A Study of Executive Functioning in Type 2 Diabetes Mellitus Patients in Relation with the Duration of Diabetes

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ABSTRACT

Background: Type 2 diabetes mellitus increases the incidence of cognitive impairment by two to three fold when compared to non-diabetics. This causes impairment in the Activities of Daily Living (ADL) in the patients which in turn leads to immeasureable caregiver burden and increase in healthcare expenditure. Effective functioning in ADL depends upon the intact executive functions controlled by the Frontal lobe. **Objective:** To measure the executive functioning in type 2 diabetes patients using Frontal Assessment Battery (FAB). **Materials and Methods:** Fifty six Type 2 diabetes mellitus patients in the age group of 30-50 yrs in both genders were screened for dementia using Mini Mental Scale Examination (MMSE). Then their executive functions were assessed using FAB under six domains- conceptualization, mental flexibility, programming, sensitivity to interference, inhibitory control and environmental autonomy. **Results:** The total scores of MMSE, FAB and the individual scores of six domains of FAB were correlated with duration of diabetes using Pearson rank correlation and a statistically significant linear correlation was obtained in the negative direction for all the variables. **Conclusion:** Type 2 diabetes is associated with poor executive functioning and the same deteriorates as the duration of disease increases.

Keywords: Type 2 Diabetes Mellitus, MMSE, executive functions, FAB.

INTRODUCTION

Cognition refers to the set of interwoven processes, such as memory, language, and problem solving, that we bring to bear to generate structures and strategies to apply to our perceptions.[1] Attention, memory, language, visuospatial abilities, speed of processing information, executive functioning, reasoning ability are various domains of cognition.

Executive functions have been recently separated from other cognitive domains as an individual entity. It refers to the capacity of the individual to engage successfully in independent, purposive, self serving behavior that is appropriate to the immediate environment. It can be defined as a set of cognitive skills required for planning, initiation, sequencing and monitoring of goal directed behavior.

One school of thought associates Executive function with specific higher functions such as insight, will, abstraction and judgment which are dependent on the Frontal lobes. According to this theory executive function is an acquired skill like memory and language.[2]

The other school of thought emphasizes that executive functions control the other cognitive domains. Thus there exist a complex interaction between executive and nonexecutive domains of cognition. Also researchers found a role for Basal Ganglia in planning and organizing particularly motor functions.[3] Animal studies on primates show association between the basal ganglia-thalamocortical circuits and frontal lobe.[4] Thus Frontal Lobe plays a very important role in Executive functions of the Brain.

Normal aging is associated with decline in cognitive abilities such as sustained attention, processing speed, short term memory, visuospatial abilities etc.[5] This decline in cognition also includes deficits in executive functioning as age advances.[6,7] likewise patients with Diabetes mellitus (DM) also show impairment of executive functions. Even the DM patients with apparently normal cognition show impaired executive functions, the reason being the cerebral microvascular compromise and chronic dysglycemia that affect the neuronal function.[8] On thorough literature review analysis most of the studies focus on the association of dysexecutive syndrome and the glycemic control in type 2 diabetes mellitus patients.

With this background this study was designed to assess the executive functioning in type 2 Diabetes mellitus patients with no cognitive impairment by a simple bedside battery of tests for frontal lobe functions. We have also tried to figure out how the duration of Diabetes affects the Executive functioning irrespective of the glycemic status.

AIM AND OBJECTIVES

The primary aim of this study is to assess the Executive functioning in individuals with Type 2 diabetes mellitus in relation to the duration of diabetes.

STUDY DESIGN

Cross-sectional Observational study done at Institute of Physiology and experimental medicine, Madras Medical College, Chennai. Subjects were recruited from the Institute of Diabetology, Rajiv Gandhi Government General Hospital, Chennai. This study was conducted between December 2016 and February 2017.

SUBJECT SELECTION

Individuals in the age group of 30-50 yrs. belonging to both genders, with Type 2 diabetes mellitus under good glycemic control were included in the study.

Individuals with

- Type 1 Diabetes Mellitus
- Dementia of any cause
- Persons with complications of DM
- Neurological disorders
- Cardiovascular disorders
- Sleep disorders
- Psychiatric illness
- Substance abuse
- Chronic drug intake were excluded from the study.

Applying the above inclusion and exclusion criteria 56 subjects were enrolled out of which 35 were males and the rest females.

INSTRUMENTS

This study is a questionnaire based study done with Mini Mental State Examination (MMSE) and Frontal Assessment Battery (FAB)[9].

MMSE is 30 point Questionnaire used in both the clinical and research setting to screen for cognitive impairment. MMSE tests the orientation, registration and recall, attention and calculation, reading, comprehension, complex commands. Total score is 30. Cut off scoring method is used for research purposes and a score of 24 and above is normal.

FAB is a brief battery of six neuropsychological tests designed for the bedside assessment of Frontal lobe functions. The six cognitive and behavioural domains explored by FAB are Conceptualization, Mental Flexibility, Programming, Sensitivity to Interference, Inhibitory Control and Environmental Autonomy.

Table 1 : How to perform Frontal Assessment Battery	
Conceptualization	Identifying similarities between two given things and categorizing them. Ex. Orange and banana are fruits
Mental flexibility	Tests the lexical fluency. Subject to tell as many words as possible starting with the letter mentioned by examiner
Programming	Luria's Fist-Palm-Edge test. Subject to perform this motor series with the examiner first and the alone.
Sensitivity to interference (conflicting instructions)	Examiner instructs the subject "Tap once when I tap twice; Tap twice when I tap once". The series performed is 1-1-2-1-2-2-2-1-1-2.
Inhibitory control (Go-No Go test)	Examiner instructs the subject "Tap once when I tap once; Do not tap when I tap twice". The series performed is 1-1-2-1-2-2-2-1-1-2.
Environmental Autonomy	Tests prehension behavior. Examiner instructs the subject " Do not take my hands". Scoring done according to the response of the subject when examiner places his hands on subject's palm.

Highest score of each domain is 3 and the lowest score is 0. Thus the total score of FAB is 18. The cut off score is 12. Higher the score better the Frontal lobe function.

METHODOLOGY

After obtaining the informed consent , the participants were screened for cognitive decline using Mini Mental Scale Examination (MMSE). Then they are subjected to Frontal lobe assessment using FAB. The total score of MMSE and FAB were correlated with duration of diabetes. Also the scores of the six domains of FAB were correlated with duration of diabetes individually.

STATISTICS

The mean values of all the parameters were statistically analysed with Pearson's Rank correlation using SPSS version 21 and MS Excel 2007.

RESULTS

Total no. of participants were 56 (35 male and 21 female). Mean age of the participants was 40.7 ± 8.05 (mean ± SD) in yrs. the FBS and PPBS in mg/dl were 122.03±4.15 and 184.93±11.69 respectively. The mean HbA1c was 6.8±0.08. The mean of systolic BP was 128.04 ± 4.30 mmHg and the mean of diastolic BP was 81.22 ± 2.82mmHg. The mean of duration of diabetes for all the 56 participants was 8.30±4.20 in years. When stratified into different duration the data obtained is depicted in the pie chart (fig no. 1)

Figure 1: Duration of diabetes in years
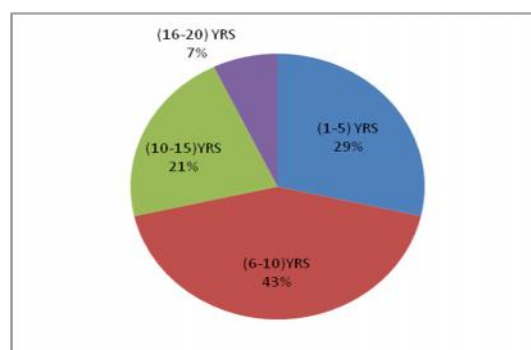
The mean of total MMSE scores was 24.85 ± 2.65. The results of total FAB scores and the scores of individual domains are depicted in the table 2.

Table.2 : Results of FAB (mean ± SD)

S. NO	PARAMETER	MEAN	SD
1.	FAB total	11.84	± 2.47
2.	FAB 1	2.39	± 0.68
3.	FAB 2	1.84	± 0.68
4.	FAB 3	1.95	± 0.67
5.	FAB 4	1.75	± 0.55
6.	FAB 5	1.64	± 0.55
7.	FAB 6	2.27	± 0.67

ANALYSIS

On statistical analysis the total MMSE and FAB scores negatively associated with the duration of diabetes with high levels of significance at $p<0.05$. The r-value for the total scores and the individual domain scores are shown in the table 3.

Table 3: Correlation table of duration of diabetes with MMSE and FAB scores

Pearson's correlation of Duration of Diabetes Vs.								
	MMSE	FAB total	FAB 1	FAB 2	FAB 3	FAB 4	FAB 5	FAB 6
r value	-0.37	-0.59	-0.29	-0.51	-0.37	-0.35	-0.45	-0.33
p value	0.005	0.000*	0.030	0.000*	0.005	0.008	0.000*	0.013
p value calculated at the level of significance p< 0.05*								

Figure 2: Correlation between Duration of DM (yrs) and MMSE

CORRELATION BETWEEN DURATION OF DM(YEARS) AND MMSE

Figure 3: Correlation between duration of DM (yrs) and FAB total
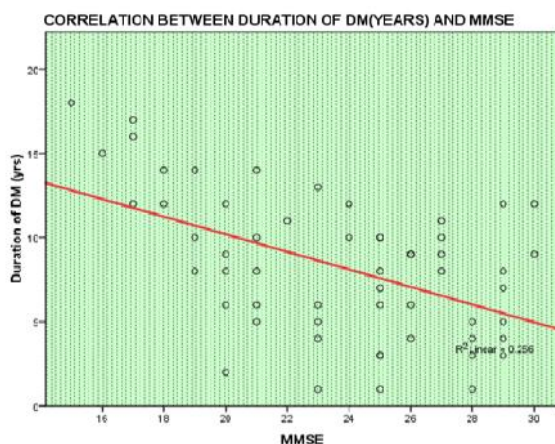

CORRELATION BETWEEN DURATION OF DM(YEARS) AND FAB TOTAL
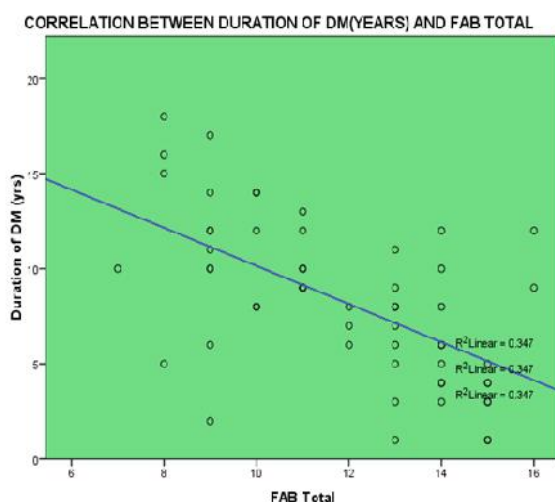
Figure 4: Correlation of duration of DM (yrs) and FAB individuals
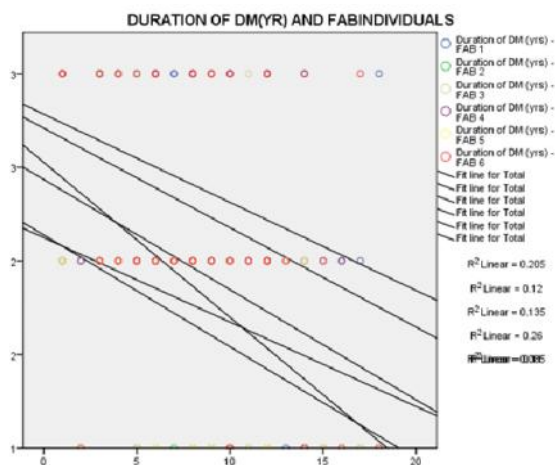

DURATION OF DM(YR) AND FABINDIVIDUALS

Regarding the association of individual domains of FAB, Lexical fluency and Inhibitory control shows a strong negative correlation with duration of diabetes with very high levels of significance.

DISCUSSION

Impairment of executive functions has adverse outcomes on many goal-directed activities like house keeping, cooking, management of finances and medication compliance. Thus an intact executive functioning is required for effective treatment of diseases like Diabetes as the affected individuals need to remain in a complex set of management protocols like insulin injections, oral drugs, lifestyle and dietary modifications.

In a four year follow up study with Digit Symbol Substitution Test (DSST) as a measure of executive function there was a decline in information-processing speed, psychomotor speed and attention domains of cognitive abilities in diabetics when compared to non diabetics.[10]

Following this a community based six year follow up study was done in diabetics to assess the cognitive decline. The tests used were DSST, Delayed Word Recall Test (DWRT) and Word Fluency Test (WFT). And the conclusion was a notable decline in executive functioning particularly in the processing speed and verbal fluency domains.[11]

Recently a large cohort study was done including the participants of Shangai Aging Study (SAS) and Mayo Clinic Study of Aging (MCSA) with a goal to compare the effect of Diabetes Mellitus on Cognitive decline of normal aging in different set of populations. Cognition was assessed in four domains viz. memory, language, executive functions and visuospatial skills. Executive functions were tested using the Trail Making Test B , Go No-go test and Modified Card sorting test. The authors have concluded that there was an early impairment of cognition particularly in the executive function domain in individuals with diabetes when compared with non-diabetes of both the populations regardless of differences in age and vascular burden.[12]

Another cohort study was done with 10963 individuals to determine the role of diabetes and hypertension in age-related cognitive changes. Cognitive testing was done with Delayed Word Recall Test (DWR), Digit Symbol Substitution Test (DSST) and first letter Word Fluency Test (WFT). The subjects were retested till 6 years in 3 years interval. The results showed a significant decline in DSST and WFT in those individuals with diabetes as a risk factor at a very early age when compared to those without diabetes.[13]

The pathophysiology of cognitive dysfunction in Diabetes Mellitus is not clear till date. Various authors emphazise on different mechanisms. Hyperglycemia seen in diabetes patients causes organ damage through activation of polyol pathway, accelerated production of Advanced Glycation End (AGE) products,

increased shunting of glucose in hexosamine pathway and activation of Protein kinase C via Diacylglycerol.[14] these mechanisms can be applied to the neuronal damage also. There is also an emerging view that diabetes per se causes "accelerated Brain aging".[15]

One another proposed hypothesis is that the alternating hyper and hypoglycemia in these diabetic individual can cause alterations in the levels and function of neurotransmitter levels. Animal studies also provide evidence of defects in neuronal plasticity particularly in the hippocampus and impairment in long-term potentiation of neurons rich in N-methyl D-Aspartate (NMDA) receptors. These mechanisms may contribute to learning deficits and consequent cognitive impairment.[16]

As seen in the above discussions diabetes mellitus definitely has a role in decline in executive functioning as part of cognitive decline. The results of this present study also shows a significant relationship of type 2 diabetes mellitus with cognitive decline as evidenced by the MMSE scores. Specifically when the executive functioning is tested as a function of the frontal lobes there was impairment in executive functions as a whole and also the individual domains.

When the individual domains are related with diabetes duration the verbal fluency domain shows a highly significant negative association which is supported by most of the previous studies. The same finding with the inhibitory control domain which is a direct function of frontal lobes suggest that frontal lobe is affected early in the course of disease even before overt dementia sets in.

Strengths of this study is this study is one where the duration of diabetes is correlated with executive functions while most of the researchers have concentrated on association of executive functions with the glycemic control. Most of the previous studies have tested executive functions as a part of other cognitive assessments. The tests used were single individual tests like Trail making test, DSST or WFT. In the present study a battery of tests have been used so that all possible domains of executive functions like concept formation, verbal fluency, motor coorrination, planning , sequencing, inhibitory control are tested.

Limitations of this study is the small sample size. Also the regression analysis of different duration of diabetes has not been done. The gender difference in executive functioning has not been taken into account. The study group consists of subjects in different age group and from varied economic, educational and occupational back ground which will definitely have an impact on the executive functioning.

To conclude there is a definite association between duration of diabetes and impairment in executive functions. As the duration of diabetes increases executive functioning declines even before overt dementia sets in.

so individuals with type 2 diabetes mellitus should be tested for impairment in executive functions as a part of clinical assessment as intact executive functioning is necessary for better treatment adherence and effective management.

Conflict of Interest : Nil.

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