Original Article

Effect of two months of structured exercises on executive functions in patients with type 2 diabetes mellitus: Randomized controlled trial

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Abstract

Background and Aim: Diabetes mellitus is an endocrine disorder characterized by metabolic abnormalities, which has been reported to be associated with cognitive dysfunctions. Exercise along with diet and medication has been considered as a cornerstone in the management of type 2 diabetes mellitus (T2DM). Therefore, the present study was undertaken to study the effect of 2 months of structured exercise therapy on executive functions of the brain in freshly diagnosed patients with T2DM.

Methods: Sixty newly diagnosed patients with type 2 diabetes and Thirty age, sex and mean education matched matched healthy controls were enrolled as study participants in this interventional randomized controlled trial. The 60 T2DM patients were divided randomly into two groups as diabetic control (patients only on dietary and medication) and interventional group (IG) (patients on structured exercise therapy along with diet and medication). Body mass index (BMI), glycated hemoglobin (HbA1c) and executive functions (Stroop test) were assessed in these subjects before and after exercise therapy.

Results: Findings showed improvement in executive functions after administration of structured exercise therapy. BMI and HbA1c values have also improved at the end of 2 months in the IG and a significant correlation was observed between BMI, and executive functions.

Conclusion: Exercise therapy along with dietary control and anti-diabetic medication has an affirmative influence on executive functions of the brain.

Key words: Body mass index, glycated hemoglobin, Stroop test

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INTRODUCTION

Diabetes mellitus is a group of common metabolic disorder and its incidence is increasing worldwide at an alarming rate. Type 2 diabetes mellitus (T2DM) results from the interaction between a genetic predisposition, behavioral, and environmental risk factors. From literature, evidences strongly suggest obesity and physical inactivity are the main nongenetic determinants of the disease.[1,2] The association of T2DM with cognitive impairments has been reported by various studies, which could be due to the metabolic abnormalities in T2DM.[3-6] The impaired glucose tolerance is associated with cognitive impairments which includes attentional control, executive function ad verbal memory.[7,8] The increased risk of dementia is reported in individuals with T2DM.[9] Moreover, various studies have documented that even mild increase in glucose levels within the nondiabetic range were also associated with impaired cognitive functions in younger individuals.[10-12]

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The majority of studies linking glucose regulation with cognitive deficits have been conducted in the elderly diabetic patients, but very limited data is available for adults with T2DM. The aged population usually have co-morbid conditions associated with aging that can contribute to decline in cognitive function and thus the relationship between glucose tolerance and cognitive performance cannot be established. Therefore, studies including

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younger population should be conducted to confirm the relationship between cognition and glucose tolerance.

Exercise has been considered a cornerstone in the management of T2DM, along with diet and medication. The benefits of exercise in preventing and treating diabetes are extensively accepted. It improves glycemic control, body composition, cardio-respiratory fitness, cardiovascular risk, physical functioning, and well-being in patients with T2DM.[13]

However, despite the accumulating evidence supporting the effects of exercise therapy in T2DM elderly patients, there is limited evidence in adults, to suggest that regular aerobic exercise and resistance exercises can augment upon executive functions of the brain. We hypothesized that exercise therapy will have a positive influence on executive functions. Stroop test response performance is commonly used in the evaluation of executive functions and as a measure of selective attention and processing speed. Therefore, we investigated the association of glycated hemoglobin (HbA1c) and body mass index (BMI) with scores on Stroop test to assess whether short structured exercise therapy of 8 weeks would improve the scoring on Stroop test response performance in adults with T2DM.

MATERIALS AND METHODS

Study population

An interventional randomized controlled trial conducted in Department of Physiology, JNMC, KLE University, Belagavi. Sixty newly diagnosed patients, attending medicine OPD KLE's Dr. Prabhakar Kore Hospital and Research Centre were included in the study. In-person assessment was done followed by a physical examination and then divided randomly into diabetic group and interventional group (IG) by computer generated, randomized number sequence. Three groups were made as mentioned below:

- Normal control (NC): Sex, age and mean education level matched healthy subjects
- Diabetic control (DC): Patients only on dietary control and anti-diabetic medication
- IG: Patients on exercise therapy along with dietary control and anti-diabetic medication.

Ethical Clearance was obtained from the Institutional Ethical Committee. Ethical Clearance No: Ref. No. KLEU/Ethic/2012-13/D-4570. Written informed consent was obtained from patients.

Inclusion criteria

Patients diagnosed with T2DM as per ADA Guidelines between the age group of 20 and 45 years, and on treatment with oral anti-diabetic drugs with normal eye sight and color vision were included in the study.

Exclusion criteria

Subject with a history of diabetes more than a year or T1DM, physical disability, neurological disorder, color blindness, with a prior regimen of physical exercise and alcoholics or smokers were excluded.

Exercise protocol

The interventional therapy consists of 8 weeks of the individually designed exercise program of regular exercise consisting of 30 min of physical activity (aerobic exercise) 5 days/week, at an intensity of 70–80% of their individualized maximum heart rate and resistance exercises performed 3 times a week targeting all major muscle groups which includes 3 sets of 8–10 repetitions at a weight that can't be lifted more than 8–10 times. Dumbbell flies, seated single leg extension, dumbbell shoulder press, dumbbell bent over row, standing leg curls, dumbbell biceps curls, dumbbell up-right row, dumbbell triceps kickbacks, and abdominal curls were included in the exercise program.[14]

Parameters assessed

Body mass index

BMI was calculated by dividing body weight in kilograms by the square of her height in meters. BMI was classified according to the BMI criteria for the Indian population.[15]

BMI ≤ 18.49 kg/m^2, underweight; BMI 18.5–22.99 kg/m^2, normal weight, BMI ≥ 23 kg/m^2 overweight or obese.

Glycated hemoglobin

HbA1c was measured by ion exchange resin method.[16]

The Stroop test

The challenge of the task was to focus on one particular feature (language), while blocking out another (color). Color words were presented in the congruent mode (e.g., the word 'red' written in a red color) and in the incongruent mode (e.g., the word 'red'

Table 1: Gender, age, BMI and HbA1c parameters of the subjects in normal control, diabetic control and interventional group expressed in mean±SD

Parameters	Normal control (*n*=30)	Diabetic control (*n*=30)	Interventional group (*n*=30)	*P*
Gender				
Males	16	12	12	0.486
Females	14	18	18	
Age	35.3±4.24	35.6±3.72	36.4±3.89	0.729
BMI (kg/m^2)	24.6±3.05	30.1±2.67***	30.3±4.05***	0.001
HbA1c	4.9±3.8	5.9±4.5**	5.6±.4.1**	0.01

Statistical analysis was done by one-way ANOVA. *P*<0.01 was considered significant. *Depicts comparison with normal group, ***P*<0.01, ****P*<0.001. BMI: Body mass index, HbA1c: Glycated hemoglobin, SD: Standard deviation written in different color). Instruction was given to read column-wise, and name the color in which the word was written. Subjects were timed on the 28 word task which was printed on A3 size paper which was held in front of subject 50 cm from eye level. The subjects were made acquainted with procedure by exposing them to the cards. The score was the time taken to complete the reading. Errors were pointed out to participants and were corrected as they proceed. The total time taken to read the whole card was noted. The average time as Stroop test response was calculated as total time divided by number of stimuli.[17,18]

Table 2: Comparison of Stroop test response time with congruent cards among the three groups before and after intervention

Groups	Mean±SD	Q1	Q2
Before intervention			
Normal control	58.3±7.58 (46-70)	52.5	66
Diabetic control	73.6±11.18*** (54-90)	63.75	83.25
Interventional group	70.6±11.11*** (48-84)	65	29.25
	F (2,8)=19.19; P<0.001		
After intervention			
Normal control	57.9±4.04 (46-61)	48	53
Diabetic control	67.3±13.51** (47-89)	67.5	67.5
Interventional group	65.8±9.39** (46-83)	73.25	73.25
	F (2,8)=19.15; P<0.001		

The values are expressed as mean±SD. Q1: Quartile 1 and Q2: Quartile 2 with minimum and maximum values. Statistical analysis was done by one-way ANOVA test. P<0.001 was considered as significant. SD: Standard deviation. *Depicts comparison with normal group, **P<0.01, ***P<0.001

Table 3: Comparison of Stroop test response time with incongruent cards among the three groups before and after intervention

Groups	Mean±SD	Q1	Q2
Before intervention			
Normal control	116±13.62 (87-136)	107.25	127
Diabetic control	137±16.95*** (110-160)	119.75	156
Interventional group	130.2±11.40*** (100-136)	106	127.5
	F (2,8)=19.87; P<0.001		
After intervention			
Normal control	108.1±13.67 (86-129)	96.5	123
Diabetic control	124.7±13.73*** (100-154)	113.5	135.25
Interventional group	110.3±9.51+++ (100-126)	101	120.25
	F (2,8)=15.67; P<0.001		

The values are expressed as mean±SD. Q1: Quartile 1 and Q2: Quartile 2 with minimum and maximum values. Statistical analysis was done by one-way ANOVA test. P<0.001 was considered as significant. SD: Standard deviation. *Depicts comparison with normal group, **P<0.01, ***P<0.001, +Depicts comparison with diabetic control, ++P<0.01, +++P<0.001

Statistical analysis of data

The Chi-square test was used for categorical data. One-way ANOVA was used for comparison of more than two groups. Student's two-tailed *t*-test was used to compare the difference in Stroop test response performance in Interventional group. Spearman's correlation coefficient was used to demonstrate the relationship between different parameters. All statistical analysis was performed by using IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. P value < 0.05 was considered statistically significant.

RESULTS

Age, gender, BMI, and HbA1c parameters of the subjects in NC, DC and IG expressed in mean ± standard deviation is depicted in Table 1. The baseline values of BMI and HbA1c are high in diabetic patients as compared to the NCs, whereas no such difference was observed between DC and IG group.

Tables 2 and 3 depicts comparison between three groups on Stroop test response time with congruent and incongruent cards, respectively before and after the intervention. The mean Stroop test response time was longer in diabetics as compared to NCs with congruent cards (P <.001). The response time decreases significantly with interventional therapy in diabetics (P < 0.001) [Table 2].

The mean Stroop test response time was longer in diabetics as compared to NCs with incongruent cards (P < 0.001). The response time decreases significantly with interventional therapy in diabetics (P <.001) [Table 3]. Table 4 depicts the number of errors made with incongruent cards among the three groups. BMI and HbA1c values have decreased with 2 months of exercise therapy as depicted in Table 5. Statistically significant correlation was observed between BMI, HbA1c and executive function assessed by Stroop test response time with congruent and incongruent cards [Table 6].

DISCUSSION

Findings of the present study revealed decreased Stroop test response performance in T2DM patients as compared to healthy controls. However, there was

Table 4: Comparison of the number of errors made with incongruent cards among the three groups

	0	1	2	3	4	5	Total
Normal control (%)	10 (33.3)	15 (50)	5 (16.7)	0	0	0	30
Diabetic control (%)	0	10 (33.3)	6 (20)	4 (13.3)	5 (16.3)	5 (16.3)	30
Interventional group (%)	0	14 (46.7)	8 (26.2)	8 (26.2)	0	0	30

Fisher exact test by *r*×c table was done and found P<0.001, was significant statistically significant improvement in the executive functions after the administration of short-term structured exercise therapy in the IG. Our findings are distinctive as we observed association between mild hyper-glycemia (newly diagnosed patients with T2DM) and decreased Stroop test performance in patients aged between 20 and 45 years. These findings are consistent with the previous reports depicting the effects of poor glucose regulation on tasks associated with fontal cortex functions.[8,19]

In the present study, decrease in BMI and HbA1c values was observed at the end of 2 months of interventional therapy, which is in agreement with the previous studies.[20,21] The impact of T2DM on cognition is established and has been reported in batteries of papers.[22,23] The association between glucose control and cognitive functions in type 2 diabetic adults was observed by the Greenwood *et al*. and found the negative relationship between cognitive performance and glucose control.[24]

Alexander *et al*. have recognized five circuits linking frontal lobe regions to subcortical areas. These five circuits pass autonomously through the caudate, globuspallidus and thalamus and may be implicated as dorsolateral, motor, and anterior cingulate. The dorsolateral circuit affords the ability to alternate between conceptual sequences and inhibition of a cognitive set. These abilities are used in the Stroop tasks. The motor loop, which passes through the putamen and ends in the supplementary motor area, is associated with choosing the action to be performed and dorsolateral circuit determines behavior.[25]

However, which stage of diabetes causes cognitive dysfunctions and how they progress over time is very unclear. Before the patients are being diagnosed as diabetic, they undergo a prediabetic state in which there is evidence of glucose intolerance with bouts of hyper- and hypo-glycemia that can cause cognitive dysfunctions. Therefore, it could be suggested that the patients before getting diagnosed with diabetes must have underwent the prediabetic state, where cognitive dysfunctions are likely to happen. Studies have reported significant difference among normal, diabetic and pre-diabetic group in executive function which is indicative of mild to moderate cognitive decline at early stages of T2DM.[26,27]

In our study diabetic group, executive functioning on Stroop response test performance were significantly less as compared to healthy controls, which may reflect the compromised efficiency of the circuits as they course through the striatal regions. There is a complex relationship between exercise and cognition. Studies have reported impaired performance of a complex task in diabetic patients, which is a function of frontal lobe and moderate intensity of exercises has been observed to improvise cognitive function in these patients by increasing pre-frontal oxygenation.[28,29]

The study by McMorris *et al*. has documented beneficial effects of acute and intermediate exercises on response speed.[30] The various studies reported differences in cognitive functions during and after exercise between different modes of exercise. These changes could be explained by changes in cerebral blood flow.[31] The physiological basis of these could be increased in the amount of release of catecholamine in central nervous system. Even neuro-imaging studies have revealed the enhanced functioning of cortical regions with exercise therapy.[32]

Limitations of the study

The difference between the groups found in our study is small reflecting the short duration of diabetes in our population. Due to less sample size we could not confirm the relationship between HbA1c and decline in executive functions of the brain.

CONCLUSION

There was a significant decrease in Stroop test performance

Table 5: Differences in BMI and HbA1c levels in interventional group at the end of 2 months of exercise therapy, expressed in mean±SD

Parameters	Baseline values	Values at the end of 2 months	*P*
BMI (kg/m^2)	30.3±4.05	27.21±3.14	0.05
HbA1c	5.6±4.1	4.89±0.49	0.05

Statistical analysis was done by Student's *t*-test. *P*<0.05 was considered as statistically significant. BMI: Body mass index, HbA1c: Glycated hemoglobin, SD: Standard deviation

Table 6: BMI and HbA1c correlation with executive function in interventional group subjects

Stroop test	Time of assessment	BMI		HbA1c	
		r	*P*	*r*	*P*
Congruent	Before intervention	0.351	0.057	−0.309	0.097
	After intervention	0.206	0.274	0.313	0.093
Incongruent	Before intervention	−0.226	0.231	−0.280	0.884
	After intervention	0.296	0.112	0.124	0.514

Statistical analysis was done by Spearman's correlation analysis. *P*<0.05 was considered as statistically significant. BMI: Body mass index, HbA1c: Glycated hemoglobin in newly diagnosed T2DM patients. Administration of structured exercise therapy for two months significantly increased Stroop test performance, and significantly decreased BMI and HbA1c levels in IG patients. Therefore, from the findings of the present study, it could be suggested that structured exercise therapy exerts a positive influence on the executive functions of the central nervous system.

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