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Effect of *pranayama* & *yoga-asana* on cognitive brain functions in type 2 diabetes-P3 event related evoked potential (ERP)

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***Background & objectives*: Electrophysiological evidence of delayed cognition as measured by P300, an evoked potential is observed in Diabetes mellitus. P300 (or P3) is a component of endogenous cerebral evoked response that assesses higher functions of the brain. Our study aims to see the role of *pranayama* and *yoga-asana* on P300 latency and amplitude in type 2 diabetic patients.**

***Methods*: Sixty patients of type 2 diabetes were recruited from diabetic clinic and divided into two groups - control group on only conventional medical therapy and *yoga*-group on conventional medical therapy along with *pranayama* and *yoga-asana*. Basal recordings of P300 and blood glucose were taken at the time of recruitment and second recordings repeated after forty five days for both the groups. P300 was recorded on Nihon Kohden Neuropack µ MEB 9100 using auditory "odd-ball paradigm". The data were analysed using repeated measures analysis of variance (ANOVA) followed by Tukey's test at 5 per cent level of significance.**

***Results*: Statistically significant improvement in the latency and the amplitude of N200, P300 was observed in the *yoga* group as compared to the control group.**

***Interpretation & conclusions*: Our data suggest that *yoga* has a beneficial effect on P300 and thus can be incorporated along with the conventional medical therapy for improving cognitive brain functions in diabetes.**

Key words Event related potential - *Pranayama* and *yoga-asana* - P300 - Type 2 diabetes

Diabetes mellitus (DM) are a group of metabolic disorders that share the common phenotype of hyperglycemia, polydipsia, polyuria and polyphagia. Although peripheral and autonomic neuropathy is a common complication of DM, the central nervous system (CNS) does not seem to be spared either. In the past few years, CNS involvement in DM has received a special attention, particularly the higher brain functions. The metabolic dysregulation influencing cerebral blood flow, metabolism and alteration in higher functions in diabetic patients has been reported and demonstrated at neurochemical, electrophysiological , structural and neurobehavioural levels[1,2]. Recently, there has been an increasing trend in the use of Evoked potentials, an electrophysiological tool to study the functional integrity of the neural substrate and the involvement

of CNS in Diabetes. Evoked potentials are changes in electrical potential (voltage) recorded from the brain during a brief period of time (epoch) after presentation of evoking stimulus. Among these potentials, event related potentials (ERP) indicates cognitive functions of the brain. P300 (or P3) wave of this ERP has been identified as a late cortical neurophysiological event reflecting the activity of cognitive and mnemonic functions in humans[3], information processing[4] and appears to be strongly associated with attention and short term memory[3]. Many authors have documented an electrophysiological evidence of delayed cognition in diabetes[5-7]. *Yoga*, a vedic science has shown improvement of oxidative stress as well as glycaemic status of diabetics through neuroendocrinal mechanism[8,9]. An attempt is made through this study to see if yogic intervention for a duration of 45 days brings about any improvement in the cognition in Type 2 diabetes using the electrophysiological test, Evoked Potential as an assessment tool.

Material & Methods

The study was conducted in the Electrophysiology laboratory of Department of Physiology, UCMS, Delhi between November 2005 to March 2007. Sixty patients diagnosed as type 2 DM according to American Diabetes Association (ADA) and who met the following criteria were selected: no history of coronary artery disease, diagnosed stroke, cerebrovascular disease, known neuropsychiatric illness or any other complications (retinopathy, nephropathy) of diabetes; age between 35-60 yrs with duration of DM beween 2-10 yr. The mean duration of DM is 4.16 ± 1.86 yr for the control group and 4.38 ± 1.98 yr for the *yoga* group). All the patients were receiving conventional medical therapy. The drugs prescribed most commonly were oral hypoglycaemic drugs like Glibenclamide and Metformin, the dose of which was not tampered with, during the entire study period. The clearance from the Ethical committee of the college was obtained and an informed written consent was taken from all the patients after the recording procedure was explained to them.

The subjects were divided into two groups matched for age and sex. Control group (n=30) with mean age 52.90 ± 6.87 yr. The *yoga* group was taught *pranayama* and *yoga-asana* (Table I) by a certified yoga instructor daily for initial 5 days and then they were called regularly at an interval of 7 days for supervision and compliance. Both the groups were tested under similar laboratory conditions. Biochemical and electrophysiological recordings of event related potential-P300 were taken twice in both the groups- initial baseline recording at the time of recruitment and the subsequent recording after 45 days for control group and with the yogic intervention for the same duration in the *yoga* group.

Table I. Various *pranayama* and *asanas* included in yogic exercises

S. No.	Name	Duration
1.	*Bhastrika- pranayama*	3-5 min/day
2.	*Kapal-bhati*	10 min/day
3.	*Anulom-viloma*	5-10 min/day
4.	*Bhramari*	5 times a day
5.	*Udgit-Om Uccharan*	5 times a day
6.	*Surya namaskar*	3-7 turns of each, the pose being maintained for ten seconds adding each turn, every fortnight
7.	*Tadasana*	¼ min to one min for adding ¼ min/wk
8.	*Trikona-asana*	¼ min to one min for each side, adding ¼ min/wk
9.	*Pashimottanasana*	¼ min to one min for each side, adding ¼ min/wk
10.	*Bhujangasana*	3-7 turns of each, the pose being maintained for ten seconds adding one turn each, every fortnight
11.	*Shavasana*	2- 5 min, adding 1 min/wk

Event related Potentials (ERP) recordings from the scalp of the patients was done using Nihon Kohden Neuropack μ MEB 9100 EP/EMG measuring system (Nihon Kohden Corp., Tokyo, Japan). Event related evoked potentials were recorded with Ag/Ag Cl electrodes from standard locations using 10-20 International system. The electrodes were placed at Fz, Cz, Pz (active electrodes at frontal, vertex and parietal areas), FPz (ground electrode on the forehead) and A1, A2 (reference electrode on the ear lobules). The recordings were obtained in response to standard auditory "Odd-ball paradigm" where a frequent and a rare stimuli were given randomly. The skin electrode contact impedance was kept below 5Ω. The subjects were instructed to press a button on the response pad with the thumb of their dominant hand on hearing Auditory 1 (target, rare) among the frequently occurring stimuli delivered by headphones. During the recording session, subjects were instructed to fix his/her eyes on a particular spot on the wall in front in order to avoid electro-oculographic artifacts due to eye movements. Data for 2 trials were obtained, stored, analyzed and averaged by software. Peak latencies and baseline to peak amplitudes of N2 and P3 were evaluated.

The data were statistically analysed using repeated measures analysis of variance (ANOVA) followed by Tukey's test at 5 per cent level of significance.

Results & Discussion

The deranged blood glucose seen in DM seems to be very effectively controlled by *yoga*, a holistic approach as shown by the result in Table II. Although improvement was seen even with control group who were on the conventional treatment but statistically significant improvement was seen only when both the modalities of interventions were combined as in *yoga* group. This finding corroborates the earlier findings[9,10-14] who reported better glycaemic control and stable autonomic functions in Type 2 diabetes with *yoga asanas* and *pranayamas* and significant reduction in hyperglycemia with decrease in oral hypoglycemic drugs for maintenance of normoglycemia in response to *yoga* therapy. Various *yoga-asanas* may be directly rejuvenating/regenerating cells of pancreas as a result of which there may be increase in utilization and metabolism of glucose in the peripheral tissues, liver and adipose tissues through enzymatic process[15].

The pattern, extent and the mechanism of damage of the central nervous system in diabetes is in the forefront of current neurological research using highly sophisticated event related evoked potentials. Many different components of the ERPs have been identified, including Nd, P165, NA, N1, P2, N2, P3, P3a, P3b, P4 and N400. The N1 and P2 components are believed to reflect the activity in neural areas that are activated by sensory modality and are independent of the subject's attention[16]. The N2 component is related to the unexpectedness of the stimulus[17]. Thus any event related potential includes an early sensory evoked potential and a late (cognitive) response P3 component. The latency of P3 is a valuable tool for studying the timing of mental events and the effects of sensory and cognitive manipulations on different stages of mental processing. P3 is a broad, positive component, peaking at around 300 msec after stimulus onset, with maximal amplitudes at parietal and central midline recording sites of the scalp measured as potential differences against the ears or the nose. The P3 wave is believed to reflect cognitive processes underlying attention allocation and memory updating[18,19]. In young Indian subjects, the latency and amplitude of P3 were comparable[20] with age and sex matched subjects of the western world.

Table II. Blood glucose (mg/dl) level in both groups

		Glucose (fasting)	Glucose (PP)
Control group	Pre	174.40 ± 36.91	260.27 ± 51.43
	Post	167.40 ± 37.32	250.23 ± 48.57
Yoga group	Pre	172.87 ± 45.55	260.50 ± 78.60
	Post	133.77 ± 38.77*	198.90 ± 63.68*

*P <0.001

P3 is evoked by an unexpected stimulus and reflects the updating of working memory. Its amplitude indicates the amount of processing required by a given stimulus. The amplitude is related to task relevance of eliciting events[21] increasing when stimulus becomes more improbable and informative[22]. Increasing the difficulty of detecting the target, decreases the amplitude and increases the latency of P300 wave. Increase in amplitude indicates functional recruitment of the neuronal pool underneath the recording electrode site. Its increase during exercise is due to increase in the cerebral blood flow[23]. Our data support earlier findings[5-7] where an electrophysiological evidence of delayed cognition was observed in diabetics. (Tables III-VI– latency and the amplitude of the baseline recording at the time of recruitment in both the groups). In non-insulin dependant DM (NIDDM), the diabetic mileu interacts with generators of N2 and P3 in the cerebral cortex so as to cause delay in cognitive processes[6].There are reports indicating that P3 generators are located in the hippocampus (HPC) of limbic system. As HPC is known to be involved in learning and memory, the delayed P3 in NIDDM therefore, reflects inhibition or possible damage of this area[6]. Chronic hyperglycemia and frequent episodes of hypoglycemia[24] and chronic stress[25] is also known to downregulate hippocampal 5HT1A receptors which in turn leads to elevations of cortisol and subsequently reduced 5HT1A receptors, finally contributing to reduced hippocampal neurogenesis and hence hippocampal atrophy and cell death. An improvement in the latency and amplitude of N2 and P3 waveform is seen in the *yoga* group which regularly and strictly performed *pranayama* and *asanas* for 45 days (Tables IV and VI), as evidenced by decrease in the latency and increase in amplitude after yogic intervention along with conventional treatment in contrast to the control group, which continued with only the conventional treatment (Tables III and V). Regular practices of *yoga* is associated with the reduction of basal cortisol and catecholamine secretion, a decrease in sympathetic activity with the corresponding increase in parasympathetic activity, reduction in metabolic rate and oxygen consumption

Table III. Mean latencies (msec) of ERP components in control group

	Montages- recording sites					
	Fz		Cz		Pz	
	Before	After 45 days	Before	After 45 days	Before	After 45 days
N2	245.70 ± 33.70	244.03 ± 22.41	234.83 ± 27.04	234.13 ± 27.94	232.73 ± 19.32	232.90 ± 16.89
P3	350.33 ± 47.07	346.60 ± 53.51	360.20 ± 47.91	358.13 ± 44.73	380.87 ± 41.10	379.13 ± 51.59

Table IV. Mean latencies (msec) of ERP components in *yoga* group

	Montages-recording sites					
	Fz		Cz		Pz	
	Pre-yoga	Post-yoga	Pre-yoga	Post-yoga	Pre-yoga	Post-yoga
N2	244.0 ± 31.55	235.67 ± 36.93	236.17 ± 26.61	227.23 ± 24.21*	230.20 ± 26.54	220.93 ± 29.19
P3	349.73 ± 36.31	328.53 ± 31.43*	360.63 ± 38.88	337.37 ± 28.13*	382.07 ± 26.11	347.10 ± 35.47**

P value *< 0.05, **<0.001. Significant decrease in the latency of N2 at Cz and P300 at all the montages

Table V. Mean amplitudes (μV) of ERP components in control group

	Montages-recording sites					
	Fz		Cz		Pz	
	Before	After 45 days	Before	After 45 days	Before	After 45 days
N2	6.56 ± 6.21	6.46 ± 5.54	7.06 ± 5.50	7.17 ± 5.01	5.51 ± 3.95	6.0 ± 3.37
P3	9.0 ± 6.47	8.03 ± 6.06	10.72 ± 5.76	10.69 ± 5.63	12.68 ± 4.88	12.75 ± 4.94

Table VI. Mean amplitudes (μV) of ERP components in *yoga* group

	Montages-recording sites					
	Fz		Cz		Pz	
	Pre-yoga	Post-yoga	Pre-yoga	Post-yoga	Pre-yoga	Post-yoga
N2	6.33 ± 3.65	7.46 ± 3.64	6.59 ± 3.94	8.51 ± 3.87*	5.04 ± 3.75	9.12 ± 4.76
P3	10.35 ± 8.70	12.12 ± 10.66	11.34 ± 7.98	13.09 ± 8.48	13.33 ± 6.82	16.08 ± 6.35*

*P** < 0.05. Significant improvement in the amplitude of wave N2 at Cz and P300 at Pz montage

with salutary effect on cognitive functions and cerebral neurophysiology[26]. *Yoga* is also known to relieve stress[27-29] and modulate the limbic system activity, which via hypothalamus may modulate the sympathetic activity and regulate endocrine secretions involved during stress[30]. Alleviation of stress by *yoga* might be involved in the upregulation of hippocampal 5HT1A receptors, decreasing cortisol level and thus reversing the pathology involved in the decline of cognition. Increase in the cerebral blood flow during various *asanas* might have brought about an increase in the amplitude. An improvement and stabilization in the basic biochemical levels and metabolic derangement might have also contributed to the positive changes seen with *yoga*. Sarang *et al*[31] also reported an improvement in P300 following *yoga*. Anand *et al*[32] reported dominance of α-rhythm in EEG activation of the persons trained in *yoga*, suggesting a positive correlation between dominant α-rhythm and an improvement in cognitive functions of the brain. In addition to the above findings, the patients also reported sense of well being with an improvement in their daily life activities. They were mentally more alert and happier. *Yoga* brings about this change by releasing opioids and altering adrenocortical activity[29,33]. More studies are needed.

Significant decrease in the latency of N2 at Cz and P300 at all the montages (Table IV) and significant improvement in the amplitude of wave N2 at Cz and P300 at Pz montage was observed in the yoga group (Table VI) while montages in the control group did not show any significant changes (Tables III and V).

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