

## A Hospital-Based Assessment of Cognitive Dysfunction in Type 2 DM during Acute Mental Stress without Overt Cerebrovascular Disease

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### Abstract

**Aim:** The objective of the present study was to assess cognitive dysfunction in Type 2 DM during acute mental stress without overt cerebrovascular disease or other vascular risk factors.

**Material & Methods:** The present study was conducted in the Department of Physiology, 200 subjects within the age group of 30–55 years were included in the study. Informed consent was taken by each subject. They were randomly distributed into two groups. Group 1 comprised of randomly chosen 100 diagnosed cases of Type 2 DM at least 2 years of duration. Group 2 comprised of 100 age and gender-matched controls.

**Results:** There was no significant difference in age in cases and controls. The mean age of Type 2 DM group was 48.2 years and the control group was 46.4 years. There was a significant statistical difference between weight and BMI. The result showed a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls. There was significant difference ART and VRT, both simple and choice during resting and during mental stress and these RTs were more prolonged in Type 2 DM when compared to controls.

**Conclusion:** The present study concluded that mental stress in Type 2 DM does affect cognition, where grades of deterioration may be related to the difficulty of the given task (mental stress) and prevalence of central nerve deficits and peripheral nerve deficits seen as side-manifestation of Type 2 DM.

**Keywords:** Cognition; Reaction Time; Mental Stress; Type 2 Diabetes Mellitus

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### Introduction

Diabetes mellitus is a complex metabolic disease which results in complications that are more devastating than the disease. The common and most studied complications of diabetes mellitus include macro vascular complications like cardiovascular and peripheral vascular diseases and micro vascular complications like nephropathy, retinopathy and neuropathy. Cognitive dysfunction is one of the least noted and poorly recognized complication of both type 1 and type 2 diabetes mellitus, though it is gaining its importance in the present days. [1] Over the past several years, evidence that showed impairment in brain insulin and Insulin-like Growth Factor (IGF) signaling, mediates cognitive impairment and neuro-degeneration has developed particularly in relation to mild cognitive impairment and Alzheimer disease(AD). [2]

Both old age and diabetes are independently associated with an increased risk of cognitive dysfunction; the risk is even greater for older adults with diabetes. [3] The most common cognitive deficits identified in patients with type 1 diabetes are slowing of information processing speed and worsening psychomotor efficiency. [4] Type-2 diabetes has been associated with a decrease in psychomotor speed, frontal lobe/executive function [5], complex motor functioning, verbal fluency [6], verbal memory, processing speed [7], working memory [5], immediate recall, delayed recall, visual retention and attention. [1]

Stress testing unveils cognitive dysfunction even before it develops at rest. Mental stress testing is easier to administer and can be precisely regulated

by the evaluator. Although Stroop color-word test, Mensa test stressful interview are different methods of inducing stress used in studies, mental arithmetic using serial subtraction is the most widely used method. [8] RT is a measure of the time taken from the onset of the stimulus to proper response which is an indicator of the rate of processing of sensory modes of stimuli by the central nervous system (CNS) and its accomplishment by the motor response. It is established that an increased difference between simple RT (SRT) and choice RT (CRT) implies cognitive dysfunction. [9] RT measures different domains of cognition such as attention, execution, and psychomotor speed. Investigators have shown that CRTs are delayed in metabolic syndrome. [10]

The aim of the present study was to find whether acute mental stress further deteriorates cognition in Type 2 DM. The hypothesis of the present study is that acute mental stress induces cognitive dysfunction in Type 2 DM. Visual RT (VRT) and auditory RTs (ART) both simple and choice were recorded, therefore cognitive performance during acute mental stress in Type 2 DM and compared with healthy controls without overt cerebrovascular disease or other vascular risk factors.

### Material & Methods

The present study was conducted in the Department of Physiology, Medical College and Hospital, Kolkata, India 200 subjects within the age group of 30–55 years were included in the study. Informed consent was taken by each subject. They were randomly distributed into two groups. Group 1 comprised of randomly chosen 100 diagnosed cases of Type 2 DM at least 2 years of duration. Group 2 comprised of 100 age and gender-matched controls.

MMSE was performed to assess the global cognitive function in these groups. Simple and choice auditory and VRTs were measured at rest and acute mental stress in these groups to assess cognitive function. The reliability of the reaction timer was tested by standard deviation obtained during the pilot study.

### Exclusion Criteria

The following criteria were excluded from the study: Hypertensives, obese, smokers, cerebrovascular disorders, cardiovascular, neuropathy, and chronic renal disorders, deformities of the spine, joints or bones, and chronic lower back spasm or pain.

### Procedure

The research participants were measured for pulse, blood pressure, height and weight, and body mass index was calculated from the collected data. Single investigator with previous expertise in anthropometry measured all the parameters. A portable stadiometer was used to measure the height to the nearest 1 mm. The weight was measured in kilogram.

The ophthalmic evaluation was performed using Snellen and Jaeger's chart. After the brief instructions, at least three trials for each of ART and VRT were given and the individual RT in milliseconds was recorded. An effort was made to get at least three acceptable recordings. Recordings of the ART and VRT were considered reproducible unless the difference between the highest and lowest values did not exceed 50 ms. During the procedure, acute mental stress was induced under time pressure by the arithmetic mental challenge. The subjects were asked to rapidly subtract seven from a three- or four-digit number. Throughout the test, investigators encouraged the subjects to perform as fast as possible.

Auditory SRT – the subject was directed to press the right button as soon as tone beeps.

Auditory CRT – the subject was directed to press the left button when tone beeps and right button when tick beeps. The differential RT was recorded.

VSRT – the subject was directed to press the right button as soon as red-light glows and RT was recorded.

VCRT – the subject was instructed to press the left button when green light glows and the right button when red light glows and differential RT was recorded.

### Statistical Analysis

All analyses were performed on a personal computer with the assistance of SPSS 20 statistical software (2012). Differences in mean values for continuous variables in Type 2 DM and controls were tested with independent t-test. Differences in mean values of RTs during resting and mental stress continuous in Type 2 DM and controls were tested with paired t-test.

### Results

**Table 1: Demographic characters in type 2 diabetes mellitus and controls**

Variables	Diabetes n=100	Controls n=100	P value
Age	48.2±4.6	46.4±5.6	0.122
Weight	68.0±8.4	64.6±9.2	0.130
BMI	22.8±2.8	23.7±2.8	0.414
SBP	122.8±5.4	120.8±6	0.022
DBP	79.1±4.3	78.2±2.2	0.316

There was no significant difference in age in cases and controls. The mean age of Type 2 DM group was 48.2 years and the control group was 46.4 years. There was a significant statistical difference between weight and BMI

**Table 2: Visual (V) and auditory (A) reaction times in type 2 diabetes mellitus and controls at rest**

Variables	Diabetes n=100	Controls n=100	P value
Visual reaction time	424.6±70.6	248.6±48.2	0.000
Auditory reaction time	350.5±85.5	220±40	0.000

**Table 3: Visual (V) and auditory (A) reaction times in type 2 diabetes mellitus and controls during mental stress**

Variables	Diabetes n=100	Controls n=100	P value
Visual reaction time	525.5±102.8	285.5±55.5	0.000
Auditory reaction time	452.8±96.4	294.6±96.4	0.000

Tables 2 and 3 showed a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls. There was significant difference ART and VRT, both simple and choice during resting and during mental stress and these RTs were more prolonged in Type 2 DM when compared to controls.

### Discussion

Individuals with schizophrenia show a substantial impairment in overall cognitive performance, which, on average, is around two standard deviations below that in healthy controls. [11] Moreover, this deficit contributes to poor clinical outcomes such as unemployment and an inability to live independently. [12] While cognitive function in schizophrenia is an area of increasing research interest [13], this has yet to translate into the development of novel treatments for cognitive problems. All currently approved pharmacological treatments for schizophrenia exert their effects via antagonism of the dopamine D2 receptor. [14,15] This mechanism of action is efficacious for symptoms that are thought to be driven by excessive striatal dopamine signalling, such as hallucinations and delusions. However, antipsychotic medications have little impact on cognitive impairments in schizophrenia, perhaps because the latter are related to different pathophysiological processes. [15]

There was no significant difference in age in cases and controls. The mean age of Type 2 DM group was 48.2 years and the control group was 46.4 years. There was a significant statistical difference between weight and BMI. The result showed a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls. There was significant difference ART and VRT, both simple and choice during resting and during mental stress and these RTs were more prolonged in Type 2 DM when compared to controls. It is important to detect cognitive dysfunction in Type 2 DM early and treat. Stress testing unveils cognitive dysfunction even before it develops at rest. There are batteries of tests available to detect cognitive dysfunction affecting different domains. [16,17] Although the most of the

earlier studies examining cognitive function in individuals with Type 2 DM such as the MMSE have focused on global cognitive function or combined measures of several cognitive tests, there is growing evidence in the literature on specific domains of cognitive function and possible distinctive association with Type 2 DM. [18,19] Studies have focused on recognizing specific domains which may contribute to identifying the mechanism by which Type 2 DM impairs cognitive function.

The majority group of researchers has agreed that mental dysfunction due to acute or chronic stress is a highly challenging issue in the present scenario. In general, stress is harmful, afflictive, and hazardous to health. Stress assessing instruments play an important role for health researchers among the doctors and psychologist to examine the deleterious effects of stress. Detecting the stress from the physiological signals and parameters is reliable. However, sometimes it is challenging. The laboratory-based experiments are highly useful to achieve more number of stress samples. Researchers consider relying on laboratory based investigations and experiments for assessing the stress more useful than real-time experiments. Among all, mental stress testing is easier to administer and can be precisely regulated by the investigator. Although Mensa test, Stroop colorword test, and stressful interview are different methods of inducing stress used in studies, mental arithmetic using serial subtraction is the most widely used technique. There are series of tests available to identify cognitive dysfunction affecting different domains. These neuropsychological tests require a lot of time, trained staff, and cooperation of the subjects. VRT is the time between the presentation of visual stimuli and subsequent motor response to stimuli. VRT and ART are considered as a suitable tool for measuring sensory-motor association. RT measures specific domains of cognition such as attention, execution, and psychomotor speed. Investigators have shown that CRTs are delayed in Type 2 DM.

## Conclusion

The present study concluded that mental stress in Type 2 DM does affect cognition, where grades of deterioration may be related to the difficulty of the given task (mental stress) and prevalence of central nerve deficits and peripheral nerve deficits seen as side-manifestation of Type 2 DM. Simple ART, VRTs, the simplest of tasks with the shortest path between the peripheral nervous system and CNS showed less delayed RTs. CVRTs will be more delayed because of the involvement of complicated circuits. The findings of this study suggested that cognition is affected in Type 2 DM patients and mental stress further deteriorates cognition.

## References

1. de la Monte SM. Relationships between diabetes and cognitive impairment. *Endocrinol Metab Clin North Am.* 2014 Mar;43(1):245–67.
2. Munshi M, Grande L, Hayes M, Ayres D, Suhl E, Capelson R, et al. Cognitive dysfunction is associated with poor diabetes control in older adults. *Diabetes Care.* 2006 Aug 1;29(8):1794–9.
3. Ryan CM, Geckle MO, Orchard TJ. Cognitive efficiency declines over time in adults with Type 1 diabetes: Effects of micro- and macrov-ascular complications. *Diabetologia.* 2003;
4. Barrou Z, Lemaire A, Boddaert J, Verny M. [Diabetes mellitus and cognition: is there a link?]. *Psychol Neuropsychiatr Vieil.* 2008 Sep ;6(3):189–98.
5. Gerald M. Reaven M, Larry W. Thompson P, David Nahum B, E. Relationship Between Hyperglycemia and Cognitive Function in Older NIDDM Patients. *Diabetes Care.* 1990 ;13:16–21.
6. Claude Messier. Impact of impaired glucose tolerance and type 2 diabetes on cognitive aging. *Neurobiol Aging .* 2005;26S:S26–30.
7. Kodl CT, Seaquist ER. Cognitive dysfunction and diabetes mellitus. *Endocr Rev.* 2008 Jun; 29(4):494–511.
8. Goi N, Hirai Y, Harada H, Ikari A, Ono T, Kinane N, Hiramatsu M, Nakamura K, Takagi K. Comparison of peroxidase response to mental arithmetic stress in saliva of smokers and non-smokers. *The Journal of Toxicological Sciences.* 2007;32(2):121-7.
9. Chiaravalloti ND, Christodoulou C, Demaree HA, DeLuca J. Differentiating simple versus complex processing speed: Influence on new learning and memory performance. *Journal of Clinical and Experimental Neuropsychology.* 2003 Jun 1;25(4):489-501.
10. Khode V, Ramdurg S, Parakh R, Ruikar K, Anupama D. Chronoscopic reading in whole body reaction times in detecting cognitive dysfunction in metabolic syndrome: a case control study. *Indian J. Med. Sci.* 2012 Sep 1; 66:222-9.
11. Keefe RS, Fox KH, Harvey PD, Cucchiari J, Siu C, Loebel A. Characteristics of the MATRICS Consensus Cognitive Battery in a 29-site antipsychotic schizophrenia clinical trial. *Schizophrenia research.* 2011 Feb 1;125 (2-3):161-8.
12. Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia?. *The American journal of psychiatry.* 1996 Mar.
13. Sabe M, Pillinger T, Kaiser S, Chen C, Taipale H, Tanskanen A, Tiuhonen J, Leucht S, Correll CU, Solmi M. Half a century of research on antipsychotics and schizophrenia: A scientometric study of hotspots, nodes, bursts, and trends. *Neuroscience & Biobehavioral Reviews.* 2022 May 1;136:104608.
14. Seeman P, Lee T. Antipsychotic drugs: direct correlation between clinical potency and presynaptic action on dopamine neurons. *Science.* 1975 Jun 20;188(4194):1217-9.
15. Kaar SJ, Natesan S, Mccutcheon R, Howes OD. Antipsychotics: mechanisms underlying clinical response and side-effects and novel treatment approaches based on pathophysiology. *Neuropharmacology.* 2020 Aug 1;172:107704.
16. Nordlund A, Pålsson L, Holmberg C, Lind K, Wallin A. The Cognitive Assessment Battery (CAB): a rapid test of cognitive domains. *International Psychogeriatrics.* 2011 Sep;23 (7):1144-51.
17. Ciesielska N, Sokołowski R, Mazur E, Podhorecka M, Polak-Szabela A, Kędziora-Kornatowska K. Is the Montreal Cognitive Assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? *Meta-analysis. Psychiatr Pol.* 2016 Oct 31;50(5):1039-52.
18. Lee AK, Rawlings AM, Lee CJ, Gross AL, Huang ES, Sharrett AR, Coresh J, Selvin E. Severe hypoglycaemia, mild cognitive impairment, dementia and brain volumes in older adults with type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) cohort study. *Diabetologia.* 2018 Sep;61:1956-65.
19. Zilliox LA, Chadrasekaran K, Kwan JY, Russell JW. Diabetes and cognitive impairment. *Current diabetes reports.* 2016 Sep;16:1-1.