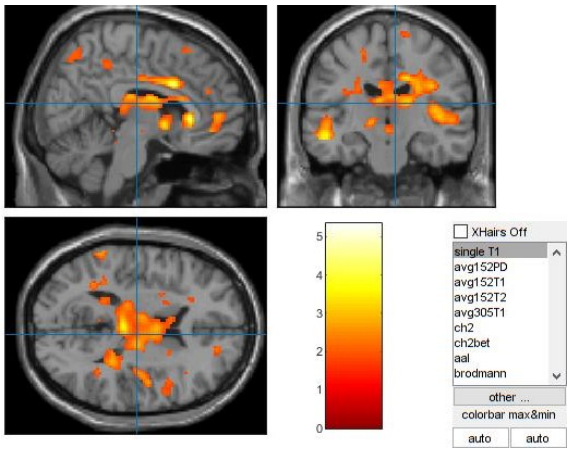
(i) Right Insula



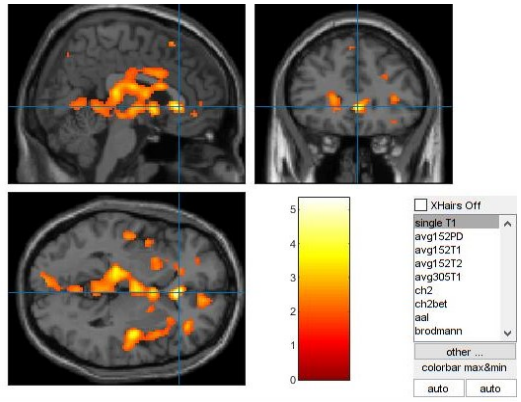
(ii) Left Insula



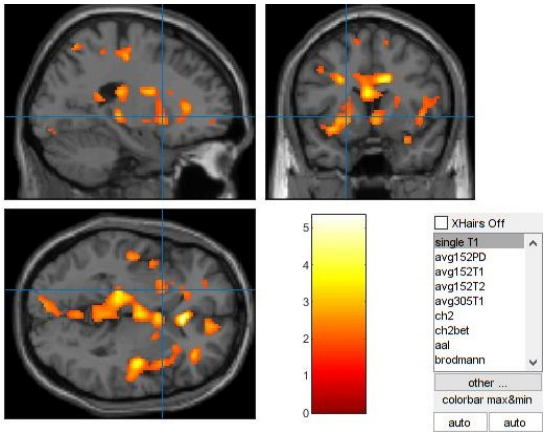
(iii) Left Thalamus



(iv) Left Thalamus

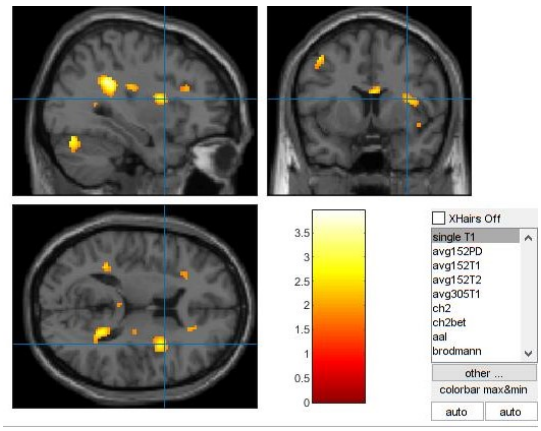


(v) Anterior Cingulate

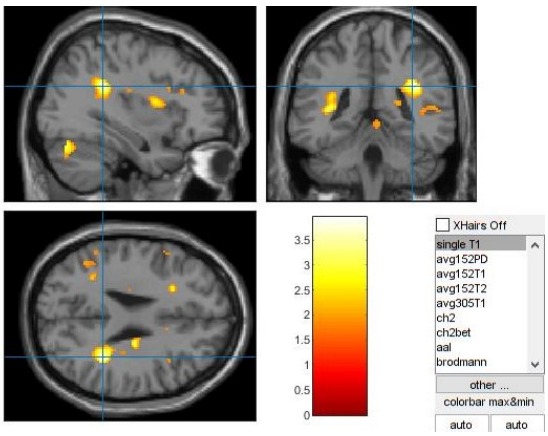


(vi) Putamen

For Relaxation Phase, maximal BOLD activation for PRACTITIONERS > CONTOL was noted over right insula and right inferior parietal lobule.(figure iv, v)

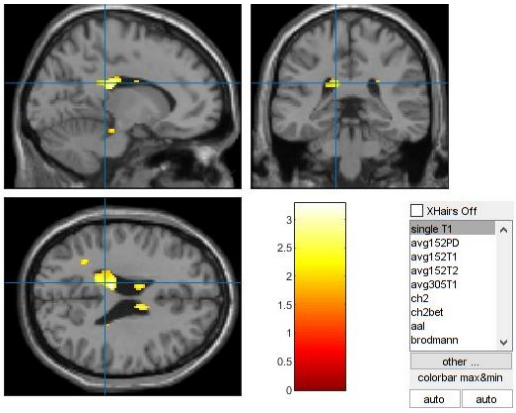


(iv) Right Insula



(v) Right Inferior Parietal Lobule.

For Rest Phase, no significant BOLD activation for PRACTITIONERS > CONTOL was noted in grematter regions, but activation was noted over over corpus callosum. (figure vi)

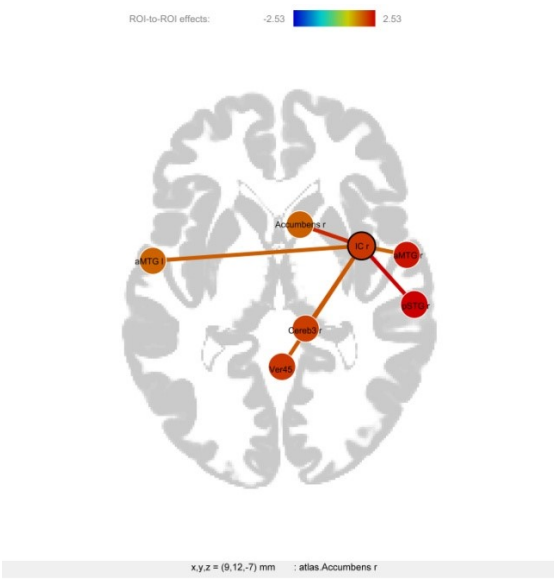


(vi) Corpuscallosum

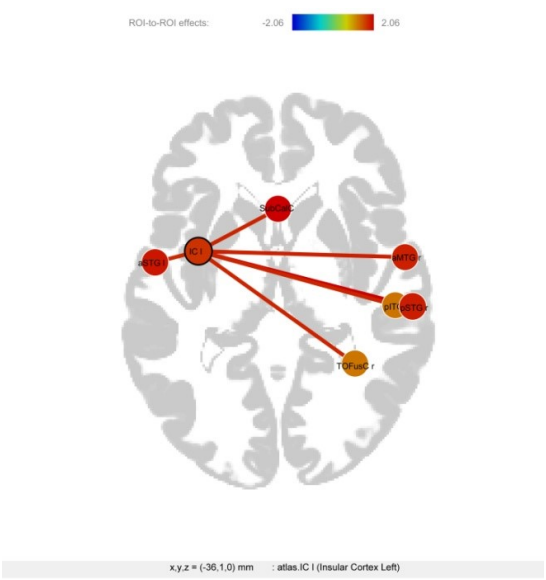
iii. Task based Connectivity

Task based connectivity analysis also followed seed based ROI to ROI connectivity method, with Practitioners > Controls. The seeds were selected with respect to the result obtained from task based activations. The regions corresponding to task activations were selected as seeds for task based connectivity. The connectivity difference for meditation phase with bilateral insula, left thalamus, anterior cigulate and left putamen were noted (Figure c,d,e,f,g,h). The connectivity corresponding to meditation condition with seeds - right insula and right inferior parietal lobule were obtained (Figure i). The regions connectected to each seed and respective uncorrected p values for meditation phase and relaxation phase are listed in the table II & table III respectively.

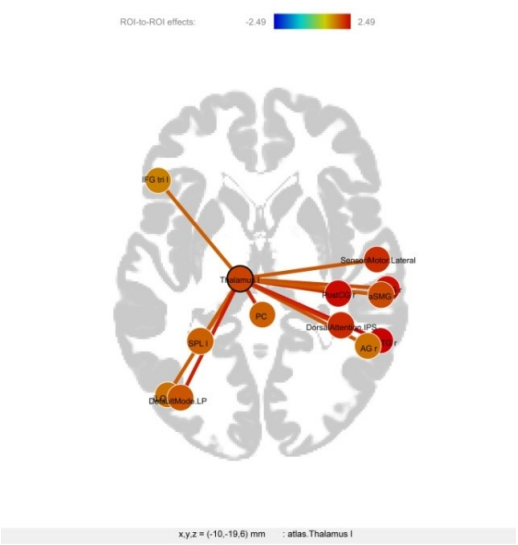
There were no significant grey matter activations in rest phase therefore no connectivity was elucidated.



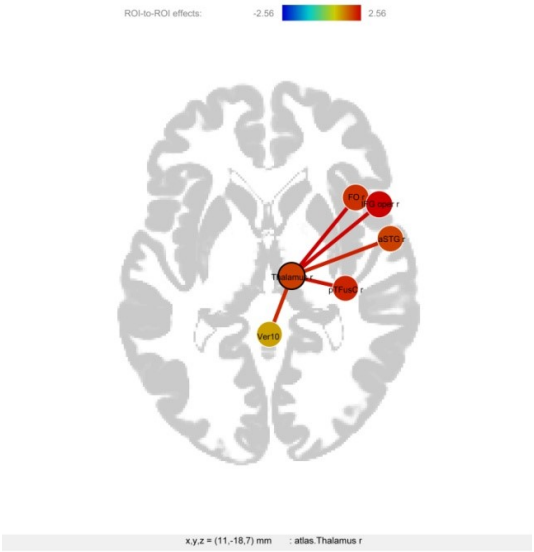
(c) Seed: Right Insula



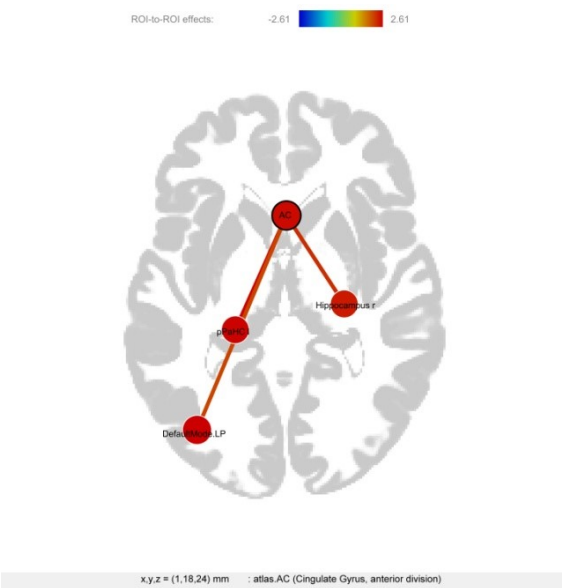
(d) Seed: Left Insula



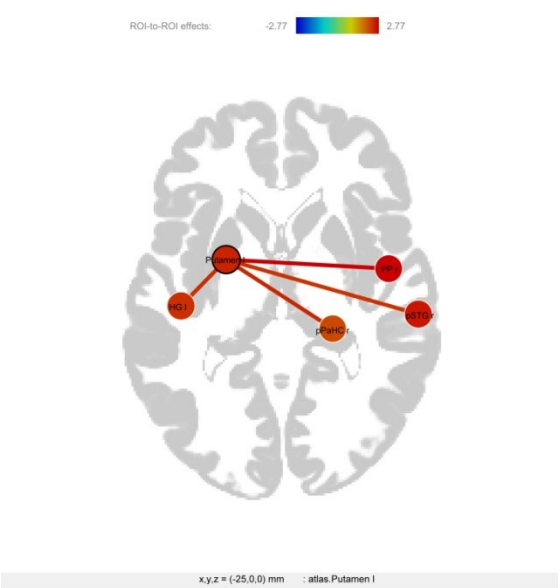
(e) Seed: Left Thalamus



(f) Seed: Right Thalamus



(g) Seed: Anterior Cingulate



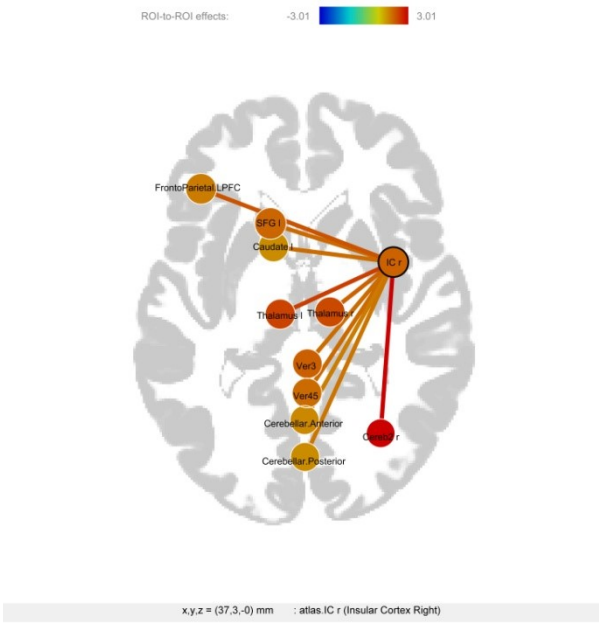
(h) Seed: Left Pulamen

RESTING STATE ROI TO ROI CONNECTIVITY - MEDITATON PHASE			
Seed	**Connection**	**T Statistic**	**p-unc**
RIGHT INSULA	pSTG r	2.53	0.0096
	Accumbens r	2.22	0.0185
	Cereb3 r	1.88	0.0365
	Ver45	1.82	0.0414
	aMTG l	1.76	0.0462
	aMTG r	1.74	0.0482
ANTERIOR CINGULATE	pPaHC l	2.61	0.0081
	Hippocampus r	2.23	0.0182
	AC -(135)	2.03	0.0274
	toMTG r	2.49	0.0105

LEFT THALAMUS	135)	2.26	0.0169
	PC	2.20	0.0193
	155)	2.16	0.021
	PostCG r	2.13	0.0225
	pSTG r	1.92	0.034
	AG r	1.85	0.0388
	(139)	1.81	0.0421
	iLOC l	1.77	0.0457
	aSMG r	1.76	0.0459
	IFG tri l	1.74	0.0476
	SPL l	1.73	0.049
Right THALAMUS	FO r	2.56	0.0089
	IFG oper r	2.53	0.0095
	pTFusC r	2.43	0.0119
	aSTG r	2.30	0.0155
	Ver10	2.25	0.0175
SUPERIOR TEMPORAL GYRUS	Pallidum r	2.78	0.0055
	Cereb9 l	2.60	0.0082
	Brain-Stem	2.58	0.0086
	IC r	2.53	0.0096
	pSTG r	2.06	0.026
	aMTG r	1.84	0.0396

LEFT INSULA	SubCalC	1.83	0.0408
	pITG r	1.82	0.0415
	TOFusC r	1.81	0.0419
	aSTG l	1.77	0.0452

Table II



(i) Seed: Right Insula

RESTING STATE ROI TO ROI CONNECTIVITY – RELAXATION PHASE			
	Analysis Unit	Statistic	p-unc
Right Insula	IC r -Cereb2 r	T(22) = 3.01	0.0032
	IC r -Thalamus l	T(22) = 2.40	0.0126
	IC r -(156)	T(22) = 2.20	0.0195

	IC r -Thalamus r	T(22) = 2.04	0.0267
	IC r -Ver45	T(22) = 1.99	0.0295
	IC r -SFG l	T(22) = 1.98	0.0299
	IC r -Ver3	T(22) = 1.95	0.032
	IC r -Caudate l	T(22) = 1.95	0.032
	IC r -(165)	T(22) = 1.87	0.0374
	IC r -(164)	T(22) = 1.79	0.0435

(ii) Result: Phase II – Mindfulness Meditation & Cognitive Retraining

ii.a Cognitive Retraining

- This arm of the study customized a ten week cognitive retraining program for adults with MCI and prodromal AD diagnosed as per the Petersen's criteria and NINCDS- ADRDA criteria with clinical dementia rating (CDR) score < 2.
- The cognitive retraining is carried out biweekly for 45 minutes. Feedback on the performance of the retraining tasks is given at the end of each session. The patient is given home based tasks for practicing during the rest of days.
- Cognitive retraining is given for the following domains: orientation, attention, mental speed/information processing, verbal fluency, response inhibition, planning, set shifting ability, visuoconstructive ability, visuospatial reasoning,

abstraction, problem solving, comprehension, sentence repetition, expressive speech, reading ability, verbal memory, visual memory.

- The sample comprised of 20 patients (14-males & 6- females). The participants are recruited through the Memory and Neuro Behavioral Disorders Clinic, SCTIMST.
- Pre and Post neuropsychological evaluation was done.
- The neuropsychology tests used to obtaining relevant data were: Addenbrooke's cognitive examination (ACE), Instrumental activities of daily living daily living (IADL), and CDR.
- Pre and Post scores were statistically evaluated by using paired t test.
- The result indicates that there is a significant difference in MMSE(p=.001), ACE total score(p=.028) and other subtests of ACE such as recall(p=.000), orientation(p=.019), language(p=.027), categorical fluency(p=.021), visuospatial abilities(p=.009), clock drawing test(p=.035)
- And also there is significant difference in CDR(p=.001)
- And there is no significant difference in tests such as ACE registration, ACE phonemic fluency, and IADL

Variables		Mean	N	Sig. (2- tailed)
Pair 1	MMSE1	26.8000	20	0.001

	MMSE2	28.1000	20	
Pair 2	ACE TOTAL SCORE 1	80.9000	20	
	ACE TOTAL SCORE 2	84.9500	20	.028
Pair 3	ACE RECALL 1	3.7500	20	
	ACE RECALL 2	6.1000	20	.000
Pair 4	ACE ORIENTATION 1	9.1000	20	
	ACE ORIENTATION 2	9.7000	20	.019
Pair 5	ACE LANGUAGE 1	26.7000	20	
	ACE LANGUAGE 2	27.4000	20	.027
Pair 6	ACE CATEGORY1	4.8500	20	
	ACE CATEGORY2	5.3500	20	.021
Pair 7	ACE VISUO SPATIAL1	3.3000	20	

	ACE VISUO SPATIAL2	4.1500	20	.009
Pair 8	CLOCK DRAWING TEST1	2.1000	20	
	CLOCK DRAWING TEST2	2.5500	20	.035
Pair 9	CDR 1	2.6500	20	
	CDR 2	1.9250	20	.001

1 & 2 represents pre and post assessment scores

ii.b Mindfulness Meditation & Cognitive Retraining

- This part of the study administered an ten week group based Mindfulness meditation (MUCBT-D) training program with cognitive retraining for adults with MCI due to AD diagnosed as per the Petersen's criteria and NINCDS-ADRDA criteria with clinical dementia rating (CDR) score < 2.
- The sample comprised of 14 patients (11-males & 3- females) after exclusion of significant anxiety and depression scale (HADS). The participants are recruited through the Memory and Neuro Behavioral Disorders Clinic, SCTIMST.
- Pre and Post neuropsychological evaluation was done.

- The neuropsychology tests used to obtaining relevant data were: Addenbrooke's cognitive examination(ACE), Rey auditory verbal learning test(RAVLT), Wechsler memory scale(WMS- visual memory, logical memory, digit span), Trail A, Trail B, Wisconsin card sorting test(WCST), Warrington recognition memory test for faces, position discrimination test, cube analysis, Instrumental activities of daily living daily living (IADL), HADS, CDR.
- Pre and Post scores were statistically evaluated by using paired t test.
- The mean age of cohort was 67years and education range was 10- 15 years.
- The result indicates that there is a significant improvement in RAVLT immediate recall (p=.038), RAVLT delayed recall (p=.035), RAVLT recognition score (p=.048) and RAVLT omission error score (p=.036).
- There is also significant improvement in WMS delayed logical memory score (p=.047).

Variables	Mean	N	Std. Deviation	Sig. (2-tailed)
RAVLT IMMEDIATE RECALL	4.0714	14	2.75860	.038
RAVLT IMMEDIATE RECALL 1	6.0000	14	4.01918	
RAVLT DELAYED RECALL	4.0000	14	3.16228	.035
RAVLT DELAYED RECALL1	5.5000	14	3.83807	
RAVLT RECONITION	12.3571	14	2.34052	.048
RAVLT RECOGNITION1	13.6429	14	.74495	
RAVLT OMISSION ERROR	2.6429	14	2.23975	.036
RAVLT OMISSION ERROR1	1.3571	14	.74495	
WMS DELAYED LOGICAL MEMORY	7.7857	14	6.02787	.047

ii.b.1 Brain Connectivity analysis results of Mindfulness Meditation Group

The Resting state connectivity analysis followed seed based ROI to ROI connectivity approach, with POST > PRE. Here we analyzed the Graph theory parameters of the resting state network seeds. The seeds were selected with respect to the standard resting state network seed sources in CONN toolbox. The connectivity difference for

POST > PRE sessions, corresponding to the graph parameter degree was analyzed. The parameter degree represents the number of connections maintained by a node. The value corresponding to degree of networks seeds pre and post training were extracted and performed a paired t test in SPSS software. The values corresponding to Anterior Cingulate Cortex (ACC) and Posterior Cingulte Cortex (PCC) were found significant as given in table below.

Variables		Sig. (2-tailed)
Pair 1	MPFC1 - MPFC2	.615
Pair 2	LPL1 - LPL2	.173
Pair 3	LPR1 - LPR2	.369
Pair 4	**PCC1 - PCC2**	**.066**
Pair 5	**ACC1 - ACC2**	**.067**
Pair 6	AIL1 - AIL2	.218
Pair 7	AIR1 - AIR2	.271
Pair 8	SRPFCL1 - SRPFCL2	.560
Pair 9	SRPFCR1 - SRPFCR2	.165
Pair 10	SMGL1 - SMGL2	.747
Pair 11	SMGR1 - SMGR2	.211

Pair 12	DAFEFL1 - DAFEFL2	.941
Pair 13	DAFEFR1 - DAFEFR2	.960
Pair 14	IPSL1 - IPSL2	.470
Pair 15	IPSR1 - IPSR2	.473
Pair 16	LPFCL1 - LPFCL2	.884
Pair 17	PPCL1 - PPCL2	.591
Pair 18	LPFCR1 - LPFCR2	.651

11. Conclusions summarizing the achievements and indication of scope for future work:

- Recruited and trained one Senior Research Fellow to work with project, specifically for conducting functional neuroimaging sessions and MR image processing. Also recruited Junior Research Fellows (2 Psychologists during project tenure) to work with the Neuropsychology assessment a as well as to facilitate cognitive retraining sessions

- GE Discovery 3Tesla MRI scanner operating software has been studied for conducting meditation fMRI studies. Evaluation and training of paradigm designing and image post processing software and brain connectivity toolbox were

carried out. Extensive literature review was made for study design conception, fMRI task development and data post processing.

- A Yoga Meditation MRI system has been setup and operated successfully. Meditation-fMRI paradigm with audio instructions detailing resting, relaxation and meditation has been developed. fMRI paradigm was generated using, Neurobehavioural Systems Presentation software, which is one of the best stimulus delivery/control software which can record stimulus and responses with high accuracy. fMRI data acquired were processed to extract BOLD activations as well as brain connectivity network using CONN toolbox.

- Achieved collaboration with Dr. Sheeba Arnold to facilitate the post processing using CONN toolbox for brain connectivity analysis. Dr. Sheeba is a data scientist and biomedical researcher and a core member of the Brain Research Department at Massachusetts Institute of Technology and the Department of Psychiatry at Massachusetts General Hospital.

- A Cognitive Retraining strategy (CR) has been devised, along with the domains to be assessed among patients with Mild Cognitive Impairment (MCI) and Prodormal AD. Multiple cognitive domains emphasised for retraining was- Attention, Orientation, Memory, Executive function, Language, Visuospatial and Problem Solving.

- Individualized domain specific cognitive retraining sessions were conducted bi weekly with one hour therapy session. Clinical Dementia Rating Scale (CDR) and Instrumental activities of daily living (IADL) were done on a monthly basis to assess the efficacy of the therapy.

- Completed Phase 1 : Recruited 13 healthy yoga practitioners & 13 age matched Controls. The brain connectivity is studied by analyzing various resting state brain networks. Taskbased BOLD activations as well as task based

- Completed Phase 2: This is the Patient phase, and so far we have recruited 10 patients acquired their Neuropsychology and MRI prior to attending the meditation sessions. Meditation training of the patient group is ongoing. The current major issue faced in patient recruitment is getting the appropriate sample; i.e. patients without co morbid psychiatric conditions like anxiety, depression as well as other vascular ailments/ physical difficulties

- In phase I, we found better BOLD signal intensity in bilateral insula, anterior cigulate, cingulate gyrus and bilateral thalamus. These regions being the focus interoceptive awareness and other cognitive skills, practice of mindfulness meditation can subserve psychological and cognitive health.

- Current study illustrates benefits of supervised cognitive retraining on memory, orientation, language, visual spatial in patients with MCI and prodromal AD.

- Our study also indicates significant benefit with a supervised Mindfulness meditation program on episodic verbal memory in MCI and prodromal AD. However a longer period of follow up is required to ascertain durable benefits of this intervention.

- Comparisons between Meditation and cognitive retraining on neuropsychological test functions were identical with greater impact on memory in the meditation arm and global functioning in the CR arm. Significant improvements in CDR were apparent.

- Network connectivity changes in pre and post rsfMRI FC values were not statistically different indicating the effect of these interventions at a functional and neuropsychological level without real impact on functional network changes in MCI due to AD. This may indicate the irreversibility of the actual disease process of the MCI subgroup despite improvements in functionality and quality of life.

- As outreach activity of the research program, organized World Alzheimer's Day Program (2018) was observed on 27th September 2018, together with interactive sessions for patients and caregivers (details: Appendix C). We also collaborated

and presented research paper in ARDSICON 2019: 23rd National Conference of Alzheimer's and Related Disorders Society of India (15-17 November 2019).

- Scientific manuscript readied for submission:

    a) Pilot paper titled "Neural Correlates and Connectivity Network Analysis based on Task Positive and Task Negative fMRI in Mindfulnes Meditation Practitioners and Meditation Naive Controls - A Pilot Study" for submission in 'Frontiers in Human Neuroscience'
    b) Impact of mindfulness training on neuropsychological test performance and resting state networks of patients with MCI due to AD - planned for submission to 'International Journal of Geriatric Psychiatry'
    c) Does cognitive retraining have short term and long-term impact on neuropsychology test performance in MCI due to AD? – intended for submission in Journal of the Neurological Sciences.

12. S&T benefits accrued:

    i. List of Research publications

S No	Authors	Title of paper	Name of the Journal/Conference	Volume	Pages	Year
1	P.G. Rajesh, M. Nandini, Ramshekhar N Menon.	Exploring Brain at the crossroads of Mindfulness Yoga Meditation & Functional MRI	Conference: Symposium of Yoga and Indian Psychology, NIMHANS, Bengaluru, June, 2017		1	2017
2	Nandini M, Mridula Mathew, Manju Mohan, Indupriya, Elsha Bava, PG Rajesh,	Validation and proof of concept pilot study on cognitive retraining strategies in early dementia	Conference: 10th World Congress for NeuroRehabilitation, Mumbai, February, 2018		1	2018

	Ramshekhar N Menon					
3	B. Thomas, R. Sheelakumari, S. Kannath, S. Sarma, and R.N. Menon	Regional Cerebral Blood Flow in the Posterior Cingulate and Precuneus and the Entorhinal Cortical Atrophy Score Differentiate Mild Cognitive Impairment and Dementia	American Journal of Neuroradiology October 2019	40 (10)	7	2019

		Due to Alzheimer Disease.				
4	Meenu KS, Rajesh PG,S. Krishnan, Lekshmy K, Nandini Mohanan, Ramshekhar N Menon	Effects of Mindfulness Yoga on Neuropsychological functions in Mild Cognitive Impairment due to Alzheimer's Disease	23rd National Conference of Alzheimer's & Related Disorders Society of India. 15-17 November 2019, Trivandrum		1	2019
5	Meenu KS, Rajesh PG,S. Krishnan,	Effects of MUCBT-D on Quality of Life, Mindfulness	Semi-Annual Continuing Education Program "Brain & Mindfulness" - 19th January 2020,		1	2020

	Lekshmy K, Nandini Mohanan, Ramshekhar N Menon	level and Perceived Stress in MCI due to AD and their Caregivers – A Pilot Feasibility Study	Trivandrum			
6		Effects of MUCBT-D on Neuropsychological functions in Mild Cognitive Impairment due to Alzheimer's Disease	Semi-Annual Continuing Education Program "Brain & Mindfulness" - 19th January 2020, Trivandrum		1	2020

Oral Presentation:
1) Neural correlates of Mindfulness and Meditation -Structural, Functional and Metabolic perspectives. At the National Workshop on Mindfulness Unified Cognitive Behavior Therapy (MUCBT), Organized by National Association for Mindfulness and Department of Psychiatry, Government Medical College, Trivandrum, February, 2018 – By Dr. Ramshekhar N Menon
2) Exploring Brain at the crossroads of Mindfulness Meditation and Functional MRI: A Pilot study in Healthy controls, Meditation Practitioners and MCI patients. At Semi-Annual Continuing Education Program "Brain and Mindfulness" Trivandrum, January 2020 – By Mr. Rajesh PG

ii. Manpower trained on the project

a) Research Scientists or Research Associates

Senior Research Fellow - 1

Junior Research Fellow – 2

No.	Name	Qualification	Post	Experience
1	Rajesh PG	MSc Computational Biology	SRF	fMRI paradigm design and Postprcessing

2	Nandini M	MA Psychology	JRF	Neuropsychology testing, Cognitive retraining
3	Meenu KS	MSc Psychology	JRF	Neuropsychology testing, Cognitive retraining

b) No. of Ph.D. produced

Nil

c) Other Technical Personnel trained

Nil

iii. Patents taken, if any

Nil

13. Financial Position:

No	Financial Position/ Budget Head	Funds Sanctioned	Expenditure	% of Total cost
I	Salaries/ Manpower costs	1666600	1839393	100%
II	Equipment	150000	150000	100%
III	Supplies & Materials	415016	325231	100%
IV	Contingencies	91584	61584	100%
V	Travel	70000	40000	100%
VI	Overhead Expenses	300000	300000	100%
VII	Others, if any	23008 (Bank interest - Year I)		
	Total	**2716208**	**2716208**	**100%**

14. Procurement/ Usage of Equipment

a)

S No	Name of Equipment	Make/ Model	Cost (FE/ Rs)	Date of Installation	Utilisation Rate (%)	Remarks regarding maintenance/ breakdown
1	Desktop PC	Dell	107100.00	2016-17	100%	AMC by SCTIMST

2	Multi Function Printer	HP	19900.00	2016-17	100%	AMC by SCTIMST
3	External Hard Disc	Seagate	10400.00	2016-17	100%	AMC by SCTIMST

b) Plans for utilizing the equipment facilities in future: For use in CBNS, SCTIMST

Name and Signature with Date

a._____

(Co-Principal Investigator)

(In the absence of PI, Dr. Ramshekhar Menon who is in London on Commonwealth Medical Fellowship)

APPENDIX A

COGNITIVE RETRAINING MANUAL

Cognitive retraining

The cognitive retraining is carried out weekly for 1 hour. Feedback on the performance of the retraining tasks is given at the end of each session. The patient is given home based tasks for practicing during the rest of the days. Cognitive retraining is given for the following cognitive domains.

Sl no	Cognitive domains	weeks
1	Orientation	Week 1-8
2	Attention	Week 1-9
3	Mental speed/ information processing	
	Letter cancellation	Week 1-2
	Grain sorting	Week 1-4
4	Working memory	
	Mental arithmetic problems	Week 1-2
	Rearrangement of jumbled words	Week 3-4
	Rearrangement of jumbled sentences	Week 4-6
5	Verbal fluency	Week 4
6	Response inhibition	
	Design coloring	Week 1-6
	Stop start task	Week 5-6
7	Planning	
	Maze completion	Week 6-8
	Planning events	Week 6-7
	Short essay writing	Week 7-8
8	Se shifting ability	
	Categorization of beads	Week 3
	Categorization of cards	Week 4-5
	Motor set shifting	Week 4-5
9	Problem solving	Week 6
10	Visuo-constructive ability	Week 5
11	Visuo spatial reasoning	Week 6
12	Abstraction	
	Similarity and differences	Week 6
	Proverb illustration	Week 7
13	Verbal memory	Week 2-6
14	Visual memory	
	Memory for location	Week 2-6
	Memory for designs	Week 6-7

ORIENTATION & WORKING MEMORY

Level 1:

Help the patient to develop a highly structured daily schedule. Schedule everything that the patient should or will do during the day. Create a simple form with times of the day organized into 30-minute slots of time. Start with the basics of getting up in the morning, washing face, brushing teeth, etc. Schedule meals, chores and "rehab" activities. Also remember to schedule in break periods several times a day, which should last 30 minutes to an hour. Every day should be similar in schedule. Create and review each day's schedule with the patient and keep the schedule posted in several places around the home. Refer to the schedule often with the patient throughout the day, especially when changing activities. Ask questions such as, "What are you supposed to do next?" When appropriate, have the patient fill out the schedule with your assistance.

Level 2:

Either use a calendar already in the patient's home or make a realistic one up on paper. Ask the patient to tell you what day, date, month, and year it is. Show the patient on the Calendar what the date is. Cross off days that have passed. Review this date with the patient often throughout the session and the day. Write important events, such as appointments and birthdays, on the calendar. Talk about the events coming up in the next several days. Encourage caregivers to keep calendars around the house and to review the date several times a day

Level 3:

Ask the patient to provide the month, date, year, and day of the week before checking the calendar. Then proceed as in Level 2. Ask the patient to provide the date of a day removed in time. For instance, ask what the date will be tomorrow, next week, in 10 days, 5 days ago, etc. Ask the number of weeks or months until, or since, important dates, such as Christmas, birthdays, etc. Refer to the calendar as necessary.

Level 4:

Once the patient is able to follow and be responsible for his own daily schedule, encourage him or her to buy a schedule book or calendar that can easily be carried. Acquire an inexpensive electronic personal organizer or scheduler, preferably one with an alarm function

on it (this will also assist with memory and problem-solving skills). These can be bought at local discount department stores or at office supply retail stores. Help the patient learn how to use the device, program the device and encourage them to use the alarm functions to increase success in recall of daily routines and schedules or even for medication times.

Level 5:
The patient is asked to remember where the items of common use are kept in house and to locate them spatially

ATTENTION

NUMBER CONNECTION

Level 1: Serially connect numbers 1-20 randomly placed on an A4 size paper. Record the time taken to complete the task and number of errors. Once the patient is able to complete the task within **1 minute** without errors, move on to the next difficult level.

Level 2: Serially connect the numbers 1-30 randomly placed on an A4 size paper. Reduce the font size of the number. Record the time taken to complete the task and number of errors. Once the patient is able to complete the task within **3 minutes** without errors, move on to the next difficult level.

Level 3: serially connect numbers 1-40 randomly placed on an A4 size paper. Further, reduce the font size of the number. Record the time taken to complete the task and number of errors. Once the patient is able to complete the task within **5 minutes** without errors discontinue the exercise.

LETTER CANCELLATION:

Level 4: The patient is required to cancel **any two** target letters from an array presented in an A4 size sheet. They are also told that they can follow a horizontal, vertical, or a random path, according to their choice. Time taken to complete the task and errors of **commission** and

omission were recorded. Once the patient is able to complete the task without errors, move on to the next difficult level.

Level 5: The patient is required to cancel **three letters** from an array presented in an A4 size sheet. Reduce the font size of the letter/symbol. Record the time taken to complete the task and errors.

Level 6: Repeat the level 4, and 5 tasks in the presence of a distracter. A music played during the task performance is a distracter

SYMBOL CANCELLATION:

Level 7: Ask the patient to cancel **two symbols** from an array presented in an A4 size sheet. Reduce the font size of the symbol further and record the time taken to complete the task and the errors.

Level 8: The patient is required to cancel **three symbols** from an array presented in an A4 size sheet. Reduce the font size of the symbol. Record the time taken to complete the task and errors.

Level 9: Repeat the tasks 7 and 8 in the presence of a distracter.

MENTAL SPEED/INFORMATION PROCESSING

LETTER NUMBER SUBSTITUTION: The task involves substituting designated numbers corresponding to the letters of the English alphabet. Ask the subject to do the task as fast as he can without omitting any boxes vacant. The task is given at three difficulty levels. Increase the task difficulty is achieved by increasing the number of targeted symbols and numbers of letters to which corresponding symbols had to be inserted. Change the distracters in different phases in terms of different sense of modalities.

Level 1: The subject is required to substitute 6 numbers corresponding to 6 letters within three minutes time. Record the number of the symbols correctly substituted. Once, the subject is able to do that, move on to the next difficulty level.

Level 2: The subject is required to substitute 8 symbols corresponding to 8 letters within three minutes time. Record the number of the symbols correctly substituted

Level 3: Repeat levels 1 and 2 in the presence of a distracter, say music. Record the number of the symbols correctly substituted.

GRAIN SORTING TASK: The task involves sorting of mixed grains into piles of similar grains with the type of grains ranging from two to four. The quantity of grains sorted in 15 minutes is measured. The task is given at five difficulty levels

Level 1: The subject is required to sort two types of big grains. The quantity of grains sorted in 15 minutes is measured. Give the task for 1 week.

Level 2: The subject is required to sort two types of small grains in week 2. The quantity of grains sorted in 15 minutes is measured

Level 3: The subject is required to sort three types of small grains in week 3. The quantity of grains sorted in 15 minutes is measured.

Level 4: In the fourth week, the subject is made to listen to the music while sorting three types of small grains to increase task difficulty. The quantity of grains sorted in 30 minutes is measured

Level 5: The subject is required to sort four types of small grains in the weeks 5 and 6. During the weeks 5 and 6, the subject is made to listen to the music while sorting four types of small grains to increase task difficulty. The quantity of grains sorted in 30 minutes is measured.

VERBAL FLUENCY

WORD GENERATION: The task consists of generating as many as words as possible starting with a selected letter and words belonging to a category within a stipulated time. The task is given in one difficulty level. The task is given during the fourth week of cognitive retraining

program. Letters and the category should be the ones other than used in the verbal fluency tests.

RESPONSE INHIBITION

STOP- START TASK: Stop- start is introduced in the week 5 and 6 of the cognitive retraining programme. In this task while the patient is performing a motor sequence for e.g. clapping hands, he is instructed to stop suddenly without a prior signal and then asked to restart the same sequence when the start signal is given. The start-stop signal is given randomly. The task is performed for 5 minutes in each therapy session,

STROOP TEST: The stroop test is given during week 5 and week 6. The task is divided into two sessions. The patient is asked to read out of the words instead of the colours. In the second phase, the patient is asked to name the colour instead of the words. The errors are noted.

PLANNING & MEMORY

Level 1:

Help the patient to make a Memory Notebook. Things that could be included can be

1)an autobiographical background section to assist the patient with long-term, recent and short-term memory, 2) a section for daily schedules, 3) a section for medication schedules, 4) important telephone numbers and family/friends' names, etc. Make it part of the patient's routine that the notebook be referenced for information several times daily in response to specific questions, (for example, "What time are you supposed to do your exercise?" or "Can you find that information in your notebook?").

Level 2:

A "daily activity" could be to check this Memory Notebook and mark off things that have been completed for that day or week. At this point the patient should be taking on more of the responsibility for keeping his notebook and daily schedule up to date and following it as appropriate. Give the patient more opportunity to use the notebook more independently by suggesting that he or she check the notebook to see if there is anything to be done or if they might have certain information handy.

Level 3:

MAZE COMPLETION TASK: Beginning with the starting point, patient had to trace the way out in the maze without tracing into a blind alley. The task is given at three difficulty levels. Increased task difficulty is achieved by the complexity of maze with increase in blind alleys and the route to reach the endpoint. The task can be given during weeks 6, 7 and 8.

Level 4:

PLANNING EVENTS: The patient is given real life situations and asked to narrate the steps taken to achieve the desired goal. For example, a situation such as planning for a picnic within a given budget is given. The therapist is required to suggest improvements to the plan. the task can be given during weeks 6 and 7.

Level 5:

SHORT ESSAY WRITING: The task involves writing a short essay on a given topic. The topics are related to activities that pertained to patient's interests and daily activities. The task is given at one level of difficulty. The task can be give at week 8.

SET SHIFTING

CATEGORIZATION OF BEADS: In week 3, 50 beads of various shapes, colours and sizes are combined together. The patient's task is to categorize the beads employing a different rule every day. The task is given during week 3. Excellent

CATEGORIZATION OF PLAYING CARDS: The patient is required to sort two decks of playing cards. this task is given during weeks 4 and 5. In week 4, the patient has to identify the sorting rule of the therapist while in week 5, the patient himself has to generate a sorting rule.

MOTOR SET-SHIFTING: Motor shifting task can be included during the weeks 4 and 5 for 5 minutes. The patient suddenly shifts from one motor sequence such as clapping hands to another sequence such as tapping feet

VISUO-CONSTRUCTIVE ABILITY

DOT BASED DESIGN CONSTRUCTION: the task involves the construction of three target designs, geometrical designs, using the dots placed in each of the boxes. The task is given at a single difficulty level. The task is given during week 5.

VISUO-SPATIAL REASONING

TRACING EMBEDDED FIGURES: the task involves tracing a embedded simple figure hidden within a complex figure. Six simple figures are placed in two rows with three figures per row. Beneath each figure, a complex figure is placed. This complex figure contains the simple figure. The task is given in at one level of difficulty. The task is given during week 6.

ABSTRACTION

PROVERB ILLUSTRATION: The task involves illustration of a given proverb. The patient is asked to write the meaning of the proverb with an example. The task is given in one level of difficulty. The task is given during week 7.

SIMILARITY: The patient is presented with a pair of objects and asked to tell the similarities between the two objects. The patient is presented with simple to complex objects in the order of difficulty.

PROBLEM SOLVING

MENTAL ARITHMETIC PROBLEMS: 10 mental arithmetic problems are given to the patient during weeks 1 and 2. The task is discontinued as the patient reaches the ceiling level.

REARRANGEMENT OF JUMBLED WORDS: the task is to rearrange the letters to make a meaningful word. Words chosen for this task are simple nouns and words, having an average of four to six letters. The task is given at one difficulty level. The task can be given during weeks 3 and 4 of the cognitive remediation programme.

REARRANGEMENT OF JUMBLED SENTENCES: 10 jumbled sentences are administered to the patient during weeks 5 and 6. Discontinue the task when the patient reaches the ceiling level.

PREDICTING THE OUTCOME OF A DESIRED SITUATION: A problem situation is presented to the subject and asks the subject "What you will do if ------- happens?

Example: What will you do if electricity goes off suddenly?

COMPREHENSION

CARRYING OUT COMMANDS: Two objects, a pen and a book were placed in front of the subject. Commands of various levels of complexity, when required manipulation of these objects, is given

SENTENCE REPETITION

A phrase or sentence should be read out to the participant and an immediate repetition was expected. The target sentence should not be very long.

EXPRESSIVE SPEECH

NAMING AND DESCRIBING THINGS (CUEING AND SEMANTIC ANALYSIS): The subject is asked to name given objects (initially cues are provided). Then he is asked to describe a thing or a picture.

READING ABILITY

SIGHT WORD APPROACH: The subject is made to read aloud selected words from a paragraph written on the flash cards and after mastering made to read the paragraph. Record the number of errors committed and the time taken to complete the task.

PHONETICS APPROACH: Reading aloud a list of words belonging to a particular phonetic family.

VERBAL MEMORY

TEMPORAL ENCODING: A list of 9 words is presented in a chunk of 3 words at a time and the patient is asked to recall. Teach the patient the strategy of semantic elaboration in the form of organizing the words and constructing a meaningful sentence for each set of words and visualizing the meaning of the sentence. The patient is asked to recall the words again in the same temporal order (immediate and delayed recall). Ensure the encoding in both verbal

and visual modality. Present three separate lists of words in each session. After the patient is able to recall all the words in the list after 1 month, the length can be increased to 12.

VISUAL MEMORY

MEMORY FOR LOCATION: Tasks for improvement of visuo spatial encoding and visual memory for locations require the patient to reproduce the location and sequence of an arrangement of objects on a table, from memory. An increasing number of objects are exposed for 10 seconds. Following maintenance in memory for another 10 seconds, the patient is asked to reproduce the arrangement. The task is given from weeks 2-6, with accuracy of reproduction as the score.

MEMORY FOR DESIGNS: The task involves drawing a given design from memory. Each abstract design contains five to eight components, which is exposed for 10 seconds. Patient is asked to observe the design carefully. After 10 seconds, the patient is asked to try to memorize the various components. In each session, there are 10 designs. The task is given at one level of difficulty. The correct number of designs forms the score. The task is given during weeks 7 and 8.

Psychotherapy sessions for the patients with psychosocial problems

Initial interview

- Assessment of current difficulties
- Goal definition
- Presentation of treatment rationale
- Beginning treatment

Subsequent therapy sessions:

- Setting the agenda
- Weekly items
- The day’s major topic
- Homework assignments
- Feedback

APPENDIX: B

(MINDFULNESS MANUAL)

APPENDIX: C

(ALZHEIMERS OUTREACH PROGRAMME)

APPENDIX: D

(PUBLICATIONS & POSTERS)

APPENDIX B

PUBLICATION & OUTREACH

Proceedings of the symposium on

'Yoga and Indian Psychology'

As a part of the International Yoga Day Celebrations

25th June 2017

Organized By

National Institute of Mental Health and Neuro Sciences (NIMHANS)
An Institute of National Importance
Bengaluru, 560029

Exploring Brain at the crossroads of Mindfulness Yoga Meditation & Functional MRI - A pilot study in Healthy Yoga Practitioners

P.G. Rajesh[1], M. Nandini[1], Ramshekhar N Menon[1]
[1]Sree Chitra Tirunal Institute for Medical Sciences & Technology
Trivandrum, India

Background

"Yoga Chitta Vritti Nirodhah" in Yoga sutra, Patanjali describes that yoga halts the disturbance of mind. Meditation as well as Yoga is effective in fortifying attention, awareness and insight. Mindfulness meditation refers to the active state of mind were we have broad attention to the present. This technique was found beneficial to people with psychological and neurological pathologies. Mild Cognitive Impairment (MCI) is featured by decline in cognitive functioning including memory and thinking abilities. MCI is a plausible precursor for dementia. Clinical evaluations suggest that individuals with MCI have a high risk of eventual progression to AD or other forms of dementia. The current study is an intervention aimed at harnessing the potential of mindfulness yoga in analyzing, evaluating and improving cognitive functioning associated with MCI with support of well-established neuroimaging modality like fMRI.

Methodology

We combined administration of Mindfulness yoga-meditation for sustaining as well as improving the quality of life in patients (MCI and prodromal AD). The effectiveness will be traced by psychological evaluation techniques; mindfulness yoga based meditation fMRI paradigms as well as resting state brain connectivity analysis. The study attempts to determine the impact of these interventions on neuropsychological performance and quality of life.

Results

The neural correlates of meditation in healthy meditators (5 Subjects) as depicted by the supra-threshold voxels ($p<0.05$) in SPM analysis were obtained at Middle temporal gyrus, parahippocampal gyrus, hippocampus and frontal regions. Hippocampus and parahippocampus being neural correlates critical in memory. Subjects were likely to demonstrate brain activation similar to that of memory encoding & recall. The study is in its infancy and ongoing. This methodology require validation in larger group of meditators, patients and healthy controls and its relevance in memory performance has to be gauged in patient group with MCI for reliable longitudinal inference.

Discussion & Conclusion

MCI is mainly attributed by cognitive impairment and the level of impairment will be greater compared to those associated with healthy ageing. At present there are no FDA approved medicines specifically for treating MCI. Besides individuals with MCI & their family, the medical fraternity and caregivers have huge concern about the associated memory decline, quality of life and management. To overcome this, there should be prospective methods to limit the number of cases progressing towards dementia. This is a unique study which makes use of the potential of mindfulness yoga in analyzing, evaluating and improving cognitive functioning associated with MCI. Such synergistic and cross disciplinary studies can ensure scientific benefits besides they can bring about changes in the treatment of irresistible neurodegenerative diseases.

Acknowledgement: Department of Science & Technology Grant under SATYAM scheme 2016

43% had academic challenges and 40% presented with cognitive complaints. On objective testing impairments were seen in executive functioning (73%), attention (>50%), and speed of processing (50%).

Conclusions: Early identification, monitoring, and appropriate intervention and rehabilitation for neuropsychological problems are required. Long-term risk of academic underperformance exists despite normal global intelligence. This study underscores an urgent need for psycho-education and awareness programmes for parents, teachers and health professionals to plan effective neuropsychological rehabilitation.

T-016: Effect of medical welfare cooperation of "vocational rehabilitation planning sheet for people with cognitive disorders after acquired brain injury"

Tamami Aida, *Mejiro University, Saitama Shi, Saitama Pref., Japan*

Objectives: In Japan, social supports in daily living and social activities for clients with Cognitive disorders (CDs) after acquired brain injuries (ABI) were started in 2011. However, VR services were not effectively used by clients with CDs. The purpose of this study is to verify the effect of promoting transition to Vocational rehabilitation (VR), according to professionals' use of the brochure for consulting clients at hospitals.

Methods: We printed an 8-page brochure in B5 size about the processes for clients and professionals which we found by a qualitative analysis from 12 professionals' interviews. Objects are professionals for CDs at seven hospitals who are members of support councils for CDs in Itabashi, Tokyo. We surveyed before and one month after the use of the brochure by the placement method. We constructed a questionnaire that has 20 items, 7 items about the Capacity of VR, 7 items about the Knowledge of VR, 6 items about the Experience of VR. We gave a presentation about the brochure at hospitals that the used it to consult about VR with clients who need RTW or reemployment. We used Mann-Whitney U for comparing before and after using the brochure. This study has been approved by the research ethics committee of Mejiro University (Permission number: 14-016).

Results: The survey period was August to September, 2016. Of 78 people, 68% were Occupational Therapists, 21% were Speech Therapists. 69 people answered again after a month. 30% used the brochure, 70% didn't have clients who must use the brochure. After using the brochure, knowledge about VR transfer items were significantly increased. There weren't significantly decreased items. Also, offering VR wasn't significantly different.

Conclusions: The brochure was effective for improvement of VR knowledge.

T-017: Neuropsychology practice in India: Online survey based study

Farzana Mulla, *Jehangir Hospital, Pune, Maharashtra, India*

Objectives: Neuropsychology is a relatively young profession in India. To date, no study has examined aspects of neuropsychological practice in India. Hence, the purpose of this online study was to identify characteristics of individuals working in the area of neuropsychology with a view to understanding their educational background, current work situation, referral pattern, existing professional and organizational support and future needs.

Methods: An online survey was administered to participants via an email link. Participants who completed the online survey were self-identified psychologists who carried out neuropsychology related work. 36 participants from geographically different parts of India completed the survey. The data was analyzed into frequencies.

Results: Findings from the online survey suggested that those practicing in neuropsychology are predominantly females, have limited training in neuropsychology in India, formally through placement during MPhil in clinical psychology or informally through guidance from senior neuropsychologists and/or through attending workshops. Majority are relatively new to the field with less than 5 years of experience and mainly practicing in the private sector. Those practicing in government or teaching hospitals constitute a minor segment. Referral numbers are currently low, and these are primarily for neuropsychological assessment rather than rehabilitation. The findings further identified a huge gap, namely a significant need for formal courses or training in neuropsychology and neuropsychological rehabilitation in India.

Conclusions: Despite some limitations, the online survey was the first evidence based exploration of the environment and needs of those practicing in neuropsychology. It provides an early insight into current working conditions, identifying future needs and direction.

T-018: Validation and proof of concept pilot study on cognitive retraining strategies in early dementia

Nandini Mohanan, *Sree Chitra Tirunal Institute For Medical Sciences, Trivandrum, Kerala, India*

Objectives: Literature from India on cognitive retraining (CR) in mild cognitive impairment (MCI) and early dementia is sparse. To develop and validate a CR strategy and to examine its utility in rehabilitation of subjects with MCI and Early Dementia.

Methods: A CR strategy was devised across multiple domains (attention, orientation, memory, executive function, language, visuospatial). Inter-examiner reliability was calculated and estimated at 0.80. Subjects were evaluated using the Malayalam versions of Addenbrooke's cognitive examination (ACE), and standard neuropsychological tests to identify the maximal affected domain. Individualised domain-deficit specific cognitive retraining was given with weekly one hour therapy sessions. Clinical dementia rating scale (CDR) and instrumental activities of daily living (IADL) assessments were done on a monthly basis to assess the efficacy of the therapy in addition to follow-up neuropsychology tests at 6 months and 1 year.

Results: Out of a total of 60 early dementia with CDR is less than 2,13 patients consented for CR therapy (amnestic MCI-6, multi-domain MCI-1; early AD-5; limbic encephalitis-1), based on the scores in neuropsychological test evaluation. CDR ranged from 0.5- 4 (calculated as sum of boxes); ACE ranged from 65-89; age at evaluationranged from 60- 85. Post retraining CDR change ranged from 0.5- 1 in more than 50% of the cohort, with stability and no further decline in the remaining participants. Subjects with amnestic MCI and the single subject with multi-domain MCI were more likely to demonstrate improvement on neuropsychological functions of attention, memory, executive functioning, planning and visuo-spatial skills.

Conclusions: This is a unique validation and proof of concept case series from India on the efficacy of CR in MCI and early dementia.

T-019: A new computer-based saccade traing program for patients with hemianopia – Preliminary results

René M. Müri, *University Hospital Inselspital, Bern, Switzerland*

Objectives: Stroke is the most common cause for hemianopia followed by traumatic brain injury and brain tumors. Though early recovery is expected in around half of cases within the first 3 months after injury, patients with persistent hemianopia are often disabled in activities of daily living. Rehabilitative compensatory approaches generally target eye movement training which are needed to improve explorative behavior in the hemianopic visual field. We developed and evaluated a computer based training tool for patients with homonymous hemianopia that is portable, inexpensive, and easy to deploy.

Methods: The computer based training program consists of two client interfaces, "Therapist" and "Patient" with an automatic difficulty adjustment. The task is a visual search task, presented on pictures or videos during 20-30 seconds. A server based user management system is used to store and synchronize data between both interfaces. The complete application was evaluated with four patients. Participants were instructed to press either the right or left arrow key depending on the stimuli presented on the background. Upon improvement, the background changed from images to videos. Patients feedback was collected via the System Usability Score and the Saccadic Eye Training questionnaire.

Results: The average usability score was 96.875. Patients who claimed to work more often with computers, and have better computer knowledge show higher SUS scores. As the difficulty increases, the completion time is longer. The reaction time in the impaired quadrants is slower compared to the other quadrants.

Conclusions: An advantage of the new training program is the automatic adjustment of the difficulty level in par with the performance and individual capacity of the patient, which will insure patient motivation and participation. The new training program will insure patient compliance and improve quality of life of patients suffering from visual field deficits.

T-020: Case study highlighting the effectiveness of intensive neuropsychological rehabilitation 13 years since brain injury

Shraddha Shah, *Synapsium Brain Health Clinic, Mumbai, Maharashtra, India*

Objectives: To highlight the relevance of rehabilitation interventions even after several years of initial injury. In the present case, neuropsychological rehabilitation began 13 years after injury and therefore, presented with various challenges including, significant amnesia and depression.

Methods: NS, a 47-year old gentleman was a high-functioning businessman prior to contracting TB Meningitis and suffering secondary hydrocephalus in 2002. He suffered several medical complications and remained in intensive care for 8 months.

Cognitively, his profile revealed improvement from 2003 to 2013. However, he remained in a state of posttraumatic amnesia and displayed significant global impairment.

Behaviourally, NS had been severely depressed and frequently threatened suicide. A neuropsychiatrist was treating him with pharmacotherapy but the symptoms persisted.

He was anxious about his right-sided hemiparesis and walking disability. He was severely apathetic, gave up easily and was not cooperative during therapy. His mood and behaviour led to significant strain on the family relations over the years.

In terms of ADLs and IADLs, NS remained dependent on the family and was largely homebound.

In July 2015, an intensive rehabilitation plan was strategized. The daily plan included 4 hours of cognitive therapy and an additional 1-hour of physical therapy from Monday to Friday spanning over 4 months.

The neuropsychological rehabilitation included cognitive stimulation, emotion-oriented psychotherapy, positive psychology interventions, social participation and mindfulness meditation.

Results: After completion of the intervention, there was an improvement in mood as well as social and occupational participation leading to better Quality of Life (QOL). He also displayed an improvement in several cognitive domains. The gains remained even 5 months after discontinuing rehabilitation.

Conclusions: This case highlights the importance of beginning rehabilitative interventions despite several years since injury. Customising rehabilitation sessions according to the patient's injury profile and functioning can lead to improvement in spite of significant global cognitive impairment.

T-021: Designing new technologies to assist memory in patients with neurological disorders

Laurie Ann Miller, *Royal Prince Alfred Hospital, University of Sydney, Sydney, New South Wales, Australia*

Objectives: Memory deficits associated with stroke, mild cognitive impairment or early dementia can include problems with wayfinding,

Regional Cerebral Blood Flow in the Posterior Cingulate and Precuneus and the Entorhinal Cortical Atrophy Score Differentiate Mild Cognitive Impairment and Dementia Due to Alzheimer Disease

B. Thomas, R. Sheelakumari, S. Kannath, S. Sarma, and R.N. Menon

ABSTRACT

BACKGROUND AND PURPOSE: Alzheimer disease is the most common degenerative dementia affecting humans and mild cognitive impairment is considered the forerunner of this devastating illness with variable progression. Differentiating between them has become all the more essential with the advent of disease-modifying medications. The aim of this study was to test the utility of the entorhinal cortical atrophy score in combination with quantitative CBF in the posterior cingulate and precuneus using arterial spin-labeling to differentiate mild cognitive impairment and early Alzheimer disease.

MATERIALS AND METHODS: We analyzed MR imaging from a prospective data base of 3 age-matched groups: 21 cognitively healthy controls, 20 patients with mild cognitive impairment, and 19 patients with early Alzheimer disease. The highest entorhinal cortical atrophy score and an atlas-based measurement of CBF in the posterior cingulate and precuneus were estimated in these groups. Statistical comparison was performed among the groups for disease-prediction probability with these parameters independently and in combination using a binary logistic regression model.

RESULTS: The entorhinal cortical atrophy score performed well in distinguishing AD from HC, with a predicted probability of .887 (area under the curve, $P < .001$). The mean CBF of the posterior cingulate and precuneus was also found to be a useful discriminator (area under the curve, 0.810, $P = < .001$). Combining the entorhinal cortical atrophy score and CBF was the best predictor (area under the curve, 0.957, $P < .001$). In distinguishing mild cognitive impairment and Alzheimer disease, entorhinal cortical atrophy also did well with an area under the curve of 0.838 ($P < .001$). However regional CBF was not useful in differentiating them (area under the curve = 0.589, $P = .339$). Entorhinal cortical atrophy scored poorly in distinguishing mild cognitive impairment from healthy controls (AUC = 0.571, $P = .493$), but CBF fared well, with an area under the curve of 0.776 ($P = .002$).

CONCLUSIONS: Combining entorhinal cortical atrophy and regional CBF could be a potential imaging biomarker in distinguishing mild cognitive impairment and Alzheimer disease.

ABBREVIATIONS: ACE-M = South Indian language of Malayalam version of Addenbrooke's Cognitive Examination; AD = Alzheimer disease; ASL = arterial spin-labeling; ERICA = entorhinal cortical atrophy; HC = healthy controls; MCI = mild cognitive impairment; PCG = posterior cingulate gyrus; PC = precuneus; ROI = region of interest

Alzheimer disease (AD) is the most common degenerative dementia affecting humans with marked socio-economic burden for care of the affected.[1,2] Mild cognitive impairment (MCI) is considered the forerunner of this devastating illness with variable progression.[3] With the advent of disease-modifying medications, early detection and classification of preclinical dementia have become essential. Exploration of possible biomarkers identifying individuals who are at high risk for developing AD is the focus of current research. Validated biomarkers for diagnosing MCI at risk of progression include Pittsburgh compound–based PET and CSF biomarkers, which are either not available in many centers worldwide or are prohibitively expensive.[4] The relevance of validating instruments from widely available multimodality imaging techniques has been demonstrated by our group previously.[5]

Received April 22, 2019; accepted after revision August 1.

From the Department of Imaging Sciences and Interventional Radiology (B.T., R.S., S.K.), Division of Cognitive and Behavioural Neurology (R.N.M.), and Achutha Menon Centre for Health Sciences Studies (S.S.), Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India.

This work was supported by CSI/90/2012, SATYAM/278/2015, and SERB N-PDF 2017 grants from the Government of India.

Please address correspondence to Bejoy Thomas, MD, DNB, PDCC, Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India; e-mail: bejoy@sctimst.ac.in; @drbejoy2002

http://dx.doi.org/10.3174/ajnr.A6219

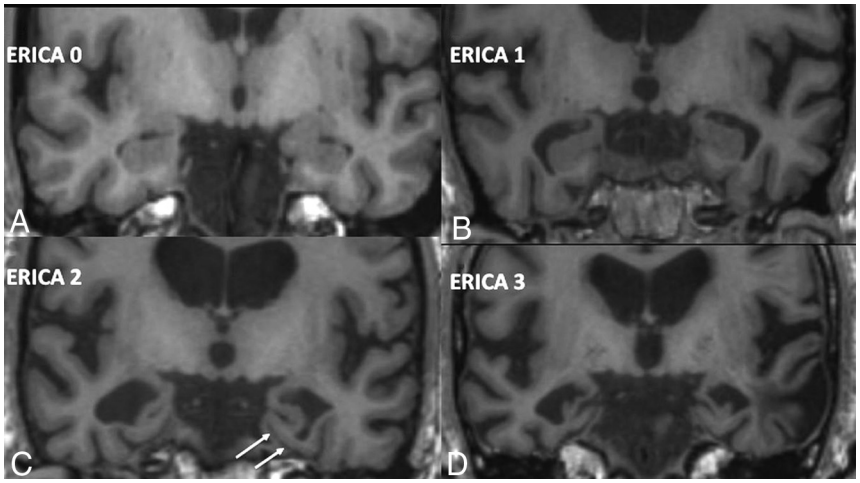


FIG 1. ERICA scoring. *A*, Score 0 with no parahippocampal atrophy. *B*, Score 1 with mild atrophy with prominence of collateral sulcus. *C*, Score 2 with moderate entorhinal cortical atrophy with tentorial cleft sign (*arrows*). *D*, Score 3 with marked parahippocampal atrophy. Adapted from Enkirch et al.[17]

Cerebral blood flow alterations in patients with AD and MCI have been identified as an important marker in understanding the neurophysiologic changes even before development of neuronal loss.[6] Arterial spin-labeling (ASL) uses tagged arterial blood as an endogenous contrast for detecting regional CBF perfusion changes. Many recent studies have highlighted its role in imaging AD and MCI, in which different brain regions have been found to show hypo- or hyperperfusion.[7-13] ASL is a noninvasive MR perfusion technique, without the use of any ionizing radiation, intravenous contrast agents, or radioactive isotopes, and it is considered a potential alternative to FDG-PET imaging.[14,15] Using ASL, many studies have consistently shown statistically significant hypoperfusion involving the posterior cingulate gyrus (PCG) and precuneus (PC), among many regions studied in MCI-AD.[10,11,13] Only a few studies have correlated quantitative CBF with neuropsychology in AD and MCI.[16] No consistent correlation has been established between CBF and gray matter volume changes in the corresponding regions in patients with AD and MCI in the existing literature.[13]

The entorhinal cortex has been shown to undergo graded atrophy in the MCI-AD complex and is thought to be one of the early areas of the brain that shows gray matter atrophy in AD.[17] A recently described numeric atrophy scale of the entorhinal cortex (ERICA) score has been shown to correlate well with the cognitive changes and the diagnosis of AD.[17] It has also been shown to be better than the previously described medial temporal lobe atrophy score in differentiating AD from subjectively reported cognitive impairment in patients.[17] The ERICA score is a 4-point atrophy rating scale from 0 to 3, where 0 indicates no evidence for atrophy of the entorhinal cortex, and 3, marked atrophy (Fig 1). This was shown to be handy because the scoring system is very simple, but powerful enough to be used for the distinction of these conditions. However, this scoring system has not yet been validated by further studies.

The aim of the present study was to test the hypothesis that the regional CBF changes measured in the posterior cingulate and precuneus (PCG + PC) region using the 3D fast spin-echo pseudocontinuous ASL sequence along with ERICA scoring of entorhinal cortical atrophy will be a better biomarker in differentiating patients with AD and MCI compared with healthy controls (HC).

MATERIALS AND METHODS

MR images from the data base of prospectively recruited consecutive subjects attending the Memory and Neurobehavioral Disorders Clinic of a tertiary referral teaching hospital in the South Indian state of Kerala, between 2016 and 2018, were included in this study. Age-matched control data were also collected during the period from the data base. Five subjects were excluded due to insufficient image quality. The final sample consisted of 21 controls, 20 patients with MCI, and 19 patients with AD. All subjects provided written consent according to procedures approved by the Institutional Ethics Committee of our institution. The diagnosis of MCI and AD was based on subjective cognitive symptoms verified by objective evidence of decline by a family member compared with the previous status and confirmed by evidence of a decline in ≥1 neuropsychological domain[4] as shown below. Participants with a global cognitive assessment score, as determined on the vernacular version (in the South Indian language of Malayalam of Addenbrooke's Cognitive Examination [ACE-M]), between 88 and 100; a Clinical Dementia Rating score of 0; with formal education of >10 years; no subjective memory symptoms; and with no serious neurologic/psychiatric issues were selected as healthy controls.[18,19] Participants with a Clinical Dementia Rating of <2 and an ACE-M score between 60 and 78 were confirmed as having AD according to standard National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association diagnostic criteria.[20]

Because we wanted to recruit patients with early AD who were largely independent for activities of daily living and capable of giving informed consent, we decided to include subjects with a Clinical Dementia Rating of only 0.5–1. Patients with MCI were diagnosed per the Modified Petersen Criteria with a Clinical Dementia Rating of ≤0.5 and an ACE-M score between 78 and 88 with evidence of impairment in ≥1 cognitive domain, defined as test performance on at least 2 tests (which also included the ACE-M subcomponent scores) for a given domain falling below a mean −1.5 SD of the normative scores for the corresponding age and education status.[21] Exclusion criteria included the presence of a major neurologic disorder (stroke), medical comorbidities (cardiovascular, renal), and psychiatric illness (clinically significant anxiety and depression [Hospital Anxiety Depression

Scale score should be <7], psychosis), similar to those in our previous study.[19]

Imaging Protocol

A 3T scanner (Discovery MR750w, GE Healthcare, Milwaukee, Wisconsin) with a 32-channel phased array head coil was used to acquire structural and ASL images. Structural images were obtained using a high-resolution 3D brain volume imaging sequence (3D-BRAVO) with the following parameters: TR/TE = 7/2.98 ms, section thickness = 1 mm, flip angle = 12°, matrix size = 256 × 256, and voxel size = 1 × 1 × 1 mm^3. A 3D fast spin-echo pseudocontinuous ASL sequence was performed with the following acquisition parameters: TR/TE = 4852/10.70 ms, flip angle = 111°, voxel size = 1.875 × 1.875 × 4, section thickness = 4 mm, NEX = 3, and postlabel delay = 2025 ms.

Data Analysis

Structural and ASL data were processed using an off-line PC workstation. For ASL processing, quantitative CBF maps with values measured in units of milliliters/100 g/min in each subject were used. All the structural images and CBF maps were oriented in the anterior/posterior commissure line using Statistical Parameter Mapping software (SPM12; http://www.fil.ion.ucl.ac.uk/spm/download/spm12/). CBF maps of all the participants were then normalized to a standard stereotactic space and spatially smoothed with an 8-mm isotropic Gaussian kernel to improve the signal-to-noise ratio. Second-level statistical procedures implemented in SPM12 were used to analyze the CBF maps. The value of total intracranial volume was used as a covariate in the statistical design to correct variability among groups. Information on regional perfusion values was extracted by means of an ROI analysis. Anatomic ROIs for the posterior cingulate and precuneus were defined by means of the WFU PickAtlas tool (https://www.nitrc.org/projects/wfu_pickatlas/) (Fig 2). Regional CBF was estimated using parameter extraction with MarsBaR (https://www.nitrc.org/projects/marsbar/). Values within ROIs of both sides were then averaged and tabulated for HC, MCI, and AD groups.

ERICA scoring was performed on coronally reformatted 3D-T1 BRAVO images in all subjects by 2 independent neuroradiologists (B.T. and S.K.) with 19 and 10 years of experience, respectively, at the level of the mamillary bodies as described by Enkirch et al.[17] The interobserver agreement was calculated using Cohen κ statistics. Values on the right and left sides were tabulated, and the highest ERICA score in consensus in each subject was used for further analysis.

Statistical Analysis

The χ^2 test was used for comparison of sex differences and vascular risk factors among groups (Table 1). The clinical differentiation scores are also summarized in the same table. For comparison of age, 1-way ANOVA was performed. The ERICA score and CBF measures in the ROI were used to derive the predicted probability of MCI and AD based on a binary logistic regression model. The derived measures were used for generating the receiver operating characteristic curves, and the area under the curve was used to compare them (Table 2 and Fig 3). Statistical analyses were performed using the software SPSS for Windows, Version 21.0 (IBM, Armonk, New York).

RESULTS

The demographics, clinical cognitive scores, and vascular risk factors of each group are summarized in Table 1. There was no significant difference in age, sex, or vascular risk factors among these 3 cohorts.

The average highest ERICA score was 0.71 ± 0.46 in HC, 0.90 ± 0.64 in MCI, and 2.15 ± 0.83 in AD. There was overall substantial interrater agreement for ERICA scoring (Cohen κ = 0.783 for the right side, 0. 777 for the left side, and 0.797 for the highest ERICA score). The mean CBF in PCG + PC was 46.64 ± 8.4, 39.08 ± 6.6, and 36.51 ± 8.4 mL/100/min in HC, MCI, and AD, respectively (Table 2).

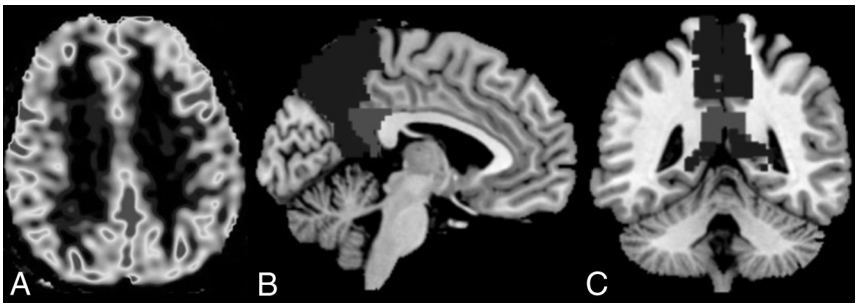


FIG 2. *A*, Axial ASL CBF gray-scale map. *B* and *C*, Sagittal and coronal representative images, respectively, of the template for automated segmentation and extraction of posterior cingulate (light gray) and precuneus (dark gray) ASL CBF perfusion maps.

Table 1: Demographic data, comorbidities, and clinical scores of subjects

Characteristic	HC (*n* = 21)	MCI (*n* = 20)	AD (*n* = 19)	*P* Value		
				MCI versus HC	AD versus HC	AD versus MCI
Sex (male/female)	11:10	11:9	11:8	.87	.77	.88
Age (mean ± SD) (yr)	64.57 ± 5.74	66.75 ± 4.08	66.68 ± 5.31	.37	.66	1.00
H/o hypertension	5/21	7/20	9/19	.33	.11	.32
H/o diabetes mellitus	5/21	8/20	10/19	.22	.06	.32
RAVLT cumulative learning score (mean)	48.52 ± 8.46	33.47 ± 10.07	25.21 ± 7.15	**<.001**	**<.001**	**.035**
RAVLT 20-min recall score (mean)	10.00 ± 2.82	5.41 ± 3.74	1.36 ± 1.73	**<.001**	**<.001**	**.001**
ACE-M	93.38 ± 4.11	81.12 ± 11.09	72.00 ± 11.09	**<.001**	**<.001**	**.020**

Note:—H/o indicates History of; RAVLT, Rey auditory verbal learning test; ACE-M, Addenbrooke's Cognitive examination. Significant *P* values are highlighted in bold.

Table 2: Performance of the ERICA score and CBF of PCG + PC in predicting HC, MCI, and AD

Parameters	HC (Mean)	MCI (Mean)	AD (Mean)	Predicted Probability of Diagnosis (Area under the Curve of ROC) with *P* Values in Parentheses		
				MCI vs HC	AD vs HC	AD vs MCI
ERICA (0–3)	0.71 ± 0.46	0.90 ± 0.64	2.15 ± 0.83	0.571 (.493)	0.887 (<**.001**)	0.838 (<**.001**)
CBF in PCG + PC (mL/100 g/min)	46.64 ± 8.4	39.08 ± 6.6	36.51 ± 8.4	0.776 (**.002**)	0.810 (<**.001**)	0.589 (.339)
Combined ERICA and CBF				0.781 (**.002**)	0.957 (<**.001**)	0.829 (<**.001**)

Note:—ROC indicates receiver operating characteristic. Significant *P* values are highlighted in bold.

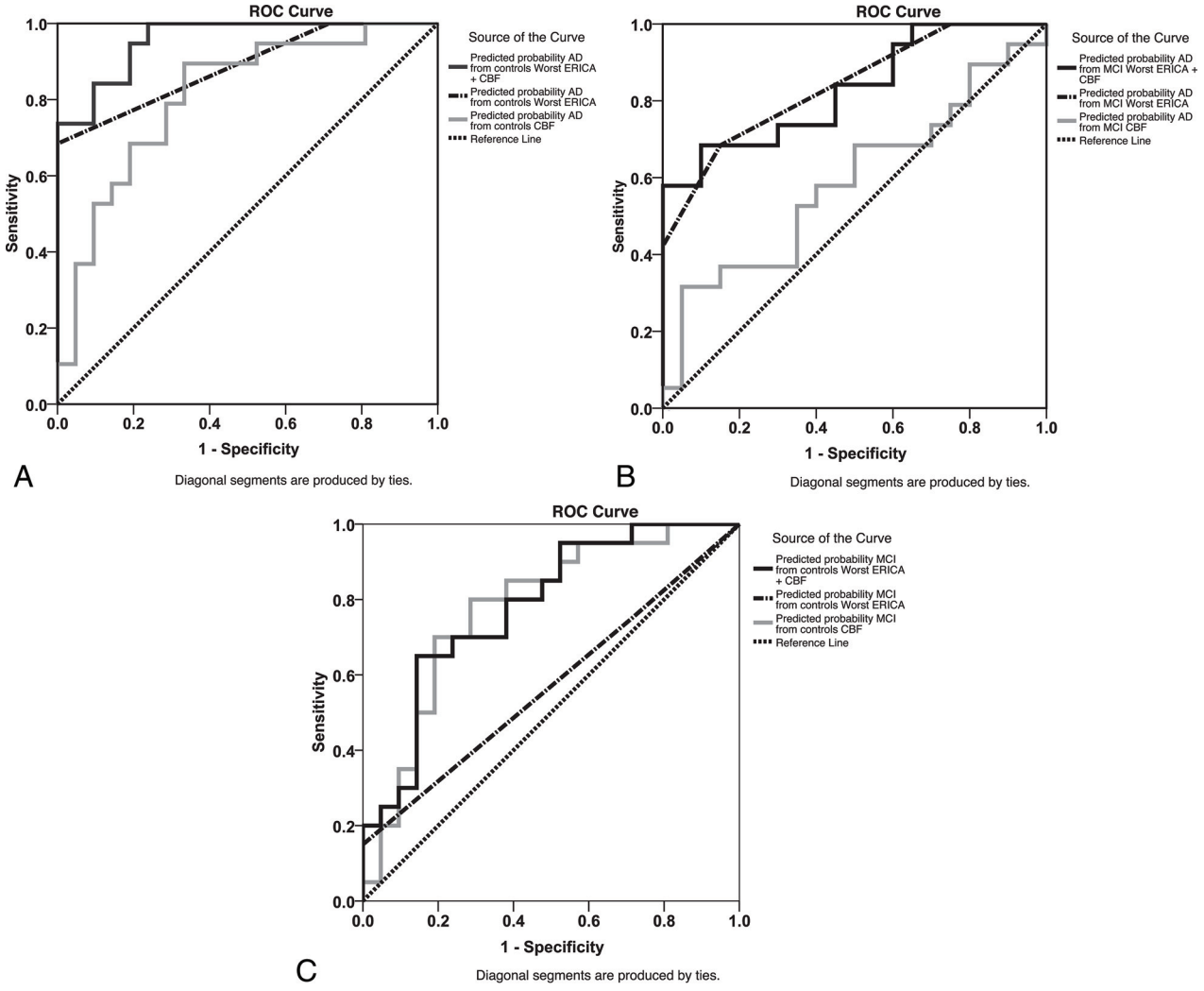


FIG 3. Receiver operating characteristic curves for predicted probability from ERICA (*dot-dash lines*) and regional CBF (*light gray continuous lines*) and a combination of both (*black continuous lines*). AD versus HC (*A*), AD versus MCI (*B*), MCI versus HC (*C*).

Both ERICA scores and mean CBF were highly predictive of distinguishing AD from HC, with a predicted probability of 0.887 ($P < .001$) and 0.810 ($P < .001$), respectively. How-ever, combining the ERICA score and mean CBF significantly increased the discriminatory power between AD and HC with the predicted probability of 0.957 ($P < .001$) (Fig 3*A*). While the ERICA score was found to be useful in distinguishing MCI from AD (predictive probability of 0.838, $P < .001$), regional mean CBF was not useful to differentiate these 2 groups (predictive probability of 0.589, $P = .339$). Marginal reduction of predictive probability (0.829, $P < .001$) was observed after a combination of ERICA scores and CBF without loss of discriminant ability (Fig 3*B*).

Significantly, the ERICA score was not found to be effective in distinguishing MCI from HC (predictive probability = 0.571, $P = .493$). On the contrary, regional CBF demonstrated a higher predictive probability of 0.776 ($P = .002$) to differentiate these groups. Combined ERICA scores and CBF maintained this predictive power, with a marginal increase of the predictive probability of 0.781 ($P = .002$). (Fig 3*C*).

The results are summarized in Table 2 and Fig 3.

DISCUSSION

ASL is a noninvasive technique for cerebral perfusion measurement using electromagnetically labeled arterial water as a diffusible tracer. Several ASL perfusion studies have highlighted regional hypo- and hyperperfusion in multiple areas of the brain in MCI-AD.[7-13] However, due to the variability of clinical subsets studied and the usage of nonreplicable sequences, these studies were not directly comparable.[13] In the past, differences in technical implementation schemes and lack of standardized protocols hindered the routine use of ASL as a robust perfusion method in the clinical setting. International consensus guidelines have been developed recently for standardized ASL acquisitions.[22] A 3D fast spin-echo pseudocontinuous ASL with a spiral readout is now generally considered the standard method of ASL in clinical research. In this study, we used a 3D fast spin-echo pseudocontinuous ASL technique on 3T MR imaging to investigate regional perfusion differences in patients with MCI and AD compared with HC. ROIs were extracted using atlas-based semiautomated techniques to avoid errors due to manual contouring.

Although several brain areas have been shown to be involved, one of the most consistent regions of hypoperfusion reported in MCI-AD is the PCG and anterior PC.[10,11,13] Identification of hypoperfusion in the PCG + PC has been reported to have a sensitivity of 91% and a specificity of 80% for diagnosing AD.[23] This method is in contrast to inclusion of a combination of different regions in subjects with amnestic and dysexecutive MCI, in which an accuracy of only 60%–70% was observed.[24] From the existing literature, it is not clear whether the hypoperfusion is the cause or consequence of the disease process.[25] In our study, the regional mean CBF in PCG + PC was 46.64, 39.08, and 36.51 mL/100/min in HC, MCI, and AD, respectively, and it performed well in distinguishing AD-HC and MCI-HC, but not between MCI and AD. This finding may be because the perfusion deficit in the PCG + PC occurs early in the course of this dementing illness spectrum, and this particular feature may be used as a reliable marker to delineate patients with MCI and AD from HC. However, from MCI to AD transformation, the perfusion reduction in these regions may be less remarkable and hence may not have significant diagnostic utility as a stand-alone measure.

There is no consistent correlation established between CBF and gray matter changes in the corresponding regions in patients with AD and MCI.[13] In the initial stages of AD, changes such as intraneuronal alterations in the form of neurofibrillary tangles and neuropil threads are observed more frequently in the entorhinal cortex compared with hippocampus.[26] This accumulation may be noted in other conditions, including normal aging, and when this is associated with neuronal loss, it leads to global cognitive decline. MR volumetric studies have also shown entorhinal cortex volume loss in dementia due to Alzheimer spectrum diseases.[27,28] It has been shown in studies that in early stages of AD, certain areas such as the prefrontal cortex or medial temporal lobe structures would eventually have the ability to compensate for the cognitive decline.[29] Simultaneously, perfusion deficits might also be present from the very early preclinical phases of AD, including MCI at risk of conversion, persisting into the advanced stages of the disease, demonstrating a progressive hypoperfusion with disease development, leading to brain atrophy and underlying neuronal loss that correlates with cognitive and functional decline.[13] With regard to the pathophysiologic interpretation of the regional hypoperfusion consistently found in the PCG + PC, in comparison with ERICA, controversy exists about whether this is a cause or consequence of the disease process.[25] It is well known that risk factors such as ischemic stroke, amyloid angiopathy, atherosclerosis, hypertension, diabetes, and cardiac disease are repeatedly implicated in the risk of MCI converting to AD.[30] While AD and vascular dementia have traditionally been considered as independent entities, there is growing evidence implicating vascular pathology in AD to the extent of suggesting an overlap between AD and vascular dementia.[31] Moreover, evidence from aging and stroke studies suggests that chronic brain hypoperfusion is the key pathophysiology that leads to neurodegeneration and consequent cognitive decline.[25] Neuropsychologic correlations have also been established between perfusion measures in the parieto-occipital region and the parietal cortex along with the PCG + PC.[32] Hypoperfusion may lead to changes in cortical thickness, as measured on structural MR imaging scans, in areas most vulnerable to aging (medial prefrontal and pericentral cortices) as well as in areas associated with amyloid aggregation (eg, occipitotemporal and basal temporal cortices), more so in *apolipoprotein E4* carriers.[33] Hence, there is the necessity to address disparate or nonconcordant topographic areas rather than looking at concordant brain volumes underlying areas of hypoperfusion while attempting to combine hypoperfusion and volumetric measures as with ERICA.

Compared with conventional MR imaging–medial temporal lobe atrophy scoring, which reported a sensitivity of 81% and a specificity of 67%, ERICA had a higher sensitivity of 83% and specificity of 98% in differentiating AD.[17,34] ERICA is also easier to comprehend and score compared with the more complex medial temporal lobe atrophy score. It is also reliable and reproducible as confirmed in our study. The tentorial cleft sign (Fig 1*C*), which indicated an ERICA score of ≥2, had a high diagnostic accuracy for AD.[17] In our study, the average ERICA score of patients with AD was 2.15. ERICA performed well in differentiating AD from MCI and AD from HC, but not MCI from HC. This performance may mean that significant parahippocampal atrophy does not happen early in MCI and probably is a much later occurrence compared with CBF reduction in PCG + PC in the course of progression of dementia. This hypothesis is further validated by the observations of neuropathology studies by Braak and Braak published in 1991.[26]

ASL hypoperfusion abnormality in PCG + PC and parahippocampal atrophy may be considered as complementary imaging biomarkers to distinguish MCI and AD. In our study combining the ERICA score with regional CBF in PCG + PC showed a promising trend to differentiate MCI, AD, and HC groups rather than individual parameters. However, MCI-AD is a more heterogeneous disease process, and not all patients with MCI are converters to AD.[17] Further prospective studies are needed to validate the usefulness of combined ERICA and regional CBF in predicting this conversion. Although the pattern of results in MCI-HC comparison indicates better utility of CBF PCG + PC as opposed to the ERICA score, nosologically, there are important considerations while stratifying MCI at risk of AD using

biomarkers. Per available criteria, to identify MCI at an intermediate or higher likelihood of AD requires combining biomarkers of -β amyloid accumulation (PET or CSF) with markers of neuronal injury (τ, FDG-PET, structural MR imaging).[35] A combined instrument using 2 MR imaging markers of neuronal injury rather than -β amyloid accumulation precludes prediction of the proportion of the MCI cohort who are likely to convert in our series.

One also needs to consider that MCI is a heterogeneous condition and potentially could be due to other causes like vascular cognitive impairment. There is evidence in the literature available from MCI negative for β amyloid, where common etiologies include vascular diseases and depression.[36] It is possible that a subset of our MCI cohort may, with time, evolve as vascular cognitive impairment or other alternative trajectories or may potentially remain stable without converting to AD. This possibility is perhaps part of the reason that the ERICA score did not show a significant difference between MCI and HC as opposed to the other 2 comparisons. Lack of longitudinal data to ascertain the trajectory of the MCI group with time precludes confirmation of the same in the present study and warrants future prospective follow-up studies. A relatively small sample size in our study also might have resulted in a lower ability to detect differences between MCI and AD using CBF alone at baseline. All these facts point to the relevance of including multiple MR imaging markers as implemented in one of our previous studies on multimodality neuroimaging.[37]

The study was performed on a prospectively acquired dataset with measurement of only 2 parameters, which could be easily reproduced in a clinical setting. We preferred to use computed segmentation of the ROI CBF to avoid any bias due to manual drawing of contours. However, this study had several limitations. Though ASL is a robust technique to measure cerebral perfusion, technical parameters and patient-specific factors could variably influence the CBF calculation and confound the results. Specific to dementia, one of the major confounders is the arterial transit time, which can be different for each subject due to associated vascular or nonvascular comorbidities. The possible vascular risk contributors like diabetes mellitus and hypertension were not considerably different in each subgroup in the present study (Table 1). Again, transit delay can be higher in some of the ROIs in dementia imaging like the posterior parietal lobes, leading to erroneous CBF measurements.[38] The appropriately increased postlabeling delay time could be used to reduce this error. Alternatively, a multidelay ASL can potentially solve this problem, but it is not ready for prime time imaging yet. Also, a small sample size and cross-sectional study design did not permit analyzing a causal relationship between the biomarkers and the development of MCI and AD, and further large longitudinal studies are needed to confirm its role in predicting progression of the disease. Additionally, head-to-head comparisons between Pittsburgh compound PET imaging and CSF biomarkers (which are currently not available at our center) and MR imaging markers would have enabled us to ascertain the sensitivity and specificity; however, this comparison remains a concern across many centers in the developing world, and only multicentric collaborative ventures can transcend the issue.

CONCLUSIONS

This study explored the utility of measuring structural and perfusion changes in specific and nonoverlapping ROIs in differentiating MCI and AD. Combining regional perfusion measurements in the PCG + PC using ASL along with the ERICA score on structural imaging has the potential to be a better imaging biomarker to distinguish among Alzheimer spectrum disorders. In centers that do not have access to nuclear imaging scans including FDG Pittsburgh compound PET, this study has shown the utility of objective multimodal imaging scores to distinguish MCI at risk of progression to AD. This use of scores has the potential to serve as a noninvasive tool to stratify MCI etiologically, which is a heterogeneous entity in itself. Future studies are needed to explore the longitudinal risk of cognitive decline in MCI due to AD (using markers of amyloid accumulation) as opposed to MCI due to non-AD pathology, including vascular cognitive impairment, in direct correlation with ERICA and regional CBF measures. This categorization should also account for confounding factors such as age, education status, hypertension, coronary artery disease, body mass index, dyslipidemia, and impaired glucose tolerance in these groups.

Disclosures: Bejoy Thomas—*RELATED*: *Grant*: Department of Science and Technology (DST), Government of India*; *Support for Travel to Meetings for the Study or Other Purposes*: DST, Government of India*; *UNRELATED*: *Grants/Grants Pending*: GE Healthcare, research grant*; *Patents (Planned, Pending or Issued)*: applied for Indian patent*; *Stock/Stock Options*: Minority stocks in Wipro India. Ramshekhar N. Menon—*RELATED*: *Grant*: Department of Science and Technology, *Comments*: grant numbers mentioned in the article*; *UNRELATED*: *Grants/Grants Pending*: Department of Science and Technology, *Comments*: Details are provided in terms of grant numbers in the article.* *Money paid to institution.

REFERENCES

1. Crous-Bou M, Minguillón C, Gramunt N, et al. **Alzheimer's disease prevention: from risk factors to early intervention.** *Alzheimers Res Ther* 2017;9:71 CrossRef Medline
2. Tolppanen A-M, Taipale H, Purmonen T, et al. **Hospital admissions, outpatient visits and healthcare costs of community-dwellers with Alzheimer's disease.** *Alzheimers Dement* 2015;11:955–63 CrossRef Medline
3. Petersen RC. **Mild cognitive impairment as a diagnostic entity.** *J Intern Med* 2004;256:183–94 CrossRef Medline
4. Apostolova LG. **Alzheimer disease.** *Continuum (Minneap Minn)* 2016;22:419–34 CrossRef Medline
5. Sheelakumari R, Kesavadas C, Lekha VS, et al. **Menon RN structural correlates of mild cognitive impairment: a clinicovolumetric study.** *Neurol India* 2018;66:370–36 CrossRef Medline
6. Hays CC, Zlatar ZZ, Wierenga C. **The utility of cerebral blood flow as a biomarker of preclinical Alzherimer's disease.** *Cell Mol Neurobiol* 2016;36:167–79 CrossRef Medline
7. Sandson TA, O'Connor M, Sperling RA, et al. **Noninvasive perfusion MRI in Alzheimer's disease: a preliminary report.** *Neurology* 1996; 47:1339–42 CrossRef Medline
8. Alsop DC, Detre JA, Grossman M. **Assessment of cerebral blood flow in Alzheimer's disease by spin-labeled magnetic resonance imaging.** *Ann Neurol* 2000;47:93–100 CrossRef Medline
9. Johnson NA, Jahng G-H, Weiner MW, et al. **Pattern of cerebral hypoperfusion in Alzheimer disease and mild cognitive impairment measured with arterial spin-labeling MR imaging: initial experience.** *Radiology* 2005;234:851–59 CrossRef Medline
10. Dai W, Lopez OL, Carmichael OT, et al. **Mild cognitive impairment and Alzheimer disease: patterns of altered cerebral blood flow at MR imaging.** *Radiology* 2009;250:856–66 CrossRef Medline

11. Binnewijzend MAA, Kuijer JPA, Benedictus MR, et al. **Cerebral blood flow measured with 3D pseudocontinuous arterial spin-labeling MR imaging in Alzheimer disease and mild cognitive impairment: a marker for disease severity.** *Radiology* 2013;267:221–30 CrossRef Medline
12. Bron EE, Steketee RME, Houston GC, et al. **Diagnostic classification of arterial spin labeling and structural MRI in presenile early stage dementia.** *Hum Brain Mapp* 2014;35:4916–31 CrossRef Medline
13. Sierra-Marcos A. **Regional cerebral blood flow in mild cognitive impairment and Alzheimer's disease measured with arterial spin labeling magnetic resonance imaging.** *Int J Alzheimer's Dis* 2017; 2017:5479597 CrossRef Medline
14. Verclytte S, Lopes R, Delmaire C, et al. **Optimization of brain perfusion image quality by cortical surface-based projection of arterial spin labeling maps in early-onset Alzheimer's disease patients.** *Eur Radiol* 2015;25:2479–84 CrossRef Medline
15. Tosun D, Schuff N, Jagust W, et al; Alzheimer's Disease Neuroimaging Initiative. **Discriminative power of arterial spin labeling magnetic resonance imaging and 18F-fluorodeoxyglucose positron emission tomography changes for amyloid-beta-positive subjects in the Alzheimer's disease continuum.** *Neurodegener Dis* 2016; 16:87–94 CrossRef Medline
16. Kaneta T, Katsuse O, Hirano T, et al. **Voxel-wise correlations between cognition and cerebral blood flow using arterial spin-labeled perfusion MRI in patients with Alzheimer's disease: a cross-sectional study.** *BMC Neurol* 2017;17:91 CrossRef Medline
17. Enkirch SJ, Traschütz A, Müller A, et al. **The ERICA score: an MR imaging-based visual scoring system for the assessment of entorhinal cortex atrophy in Alzheimer disease.** *Radiology* 2018;288:226–33 CrossRef Medline
18. Mathuranath PS, Hodges JR, Mathew R, et al. **Adaptation of the ACE for a Malayalam speaking population in southern India.** *Int J Geriat Psychiatry* 2004;19:1188–94 CrossRef Medline
19. Menon R, Lekha V, Justus S, et al. **A pilot study on utility of Malayalam version of Addenbrooke′s Cognitive Examination in detection of amnestic mild cognitive impairment: a critical insight into utility of learning and recall measures.** *Ann Indian Acad Neurol* 2014;17:420 CrossRef Medline
20. McKhann G, Drachman D, Folstein M, et al. **Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease.** *Neurology* 1984; 34:939–44 CrossRef Medline
21. Petersen RC, Stevens JC, Ganguli M, et al. **Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review)—report of the Quality Standards Subcommittee of the American Academy of Neurology.** *Neurology* 2001;56:1133–42 CrossRef Medline
22. Alsop DC, Detre JA, Golay X, et al. **Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: a consensus of the ISMRM Perfusion Study group and the European Consortium for ASL in Dementia.** *Magn Reson Med* 2015;73:102–16 CrossRef Medline
23. Yoshiura T, Hiwatashi A, Noguchi T, et al. **Arterial spin labelling at 3-T MR imaging for detection of individuals with Alzheimer's disease.** *Eur Radiol* 2009;19:2819–25 CrossRef Medline
24. Chao LL, Pa J, Duarte A, et al. **Patterns of cerebral hypoperfusion in amnestic and dysexecutive MCI.** *Alzheimer Dis Assoc Disord* 2009;23:245–52 CrossRef Medline
25. Austin BP, Nair VA, Meier TB, et al. **Effects of hypoperfusion in Alzheimer's disease.** *J Alzheimer's Dis* 2011;26(Suppl 3):123–33 CrossRef Medline
26. Braak H, Braak E. **Neuropathological stageing of Alzheimer-related changes.** *Acta Neuropathol* 1991;82:239–59 CrossRef
27. Jessen F, Feyen L, Freymann K, et al. **Volume reduction of the entorhinal cortex in subjective memory impairment.** *Neurobiol Aging* 2006;27:1751–56 CrossRef Medline
28. deToledo-Morrell L, Stoub TR, Bulgakova M, et al. **MRI-derived entorhinal volume is a good predictor of conversion from MCI to AD.** *Neurobiol Aging* 2004;25:1197–1203 CrossRef Medline
29. Chen W, Song X, Beyea S, et al. **Advances in perfusion magnetic resonance imaging in Alzheimer's disease.** *Alzheimers Dement* 2011; 7:185–96 CrossRef Medline
30. Mazza M, Marano G, Traversi G, et al. **Primary cerebral blood flow deficiency and Alzheimer's disease: shadows and lights.** *J Alzheimers Dis* 2011;23:375–89 CrossRef Medline
31. Zhang Q, Stafford RB, Wang Z, et al. **Microvascular perfusion based on arterial spin labeled perfusion MRI as a measure of vascular risk in Alzheimer's disease.** *J Alzheimers Dis* 2012;32:677–87 CrossRef
32. Alsop DC, Detre JA, Grossman M. **Assessment of cerebral blood flow in Alzheimer's disease by spin-labeled magnetic resonance imaging.** *Ann Neurol* 2000;47:93–100 CrossRef
33. Espeseth T, Westlye LT, Fjell AM, et al. **Accelerated age-related cortical thinning in healthy carriers of apolipoprotein E epsilon 4.** *Neurobiol Aging* 2008;29:329–40 CrossRef Medline
34. Scheltens P, Leys D, Barkhof F, et al. **Atrophy of medial temporal lobes on MRI in "probable" Alzheimer's disease and normal ageing: diagnostic value and neuropsychological correlates.** *J Neurol Neurosurg Psychiatry* 1992;55:967–72 CrossRef Medline
35. Albert MS, DeKosky ST, Dickson D, et al. **The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.** *Alzheimers Dement* 2011;7:270–79 CrossRef Medline
36. Landau SM, Horng A, Fero A, et al. Alzheimer's Disease Neuroimaging Initiative**. Amyloid negativity in patients with clinically diagnosed Alzheimer disease and MCI.** *Neurology* 2016;86:1377–85 CrossRef Medline
37. Sheelakumari R, Sarma SP, Kesavadas C, et al. **Multimodality neuroimaging in mild cognitive impairment: a cross-sectional comparison study.** *Ann Indian Acad Neurol* 2018;21:133–39 CrossRef Medline
38. Alsop DC, Dai W, Detre JA, et al. **Arterial spin labeling blood flow MRI: its role in the early characterization of Alzheimer's disease.** *J Alzheimers Dis* 2010;20:871–80 CrossRef Medline

23rd ALZHEIMER'S AND RELATED DISORDERS SOCIETY OF INDIA (ARDSI) NATIONAL CONFERENCE 2019

ARDSICON 2019

ARDSI. REMEMBER THOSE WHO CANNOT REMEMBE

Hosted by: ARDSI Trivandrum Chapter

Date: 15th, 16th & 17th November 2019

Venue: IMA Kerala Doctor's Club, Near Chakka Junction, Trivandrum

EFFECT OF MINDFULNESS YOGA ON NEUROPSYCHOLOGICAL FUNCTIONS IN MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE

Meenu. K.S[1], Rajesh PG[1], S. Krishnan[2], Lekshmy. K1[3], Nandini Mohanan1, Ramshekhar N Menon[1]

1 Cognition & Behavioral Neurology sub-section, Dept of Neurology, SCTIMST, Trivandrum

2 Department of Psychiatry, MCH, Trivandrum; 2 Mindfulness Practitioner

Background: The current lack of an effective cure for Alzheimer's disease (AD) in its prodromal state i.e. mild cognitive impairment (MCI) impacts health care and the social fabric of the elderly and care-givers. Growing evidence has linked yoga and mindfulness to cognitive and psychological improvements that could be relevant for MCI. In this study, effect of Mindfulness Yoga (MY) on neuropsychological function in mild cognitive impairment (MCI) due to AD is evaluated.

Methods: This prospectivepilot study customized an eight-weekgroup-based MY training program for older adults with MCI due to AD diagnosed as per Petersen's criteria and NINCDS–ADRDA criteria with clinical dementia rating score of < 2 with and sample comprised of 14 patients (males -11, females-3) after exclusion of significant anxiety and depression on Hospital anxiety depression scale (HADS). The participants are recruited through the Memory & Neurobehavioral Disorders Clinic of SCTIMST, Trivandrum. The neuropsychology tests used to obtaining relevant data were:Addenbrooke's Cognitive Examination (ACE), Rey Auditory Verbal Learning Test (RAVLT), Wechsler Memory Scale (WMS- visual memory, logical memory, digit span), TRAIL A, TRAILB, Wisconsin card sorting test (WCST), Warrington Recognition Memory Test for Faces, Position Discrimination test, Cube Analysis, Instrumental Activities of Daily living, HADS, and CDR. Pre and post intervention scores after 3 months were statistically compared using paired samples t-test.

Results: The mean age of the cohort was (67years; range 50-85; education range10-15 years). The results indicate that participants showed significant improvement in RAVLT Immediate Recall(p=.038), RAVLT Delayed Recall(p=.035), RAVLT Recognition(p=.048), and Omission error-score (p=.036). There was also significant improvement on WMS Delayed Logical Memory score (p=.047). There were no significant differences in WMS Visual Memory and Digit Span,

TRAIL A, TRAIL B, WCST, Warrington Recognition Memory Test for Faces, Position Discrimination, Cube Analysis, HADS,IADL, and CDR.

Conclusions: Our study indicates significant benefit with a supervised MY program on episodic verbal memory in MCI due to AD. This is the first proof of concept study from the subcontinent on the effectiveness of a holistic mindfulness practice in improving cognitive performance in prodromal AD. A longer period of follow-up is required to ascertain durable benefits of this intervention.

Keywords: Yoga, Mindfulness,Neuropsychological Functions, Mild Cognitive Impairment, Prodromal AD.

EFFECT OF MUCBT-D ON QUALITY OF LIFE, MINDFULLNESS LEVEL AND PERCEIVED STRESS IN MCI DUE TO AD AND THEIR CAREGIVERS - A PILOT FEASIBILITY STUDY

Meenu. K.S, Rajesh PG, S. Krishnan, Lekshmy. K, NandiniMohanan,Ramshekhar N Menon

Cognition and Behavioural Neurology Section(CBNS), Department of Neurology Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, Kerala, India

BACKGROUND

Mild cognitive impairment (MCI) impacts health care and the social fabric of the elderly and care-givers. Growing evidence has linked mindfulness to improvement in quality of life, mindfull living and declaine in stress. In this study, the effect of MUCBT-D on mindfullness level quality of life and percevied stress in MCI due to AD and their care givers is evaluated.

OBJECTIVE

To study the effect of MUCBT-D and its continued practice in reinforcing quality of life, mindfullness level and reducing perceived stress in individuals with MCI and prodromal AD and their care givers by validating and comparing information from established modalities.

METHOD

* This pilot study customized an eight-week group-based MUCBT-D training program for older adults with MCI due to AD diagnosed as per Petersen's criteria and NINCDS–ADRDA criteria with clinical dementia rating score of < 2 and their care givers the sample comprised of 14 patients (males -11, females-3) and 14 care givers (males -3, female-11) after exclusion of significant anxiety and depression on Hospital anxiety depression scale (HADS). The participants are recruited through the Memory & Neurobehavioral Disorders Clinic, Dept of Neurology SCTIMST, Trivandrum.
* The questionnaires used to obtaining data were: five facet mindfullness questionnaire, precevied stress scale and quality of life scale by WHO.
* Pre and post intervention scores were statistically evaluated by using paired t test.

RESULT

The result indicates that patients and care givers shows a difference in pre and post means scores in perceived stress scale (PSS) and quality of life (QOL). PSS of MCI (pre mean -13.86, post mean -11.57) and QOL of MCI (pre mean - 82.57, post mean- 88.21) and PSS of care givers (pre mean -15.86, post mean -13.93) and QOL of care givers (pre mean -87.4, post mean - 89.17)

Variable	Mean MCI/EAD (N=14)	Mean Care Givers (N=14)
PSS before intervention	13.86	15.86
PSS after intervention	11.57	13.93
QOL before intervention	82.57	87.14
QOL after intervention	88.21	89.17

p value

CONCLUSION

Preliminary data from this small pilot study shows trends towards improvement in perceived stress and quality of life amoung individuals with MCI /EAD and also their care givers following MUCBT-D training by compairing pre and post mean scores But there is no significance in t -test as our sample size is very small . Our study is the first proof of a concept study from the Indian continent on the effectiveness of a mindfullness practice in improving quality of life and reducing perceived stress expressed by patients and care givers.

REFERENCES

1. Alzheimer's Association, Alzheimer's disease Facts and Figures 2014, Alzheimer's & Dementia, Volume 10, Issue 2.
2. B.K. Hölzel et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Research: Neuroimaging 191 (2011) 36–43
3. Bahar-Fuchs et al. Cognitive training and cognitive rehabilitation for persons with mild to moderate dementia of the Alzheimer's or vascular type: a review. Alzheimer's Research & Therapy 2013, 5:35
4. Bhargav et al. Frontal hemodynamic responses to yoga breathing. frontiers in psychiatry 2014 5 (29) 1-6 5/3(2009). 672–678

AKNOWLDGEMENT

Department of Science & Technology Grant under SATYAM scheme 278/2015

EFFECT OF MUCBT-D ON NEUROPSYCHOLOGICAL FUNCTIONS IN MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE

Meenu. K.S, Rajesh PG, S. Krishnan, Lekshmy. K, NandiniMohanan,Ramshekhar N Menon

Cognition and Behavioural Neurology Section(CBNS), Department of Neurology Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, Kerala, India

BACKGROUND

Mild cognitive impairment (MCI) impacts health care and the social fabric of the elderly and care-givers. Growing evidence has linked yoga and mindfulness to cognitive and psychological improvements that could be relevant for MCI. In this study, effect of MUCBT-D on neuropsychological function in mild cognitive impairment (MCI) due to AD is evaluated.

OBJECTIVE

To study the effect of MUCBT-D and its continued practice in reinforcing cognitive abilities as well as in improving the quality of life in individuals with MCI and prodromal AD by validating and comparing information from established modalities.

METHOD

* This prospective pilot study customized an eight-week group-based MUCBT-D training program for older adults with MCI dueto AD diagnosed as per Petersen's criteria and NINCDS–ADRDA criteria with clinical dementia rating score of < 2 with and sample comprised of 14 patients (males -11, females-3) after exclusion of significant anxi ety and depression on Hospital anxiety depression scale (HADS). The participants are recruited through the Mem ory & Neurobehavioral Disorders Clinic, Dept of Neurology SCTIMST, Trivandrum.
* The neuropsychology tests used to obtaining relevant data were: Addenbrooke's cognitive examination (AC E), Rey auditory verbal learning test (RAVLT), Wec hsler memory scale(WMS- visual memory, logical me mory, digit span), Trail A, Trail B, Wisconsin card Sorting test (WCST), Warrington recognition memory test for faces, Position discrimination test, Cube anal ysis, Instrumental activities of daily living, HADS, and CDR.
* Pre and post intervention scores were statistically evaluated by using paired t test.

RESULT

The mean age of cohort was (67years; range 50-85; education range 10-15years). The results indicate that participants showed a difference in mean of pre and post scores in the following neuropsychological tests such as WMS- visual immediate recall (pre-24.43, post - 28, p= .147). WMS -visual delayed recall (pre- 17.93, post - 19.43, p=.573) Trail A (pre- 124.86, post -104.5, p= .064) Trail A error (pre-.21, post - .07, p= .336) Trail B (pre - 254.86, post - 231.29, p= .063) Trail B error (pre- 2.5, post- .93, p=.414). Face recognition test (pre- 19.07, post- 20.5, p=.081) ACE (pre . 85.79, post 86.93, p=.533). RAVLT (pre- 32.5, post - 37.36, p= .07) IADL (pre- 3.43, post 2.64, p= .359) Anxiety (pre- 3.43, post- 3, p= .435) Depression (pre-3.43, post- 2.14, p= .162)

SPSS Result Table

Parameter	Pre-mean	Post mean	p value
WMS Visual immediate recall	24.43	28	.147
WMS – visual delayed recall	17.93	19.43	.573
Trial A	124.86	104.5	.064
Trial A error	.21	.07	.336
Trial B	254.86	231.29	.063
Trial B error	2.5	.93	.414
Faces	19.07	20.5	.081
Ace	85.79	86.93	.533
RAVLT	32.5	37.36	.070
IADL	3.43	2.64	.359
Anxiety	3.43	3	.435
Depression	3.43	2.14	.162

CONCLUSION

Our study indicates benefit of a supervised MUCBT-D program on memory and other cognitive functions in MCI due to AD. As there is a difference in the mean of pre and post scores it shows a trend for improvement eventhough the p value is not significant (may be because of small sample size) This is the first proof of concept study from the subcontinent on the effectiveness of a holistic mindfulness practice in improving cognitive performance in prodromal AD. A longer period of follow-up is required to ascertain durable benefits of this intervention.

REFERENCES

1. Alzheimer's Association, Alzheimer's disease Facts and Figures 2014, Alzheimer's & Dementia, Volume 10, Issue 2.
2. B.K. Hölzel et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Research: Neuroimaging 191 (2011) 36–43
3. Bahar-Fuchs et al. Cognitive training and cognitive rehabilitation for persons with mild to moderate dementia of the Alzheimer's or vascular type: a review. Alzheimer's Research & Therapy 2013, 5:35
4. Bhargav et al. Frontal hemodynamic responses to yoga breathing. frontiers in psychiatry 2014 5 (29) 1-6 5/3(2009). 672–678

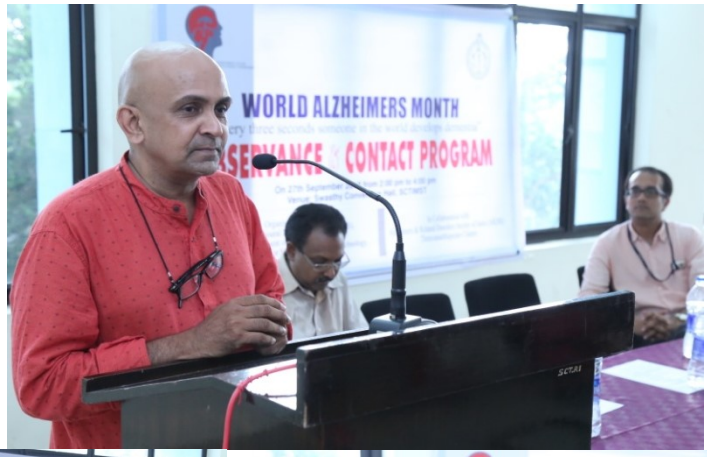
AKNOWLDGEMENT

Department of Science & Technology Grant under SATYAM scheme 278/2015

WORLD ALZHEIMERS MONTH 2018

World Alzheimers Month was observed on September 27th ,2018 from 2:00 pm to 4:00 pm at Swasthy Convention Hall at Sree Chitra Tirunal Institute for Medical Sciences & Technology in collaboration with Alzheimers & Related Disorders Society of India (ARDSI), Trivandrum Chapter. An observance and patient contact program was conducted with special focus on psycho social and physical issues in dementia and mild cognitive impairment. Care giver burden reduction was also emphasised. Physical exercises to improve gait was discussed in detail. A group activity for patients were arranged as memory games and activities using cognitive retraining interventions.


WORLD ALZHEIMERS MONTH


WORLD ALZHEIMERS MONTH


WORLD ALZHEIMERS MONTH
OBSERVANCE & CONTACT PROGRAM


WORLD ALZHEIMERS MONTH