PROJECT COMPLETION REPORT

1. **Title of the project**: Effects of Yoga on Motor Cortex plasticity, Motor Learning and Motor Deficits of Parkinson's disease

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3. **Implementing Institution:** Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

4. **Date of commencement**: 13-06-2016

5. **Planned date of completion**: 12-06-2019

6. **Actual date of completion**:12-12-2019 (Project extended for 6 months from planned date of completion)

7. **Objectives as stated in the project proposal**:

   (a.) To study the effects of Yoga on motor cortex plasticity by measuring the same assessed by Paired Associative Stimulation (PAS)- a Transcranial Magnetic Stimulation (TMS) based technique to induce plasticity of brain in the motor cortex- before and after 4 weeks and 12 weeks of regular sessions of Yoga versus 30 minutes regular aerobic exercise, in healthy volunteers.

   (b.) To study the effects of Yoga on motor learning by measuring the same, assessed by a motor sequence learning task and a sensori-motor adaptation task at baseline and after 4 weeks and 12 weeks of Yoga versus aerobic exercise, in healthy volunteers.

   (c.) To measure the effects of Yoga on the severity of motor symptoms (tremor, stiffness, slowness, postural instability etc.) of Parkinson's disease (PD) by measuring the same before and after 12 weeks of Yoga versus aerobic exercise in patients with PD.

8. **Deviation made from original objectives if any, while implementing the project and reasons thereof**: No deviations were made from the original objectives.

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

   Experimental set up & Methods

   We conducted a randomized control study that had two parts. *In the first part of the study*, healthy volunteers who are non-practitioners of yoga (n= 45) were recruited. Healthy volunteers who were trained musicians or typists were excluded from the study. On Day 1, each subject underwent paired associative stimulation (PAS) using TMS to assess their baseline motor cortex plasticity. They also performed a standardized motor sequence learning (sequential finger movements) task and a motor adaptation (Visuo-motor adaptation) task. The subjects were later randomized to three groups: yoga group, aerobic exercise group and a non-exercise group who did not practice any specific exercise besides routine activities. The Yoga group received one week of supervised Yoga training from a trained instructor on site and the aerobic exercise group, received training for aerobic exercises. Similarity in the

exercise regimens in terms of energy expenditure and duration was monitored using a wrist actimeter during the on-site training. After one week, subjects continued the regimen at home regularly for at least 30 minutes a day, 5 days a week for the next 12 weeks. All subjects were reassessed at 4 weeks and at 3 months. During the reassessment visits, subjects underwent PAS for motor cortex plasticity assessment and repeated the motor sequence learning and motor adaptation tasks.

In the second part of the study, 120 Parkinson's disease patients in Hoehn and Yahr stage I to III were recruited. Patients with dementia, severe gait and balance impairment, uncontrolled psychiatric co-morbidities (depression, psychosis) were excluded. At baseline, severity of Parkinsonism was assessed using the UPDRS score. Following these patients were randomized in 1:1 ratio to the Yoga group or aerobic exercise group. Routine physiotherapy was allowed to continue in both groups. A subset of subjects (n=30, 15 from the Yoga group and 15 from aerobic exercise group) was selected to undergo TMS and motor learning assessments. In this subset, motor cortex plasticity was assessed using PAS in the Parkinsonian medication ON (1 hour after usual dose of medication) and OFF (after overnight withdrawal of medications) states, on 2 separate days separated by one week and in random order. After PAS assessment, they also performed the motor sequence learning and sensori-motor adaptation tasks.

After baseline assessments, the Yoga group received one week of supervised Yoga training from a trained instructor on site and the exercise group, received training for aerobic exercises. Similarity in the exercise regimens in terms of energy expenditure and duration was monitored using a wrist actimeter during the on-site training. After one week, subjects continued the regimen at home regularly for at least 30 minutes a day, 5 days a week for the next 12 weeks. For PD, the intervention regime was performed in medication ON state and standard physiotherapy as practiced was allowed to continue in both the groups. Subjects documented the hours spent performing the target intervention on a diary provided. Fortnightly visits were arranged during the intervention period to confirm compliance and documentation. At the end of 12 weeks, all subjects underwent reassessment of UPDRS after medication intake and after overnight medication withdrawal. The TMS subset underwent reassessment of plasticity and motor learning in these two states.

TMS assessment: TMS assessment was done at the Non-Invasive Brain Stimulation laboratory. For PAS, electric stimulation pulses were delivered over the median nerve. Each pulse will be followed 25ms later by a magnetic pulse delivered over the primary motor cortex over the hotspot for abductor pollicis brevis muscle. Six hundred pairs of stimuli are delivered at 5 Hz. Motor evoked potentials were elicited at baseline (T0) and 5, 15, 30 and 45 minutes after PAS. Short Interval Intracortical Inhibition (SICI) and Long Interval Intracortical Inhibition (LICI) were also recorded at baseline and 30 minutes after PAS.

Motor learning tasks: Motor sequence learning was assessed using a sequential finger tapping task in which the subject had to learn and press the keys on a computer keyboard using four fingers of the non-dominant left hand in a particular sequence repeatedly (4-1-3-2-4). The actual task consisted of 8 blocks of 20 sequences. With practice the time taken to complete the sequence decreases and accuracy improves. For motor adaptation an eight-target tracking

task was used, the subject was asked to move a cursor positioned at the center of the screen to one of the 8 targets following a straight trajectory using a joystick with the dominant hand. The task consisted of 4 blocks of 32 trials each. Out of 4 blocks, 2 blocks are executed with zero-degree deviation and the other 2 blocks with 60-degree deviation from target which the subject had to recognize and compensate for. Number of attempts required to reach asymptotic performance and accuracy improves with repeated cycles.

Pegboard test: Purdue pegboard test (PPT)was done to assess the manual hand dexterity of the subjects. PPT (Model 32020A) consists of four subsets: right hand, left hand, bimanual and an assembly task. The subjects will attempt to put as many pegs as possible in the first 3 tasks, in 30 seconds. In the assembly task, subjects should assemble pins, collars and washers onto the board, in 60 seconds. The score is the total number of pegs or parts placed on the board.

Yoga protocol: The study needed a standardized yoga therapy protocol specific to PD. The co-investigator along with the other investigators developed a clinically relevant yoga therapy protocol specific to PD. This highly evolved protocol was offered to patients by a qualified and certified Yoga therapist under the supervision of the co-investigator who is a Yoga expert. The yoga intervention included postures, voluntary regulated breathing, relaxation techniques and meditation

Outcome variables: For the motor cortex plasticity assessment, percentage change in the amplitude of motor evoked potentials recorded after PAS was the outcome variable. For motor sequence learning, outcome variables computed were the mean time per sequence and accuracy (number of sequences executed correctly). For motor adaptation task, time taken by the subject to reach target and area under the trajectory was recorded as outcome. To assess the deficits of PD, Unified Parkinson's Disease Rating Scale (UPDRS) total scores, tremor, rigidity and bradykinesia scores was used. For the Pegboard test, the total number of pegs or places on the board was taken as the outcome measure. Outcome assessment was done by an investigator who is blinded to the intervention allotted to the subject. Comparison of outcome variables before and after intervention (Yoga/ aerobic exercise/ non-exercise) at 4 weeks and 12 weeks in healthy volunteers identified the acute and long-term effect of Yoga in comparison to regular exercise and no exercise. In PD patients, comparison of changes in outcome variables including UPDRS score at 12 weeks identified the effect of Yoga in comparison to aerobic exercise.

Fig1.A
TMS procedure being done on a healthy volunteer

Fig1.B
Motor sequence learning task being done by a PD patient

Fig1.C
Motor Adaptation task being done by a Healthy volunteer

Data Collected

In the first part of the study, 45 Healthy volunteers were recruited, out of which 42 completed the study. All recruited were randomized to three groups; hence full data of 14 subjects are available in each group for the Healthy volunteer arm of the study. In the second part of the study, 120 PD patients were recruited, out of which 100 patients completed the study. All recruited were randomized into two groups; hence full data of 51 patients in Yoga group and 49 patients in Aerobics group is available for the patient arm of the study. A subset of 30 patients from the 120 PD patients were selected to undergo TMS and motor learning assessments, out of which 28 completed the study and data is available for 14 subjects in each group of the Patient arm of the study.

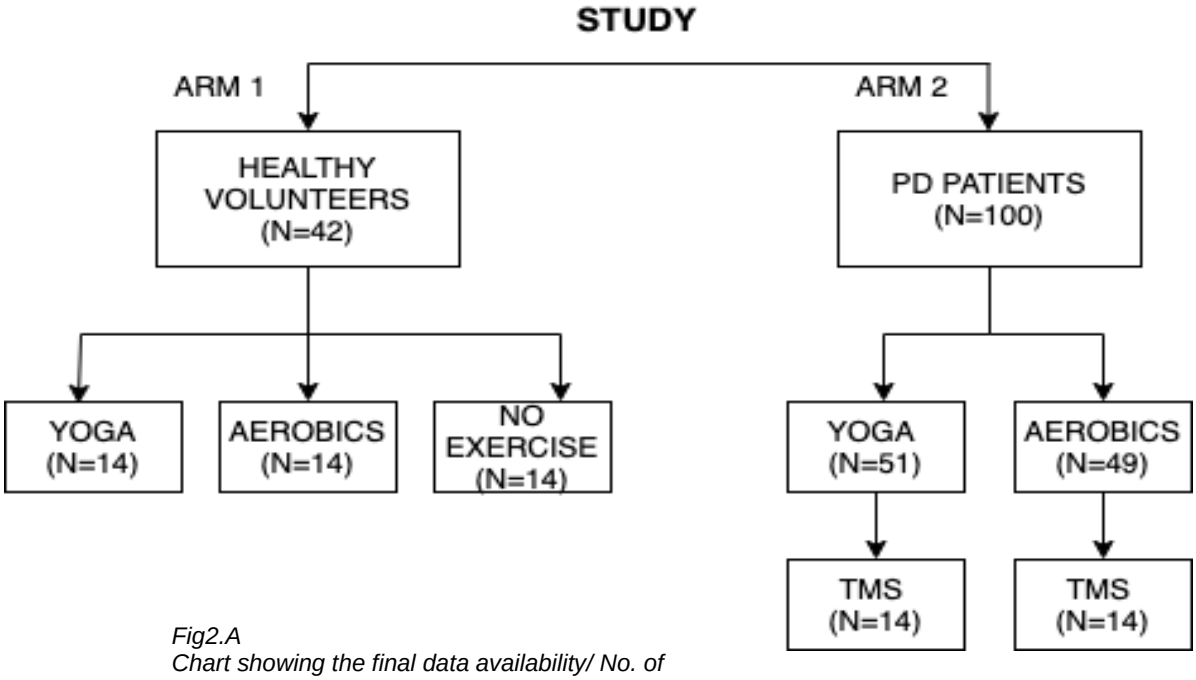

Fig2.A
Chart showing the final data availability/ No. of subjects who completed the study in each arm.

Non-motor assessments

In PD patients, non-motor assessments were done pre and post intervention. Becks Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS), Non-Motor Symptoms Scale (NMSS), Fatigue Severity Scale (FSS) and PDQ-39 were the various assessments used.

PD patient data: Demographics

The 2 groups (n = 100) were not significantly different regarding age, duration of illness, age at onset, HY, UPDRS total in ON and UPDR part 3 in ON (unpaired T test all P between 0.2 and 0.7). In the yoga group 30 patients experienced motor fluctuations and 14 had dyskinesias; in the aerobic group 32 patients had motor fluctuations and 14 had dyskinesias.

	Mean	Std. Dev.
age, Total	54,380	7,967
age, yoga	53,608	8,256
age, aerobic	55,184	7,656
age onset, Total	47,880	8,565
age onset, yoga	47,412	9,023
age onset, aerobic	48,367	8,126
duration ill ness, Total	6,487	3,752
duration ill ness, yoga	6,167	3,687
duration ill ness, aerobic	6,820	3,828
UPDRS ON, Total	23,880	12,862
UPDRS ON, yoga	23,373	12,706
UPDRS ON, aerobic	24,408	13,132
UPDRS III ON, Total	18,130	9,335
UPDRS III ON, yoga	17,059	9,056
UPDRS III ON, aerobic	19,245	9,582
HY, Total	2,405	,540
HY, yoga	2,451	,492
HY, aerobic	2,357	,586

Table showing demographics of all PD patients in the study

PD TMS data

		BASELINE DATA			3RD MONTH DATA	
		YOGA	AEROBICS		YOGA	AEROBICS
	Age	54.07±6.62	54.64±7.32	Age	54.07±6.62	54.64±7.32
PRE INTERVENTION	RMT	49.07±7.14	48.64±3.98	RMT	48.29±6.61	48.43±5.15
	AMT	38.07±7.22	38.64±5.46	AMT	38.79±5.71	37.93±4.42
	test	0.82±0.26	0.93±0.17	test	0.82±0.19	0.8±0.24
	sici	0.53±0.26	0.6±0.26	sici	0.54±0.19	0.5±0.21
	lici	0.44±0.26	0.53±0.29	lici	0.29±0.17	0.5±0.32
	sici/test	0.67±0.24	0.63±0.21	sici/test	0.66±0.18	0.63±0.2
	lici/test	0.6±0.38	0.59±0.32	lici/test	0.36±0.23	0.65±0.35
	test	0.69±0.22	0.8±0.2	test	0.77±0.19	0.77±0.19
	lai	0.45±0.25	0.59±0.36	lai	0.46±0.19	0.51±0.29
	sai	0.45±0.17	0.54±0.23	sai	0.49±0.18	0.51±0.28
	lai/test	0.68±0.3	0.69±0.29	lai/test	0.6±0.2	0.64±0.29
	sai/test	0.66±0.14	0.67±0.18	sai/test	0.63±0.17	0.64±0.28
TEST ANALYSIS	T0	0.76±0.23	0.86±0.17	T0	0.8±0.18	0.79±0.2
	T5	0.85±0.29	0.92±0.25	T5	1.05±0.26	0.96±0.34
	T15	0.79±0.19	0.99±0.29	T15	1.05±0.22	1±0.36
	T30	0.81±0.32	0.96±0.26	T30	1.02±0.25	0.93±0.3
	T45	0.82±0.28	0.9±0.27	T45	0.96±0.26	0.87±0.32
	TEST AVG	0.82±0.26	0.94±0.23	TEST AVG	1.02±0.24	0.94±0.32
	TEST AVG/T0	1.1±0.22	1.09±0.15	TEST AVG/T0	1.29±0.17	1.18±0.2
POST INTERVENTION	RMT	48.36±6.98	47.5±4.17	RMT	47.57±6.64	48.21±5.37
	AMT	38.14±7.39	37.79±4.89	AMT	38.14±5.87	37.5±4.45
	test	0.77±0.28	1.04±0.35	test	0.92±0.26	0.87±0.31
	sici	0.55±0.25	0.61±0.33	sici	0.49±0.21	0.59±0.25
	lici	0.45±0.29	0.48±0.25	lici	0.32±0.16	0.51±0.32
	sici/test	0.72±0.17	0.6±0.26	sici/test	0.53±0.15	0.67±0.16
	lici/test	0.59±0.27	0.48±0.22	lici/test	0.35±0.17	0.58±0.25
	test	0.81±0.31	0.92±0.31	test	0.85±0.22	0.88±0.3
	lai	0.48±0.13	0.61±0.36	lai	0.45±0.16	0.59±0.3
	sai	0.49±0.21	0.58±0.34	sai	0.52±0.13	0.56±0.29
	lai/test	0.68±0.34	0.65±0.22	lai/test	0.56±0.21	0.67±0.21
	sai/test	0.65±0.28	0.63±0.26	sai/test	0.64±0.21	0.61±0.17

Table showing all TMS data for all 28 patients ;14 subjects in each group of the Patient arm of the study.

HV TMS Data

	YOGA					AEROBICS					NO INTERVENTION			
	Age	23.5±2.77	23.5±1.72	24±1.6		Age	23.5±2.77	23.5±1.72	24±1.6		Age	23.5±2.77	23.5±1.72	24±1.6
PRE INTERVENTION	RMT	46.86±5.55	49.36±5.8	47.5±4.85	PRE INTERVENTION	RMT	46.64±6.22	49.21±4.51	47.57±5.77	PRE INTERVENTION	RMT	47±6.73	50.29±5.3	47.21±6.36
	AMT	36.86±5.72	38.93±5.6	38.07±5.02		AMT	36.86±6.69	38.79±3.61	37.43±6.03		AMT	37.43±6.88	40.64±4.78	36.29±5.34
	test	0.92±0.15	0.91±0.16	0.91±0.16		test	0.92±0.16	0.92±0.15	0.85±0.22		test	0.89±0.17	0.96±0.12	1.04±0.15
	sici	0.62±0.13	0.61±0.19	0.58±0.23		sici	0.51±0.16	0.57±0.11	0.53±0.21		sici	0.49±0.14	0.54±0.12	0.53±0.18
	lici	0.37±0.23	0.49±0.27	0.32±0.14		lici	0.32±0.15	0.29±0.16	0.4±0.22		lici	0.34±0.14	0.37±0.19	0.43±0.19
	sici/test	0.68±0.12	0.68±0.2	0.64±0.22		sici/test	0.56±0.14	0.63±0.1	0.64±0.24		sici/test	0.55±0.12	0.57±0.14	0.51±0.16
	lici/test	0.4±0.22	0.53±0.29	0.37±0.23		lici/test	0.37±0.19	0.32±0.17	0.46±0.19		lici/test	0.38±0.16	0.39±0.2	0.42±0.19
	test	0.86±0.14	0.84±0.15	0.84±0.14		test	0.82±0.15	0.84±0.13	0.87±0.18		test	0.85±0.18	0.89±0.13	0.95±0.11
	lai	0.54±0.21	0.58±0.2	0.52±0.22		lai	0.5±0.21	0.47±0.16	0.47±0.2		lai	0.51±0.25	0.48±0.22	0.44±0.14
	sai	0.66±0.18	0.53±0.15	0.61±0.23		sai	0.54±0.18	0.5±0.18	0.57±0.22		sai	0.51±0.24	0.5±0.15	0.45±0.13
	lai/test	0.63±0.25	0.68±0.22	0.6±0.18		lai/test	0.62±0.23	0.55±0.14	0.54±0.18		lai/test	0.58±0.24	0.53±0.22	0.47±0.15
	sai/test	0.77±0.2	0.63±0.17	0.73±0.22		sai/test	0.64±0.15	0.59±0.15	0.66±0.18		sai/test	0.6±0.22	0.57±0.17	0.48±0.15
		#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!
TEST ANALYSIS	T0	0.89±0.11	0.88±0.14	0.87±0.15	TEST ANALYSIS	T0	0.87±0.14	0.88±0.13	0.86±0.2	TEST ANALYSIS	T0	0.87±0.16	0.93±0.12	0.99±0.11
	T5	0.98±0.22	0.98±0.18	1.05±0.15		T5	1.07±0.21	1.02±0.19	1.02±0.24		T5	1.16±0.24	1.18±0.18	1.18±0.14
	T15	0.98±0.12	1.01±0.2	1.03±0.16		T15	1.16±0.15	1.08±0.18	1.01±0.21		T15	1.17±0.23	1.26±0.16	1.2±0.14
	T30	1.06±0.16	1.01±0.22	1.05±0.17		T30	1.17±0.19	1.04±0.24	0.99±0.23		T30	1.19±0.22	1.2±0.13	1.13±0.1
	T45	1±0.23	0.98±0.18	1±0.23		T45	1.12±0.21	1.07±0.21	0.96±0.18		T45	1.17±0.26	1.22±0.16	1.15±0.14
	TEST AVG	1.01±0.15	1±0.17	1.03±0.15		TEST AVG	1.13±0.17	1.05±0.19	1±0.2		TEST AVG	1.17±0.22	1.21±0.12	1.17±0.1
	TEST AVG/T0	1.13±0.1	1.14±0.13	1.2±0.17		TEST AVG/T0	1.31±0.1	1.2±0.14	1.17±0.12		TEST AVG/T0	1.35±0.08	1.32±0.15	1.18±0.13
		#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!
POST INTERVENTION	RMT	45.64±5.46	48.57±6.07	46.5±4.98	POST INTERVENTION	RMT	46.07±6.2	48.79±4.44	47.14±5.71	POST INTERVENTION	RMT	46.14±6.54	49.29±5.5	46.21±6.21
	AMT	35.5±5.56	38.43±5.82	37±5.26		AMT	36.14±6.61	38.14±3.76	36.43±5.82		AMT	36.43±6.48	39.64±4.88	35.29±5.16
	test	0.98±0.19	1.02±0.24	1.01±0.14		test	1.03±0.23	1.01±0.22	1±0.35		test	1.06±0.21	1.06±0.18	1.05±0.14
	sici	0.58±0.26	0.58±0.16	0.63±0.3		sici	0.54±0.21	0.62±0.16	0.64±0.27		sici	0.63±0.2	0.57±0.22	0.57±0.24
	lici	0.42±0.25	0.44±0.31	0.35±0.11		lici	0.39±0.23	0.42±0.2	0.42±0.29		lici	0.4±0.17	0.39±0.21	0.39±0.26
	sici/test	0.59±0.21	0.6±0.2	0.6±0.22		sici/test	0.53±0.15	0.64±0.21	0.65±0.18		sici/test	0.59±0.15	0.54±0.18	0.54±0.22
	lici/test	0.45±0.27	0.43±0.27	0.35±0.11		lici/test	0.38±0.21	0.49±0.4	0.42±0.25		lici/test	0.39±0.17	0.37±0.21	0.38±0.25
	test	0.89±0.26	0.84±0.21	0.92±0.15		test	0.91±0.25	0.91±0.18	0.92±0.28		test	0.98±0.29	0.99±0.14	1.01±0.19
	lai	0.46±0.23	0.61±0.31	0.47±0.24		lai	0.51±0.19	0.5±0.19	0.52±0.28		lai	0.54±0.26	0.47±0.21	0.52±0.21
	sai	0.56±0.22	0.6±0.24	0.54±0.3		sai	0.59±0.26	0.61±0.22	0.59±0.25		sai	0.58±0.27	0.49±0.21	0.5±0.24
	lai/test	0.53±0.25	0.71±0.33	0.52±0.27		lai/test	0.58±0.2	0.55±0.19	0.59±0.25		lai/test	0.56±0.2	0.49±0.22	0.52±0.22
	sai/test	0.64±0.25	0.7±0.2	0.59±0.36		sai/test	0.65±0.24	0.66±0.23	0.67±0.22		sai/test	0.62±0.24	0.5±0.19	0.49±0.2

Table showing all TMS data for all 42 Healthy volunteers ;14 subjects in each group of the HV arm of the study.

RMT-Resting Motor threshold
AMT-Active Motor threshold
SICI-Short interval intra cortical inhibition
LICI-Long interval intra cortical inhibition
LAI-Long Afferent Inhibition
SAI-Short Afferent inhibition

PAS- Paired Associative Stimulation
T0- Pre-PAS Test
T5- 5 minutes Post PAS Test
T15- 15 minutes Post PAS Test
T30- 30 minutes Post PAS Test
T45-45 minutes Post PAS Test
TEST AVG- Average of T5, T15, T30 and T45

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

Major finding: I

For the first time we show that 12 weeks of daily yoga or aerobic training enhance in healthy volunteers naive to yoga practice, the responsiveness of the primary motor cortex (M1) to plastic interventions (in other words it makes the motor cortex more amenable to change the efficacy of the synapses connecting the neurons when needed). We show that yoga training is faster than aerobic training to drive this change in plastic responsiveness: after 1 month of daily training the yoga practitioners have already reached the plateau of the effect while this was not achieved for the aerobic practitioners.

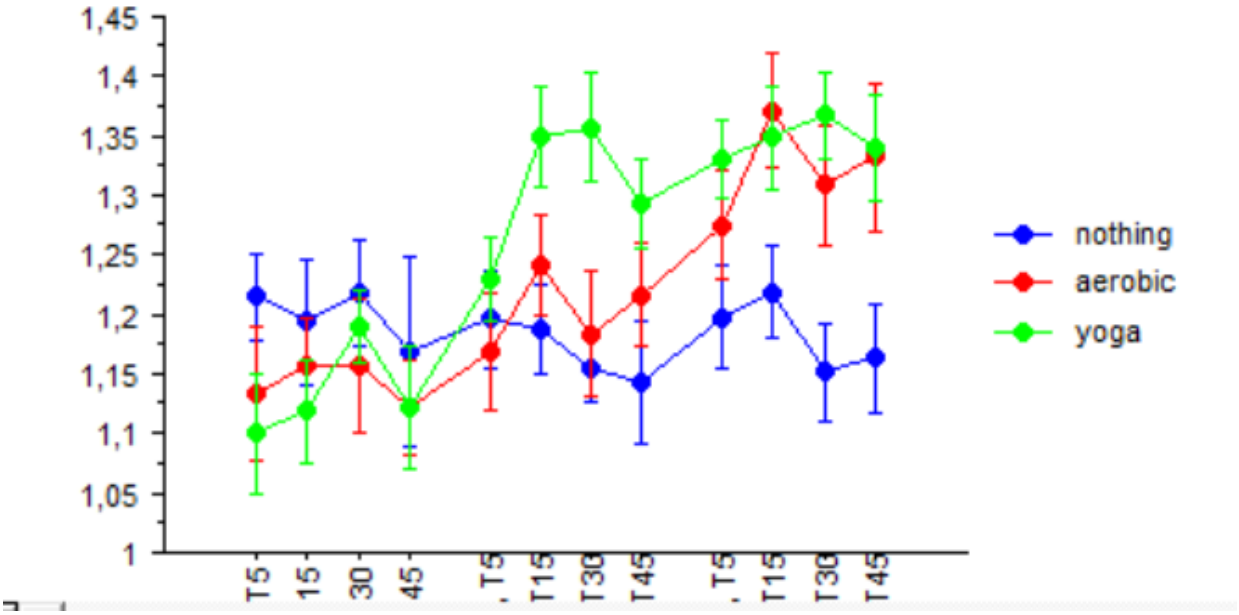

FIG 3.A PAS response at Baseline, 4 weeks of intervention and at 12 weeks of intervention in Healthy volunteers.

According to the effect of TIME we ran separate ANOVAs for baseline, 1 month and 3 months

- Baseline: there was no difference in the PAS effect between the 3 groups (GROUP : F 2, 39 = 0.9 P = 0.4, PAS : F 3, 117 = 0.9 P = 0.4)
- Month 1: the yoga group had significantly more PAS effect than the 2 other groups (GROUP : F 2, 39 = 4.5 P = 0.01, PAS : F 3, 117 = 2.1 P = 0.1 ; post hoc Scheffe no training versus yoga P = 0.02)
- Month 3: the Yoga and the aerobic groups have more PAS effects than the no training group (GROUP : F 2, 39 = 6.8 P = 0.003, PAS : F 3, 117 = 1.0 P = 0.4 ; post hoc Scheffe no training versus yoga P = 0.006, no training versus aerobic P = 0.02, aerobic versus yoga).

PAS effects are enhanced to a same extent (compared to no training) after 3 months of aerobic or yoga training but the effects develop earlier after yoga (already there at 1 month) than after aerobic.

A striking result is that a similar enhancement of the plastic responsiveness of M1 was observed in PD patients.

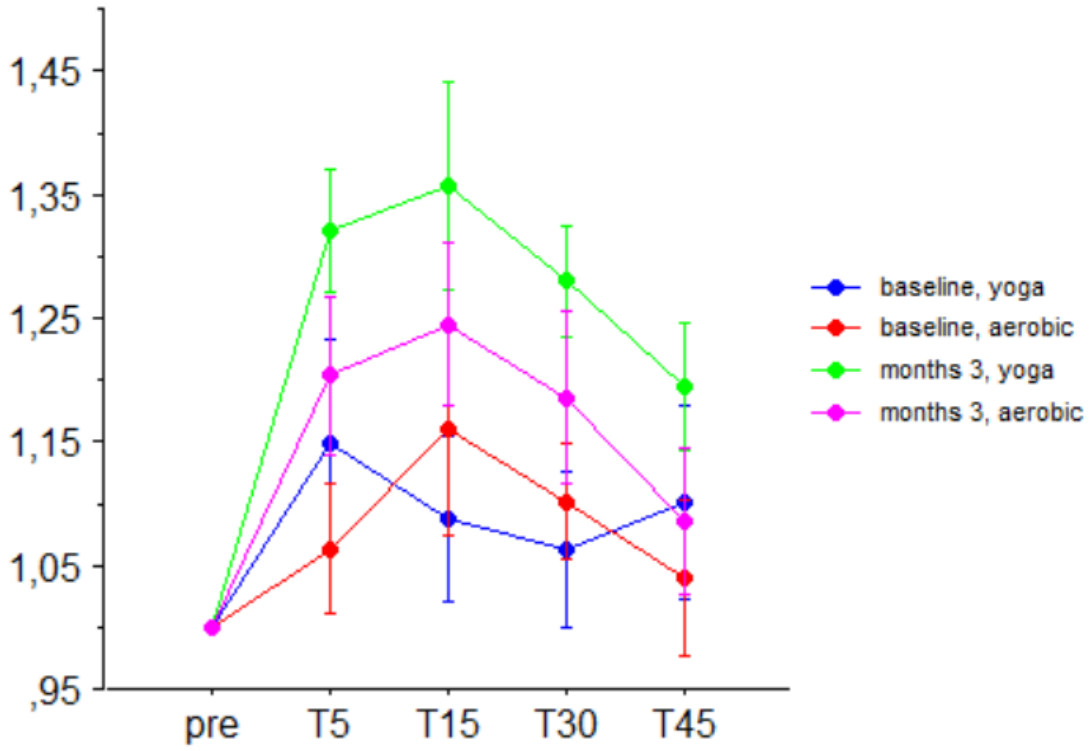

FIG 3.B PAS response at Baseline and after 12-week intervention in Patients with PD.

- To compare the effects of 3 months of aerobic versus yoga training on PAS-induced plasticity we ran a 2 level rANOVA with the 8 normalized values of the MEPs (MEP_{T5}/MEP_{pre}, MEP_{T15}/MEP_{pre}, MEP_{T30}/MEP_{pre}, MEP_{T45}/MEP_{pre} at baseline and at 3 month) forming the repeats and group being the inter subject variable (aerobic/yoga). There was a significant effect of training ($F_{1, 26} = 10.9$ $P = 0.003$), with similar effect of yoga and aerobic ($F_{1, 26} = 0.9$ $P = 0.3$). PAS effects were over 45 minutes after the end of the intervention ($F_{3, 78} = 3.5$ $P = 0.02$, post hoc Scheffé test T_{15} versus T_{45} $P = 0.02$).

Such a change in plastic responsiveness may impact various activities by allowing a better adaptation to changes in the environment, like walking in difficult terrain or to internal changes, like adapting to a new position. It has been suggested that with yoga, because of its resilience effects on basal ganglia cortico-thalamic circuits, one could unlearn old maladaptive behavioral patterns and to establish new adaptive ones. Enhanced plastic capabilities of the motor cortex by yoga indicate that this may be also the case in the motor domain. We will show in the next paragraph that enhanced plastic responsiveness in M1 hand representation is paralleled by improvement of hand dexterity.

Perspectives

It has been shown that plastic responsiveness of M1 is decreased in PD with motor complications. Whether long term yoga practice may delay the occurrence of motor complications or decrease their extent is a challenging question that will need further research. Interestingly the type of plasticity that we tested involves both a somatosensory and a motor aspect and sensori integration is a crucial aspect of yoga training. It will be interesting, in the future to test whether the enhancement of the plastic responsiveness of M1 after yoga training is also present when other types of plasticity are tested.

Major Finding: II

PD patients report impaired manual dexterity and have problems with fine manipulative skills. This has a detrimental impact on their daily living activities and quality of life. The Purdue Pegboard test (PPT) assesses the gross movements of fingers, hand and arms and through the assembly test the fingertips dexterity. To our knowledge it is the first time that this test is used in yoga or aerobic training evaluation. In PD patients we observed a highly significant and specific effect of yoga training on the assembly score. It shows that yoga, which has a broad general aim to promote mind-body connections and does not focus on hand or fingers movements per se, is able to improve fine hand dexterity. This effect may explain other effects like the decrease of the PDQ1 (mobility) and PDQ2 (daily living activities) sub scores at PDQ39.

		T tests	sigificant if P<0.007		
		aerobic	yoga	comparison	
		paired T test raw values		between aerobic and yoga	
				unpaired T test normalized values	
PEGBOARD	right	0.0002	<0.0001	ns	
	left	<0.0001	0.0001	0.02	
	both	<0.0001	<0.0001	0.03	
	total	0.006	<0.0001	<0.0001 yoga>aerobic	
	assembly	<0.0001	<0.0001	0.002 yoga > aerobic	

Table showing significant improvement at 3rd month compared to baseline. Yoga had a stronger effect than aerobic for the assembly score and for the total score.

Interestingly there is a correlation between the enhancement of the plastic responsiveness of the hand representation in M1 and the improvement of the assembly score.

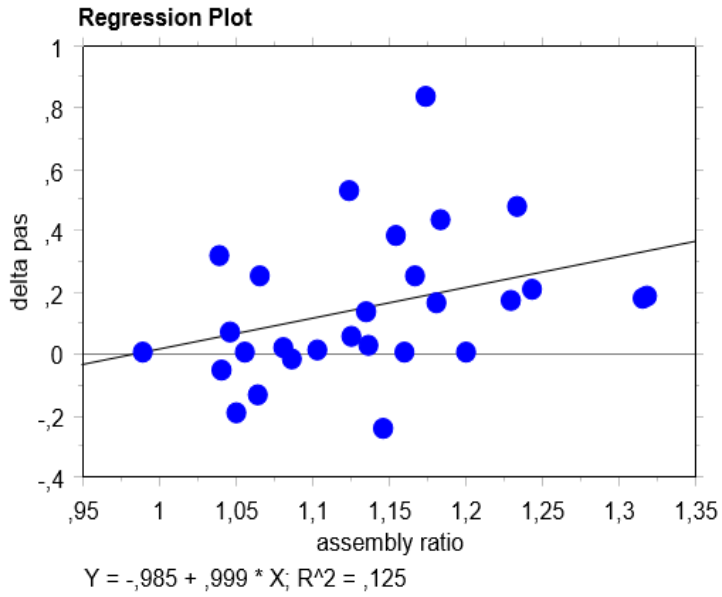

FIG 3.C Correlation between PAS effect and increase of assembly score

- Correlation in the PD group (N = 28) between the increase of the overall PAS effect between baseline and 3 month and the increase of the assembly score at the pegboard test
- Spearman test P = 0.026 R = O.4

In HV yoga training improves the score obtained with the LEFT hand at the pegboard test , probably the score with the right hand is maximized at baseline and can't increase.
Better the increase of the score of the left hand, less is the PAS increase in the ipsilateral hemisphere, showing that improvement of the left-hand dexterity is paralleled by tuning down the plastic responsiveness of the ipsilateral hemisphere.
Correlations obtained in HV and PD groups between the extent of the changes of M1 plastic responsiveness and the scores for hand motricity (HV) or hand dexterity (PD) stress how important is the physiological impact of yoga on plastic responsiveness of M1.

Major Finding III
Training led to a decrease (same for aerobic and yoga) of the tremor score measured in the OFF condition on the right side. Rigidity and Bradykinesia scores and subscores were not modified. This selective effect on tremor is possibly linked to the beneficial effects of training on anxiety, a feeling well known to accentuate tremor.

In addition to these new findings the study also confirms prominent effects of yoga on non motor signs in PD like anxiety, depression, fatigue and attention

		T tests	sigificant if P<0.007		
		aerobic	yoga	comparison	
		paired T test raw values		between aerobic and yoga	
				unpaired T test normalized values	
BDI		0.002	0.0008	ns	
HADS A		0.003	0.004	ns	
HADS D		ns	0.0001	0.04	
MOCA		0.7	0.09	ns	
FSS		0.2	<0.0001	0.02	
PDQ39	SI	<0.0001	<0.0001	ns	
	PDQ1	0.01	0.003	ns	mobility
	PDQ2	0.1	0.0006	ns	activity of daily living
	PDQ3	0.2	0.0006	ns	emotional well being
	PDQ4	0.2	0.4	ns	stigma
	PDQ5	0.1	0.01	ns	social support
	PDQ6	0.4	0.09	ns	cognition
	PDQ7	0.05	0.9	ns	communication
	PDQ8	0.1	0.01	ns	bodily discomfort
NMSS	total	0.002	0.006	ns	
	NMSS1	0.9	0.2		cardiovasc falls
	NMSS2	0.06	0.08		sleep fatigue
	NMSS3	0.002	0.01	ns	mood cognition
	NMSS4	0.5	0.5		perceptual pbs hallucination
	NMSS5	0.04	0.001	ns	attention memory
	NMSS6	0.5	0.1		gastro intestinal
	NMSS7	0.5	0.5		urinary
	NMSS8	0.8	0.2		sexual functions
	NMSS9	0.02	0.08		miscellaneous

- Scores at BDI were significantly improved by either training. Despite better scores at 3 months in the yoga group than in the aerobic group, difference between the groups did not reach statistical significance.
- Scores at MOCA were not significanly changes at 3 months versus baseline in either group.
- Scores at FSS were significantly improved in the Yoga group but not in the aerobic group.
- Scores at HADS part A were improved similarly in both groups while scores at HADS part D were only improved in the yoga group.

- The NMSS total score (sum of the items) was improved in both groups. This was due to a significant effect of the training on the scores at items NMSS3 (for aerobic) and 5 (for Yoga).
- The PDQ39 sumamry index was improved similarly in both groups. There was a specific effect of yoga on items 1, 2, 3

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

As part of this research study, a Yoga protocol for patients with Parkinson's disease has been developed. This was administered to patients with Parkinson's disease participating in the study and others who are interested. The study yielded useful and quantitative information on how Yoga may influence cortical plasticity and motor learning and acts as a supplementary therapy to patients with motor disorders like Parkinson's disease. This has provided a scientific rationale for the practice of Yoga by healthy subjects as well as patients with Neurological conditions like Parkinson's disease. Supported by evidence from this systematically conducted study registered in the Clinical Trial Registry of India (CTRI), this protocol can be popularized among clinicians treating patients with PD, for the benefits of the patients and the society. This study provides a scientific basis for the practice of Yoga

More extensive, well-designed, and multimodal/ multiparametric research studies with the control group are required. Especially the integration of Neuro imaging techniques like fMRI, DTI etc. will provide further insights. The integration of both neuroimaging and neurophysiological techniques such as EEG, MEG etc. will further allow to investigate and bridge imaging findings with neurophysiological and behavioral assessment.

11. **S&T benefits accrued**:

i. List of Research publications
The articles are being submitted to top international journals.

ii. Manpower trained on the project

a) Research Scientists or Research Associates: Nil
b) No. of Ph.D. produced: Nil
c) Other Technical Personnel trained: 2

iii. Patents taken, if any: NA

iv. Any other outcome.

Nil

12. **Financial Position**:

Sr.	Budget Head	Funds Sanctioned	Expenditure	%of Total cost
1.	Manpower	1666600	1839393	110 %
2.	Consumables	415016	302223	73 %
3.	Contingencies	91584	61584	67 %
4.	Travel	70000	40000	57%
5.	Overhead Expenses	300000	300000	100 %
6.	Equipment	150000	150000	100 %
	Total	2693200	2693200	**100 %**

13. **Procurement/Usage of Equipment**

a)

Sr.	Name of Equipment	Make / Model	Cost (FE/ Rs.)	Date of Installation	Utilization Rate (%)	Remarks regarding maintenance/ breakdown
1	Actimeter with flow link-10	FT7/POLAR	INR 95,000	15-07-2016	100	Working

b) Plans for utilizing the equipment facilities in future

The actimeter is an instrument for measuring the physical activity of the human body. Since most of our projects are movement related, this particular equipment will act as an essential component in ensuring uniform activity in various groups in prospective intervention studies.

Name and Signature with Date

a_____
(Principal Investigator)

निदेशक / Director
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