

Detection of Cognitive Impairment in Type 2 Diabetes Mellitus by Choice Auditory and Visual Reaction Times During Acute Mental Stress: A Case–Control Study

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Abstract

Aim: Detection of cognitive impairment in Type 2 diabetes mellitus by choice auditory and visual reaction times during acute mental stress.

Methods: This prospective observational study was carried out in the Department of Physiology, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar, India for 6 months. 80 subjects within the age group of 33–53 years were included in the study. Informed consent was taken by each subject. They were cleaved into two groups. Group 1 comprised of randomly chosen 40 diagnosed cases of Type 2 DM at least 2 years of duration. Group 2 comprised of 40 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.

Results: The mean age of Type 2 DM group was 45.7 years, and the control group was 43.6 years. There was a significant statistical difference between weight and BMI. Tables 2 and 3 show a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls. These RTs further increased during mental stress in diabetes. Table 4 shows that 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: we can conclude 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

The incidence of type 2 diabetes mellitus (T2DM) is increasing worldwide and has become a significant public health problem[1]. It is associated with mortality and significant morbidity, including neurological disability. Although the effects of diabetes on the peripheral nervous system (PNS) are well established, its effects on higher mental functions (HMF) are often overlooked, due to lack of clear signs and unavailability of standard assessment techniques[2,3]. Even mild form of cognitive dysfunction might hamper everyday activities depending on the work and situation, which requires various cognitive domains such as general intelligence, processing speed, psychomotor efficiency, attention, perception, learning, memory, and executive functions[4]. Several studies have reported a cognitive decline in T2DM[5,6]. However, there is no consensus as to the specific domains of cognition that may be affected by T2DM, and thus, which domains can be recommended for testing. 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[7]. RT measures different domains of cognition such as attention, execution, and psychomotor speed. Investigators have shown that CRTs are delayed in metabolic syndrome[8]. The intention of this study is 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. We recorded visual RT (VRT) and auditory RTs (ART) both simple and choice, 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 and methods

This prospective case control study was carried out in the Department of Physiology, Narayan Medical College and Hospital, Jamuhar, Sasaram, Bihar, India, for the period of 6 months.

Methodology

80 subjects within the age group of 33–53 years were included in the study. Informed consent was taken by each subject. They were divided into two groups.

Groups

Inclusion criteria

- Age above 30 years
- Type 2 Diabetic patients (at least for 2 years)
- Either sex
- Given Informed consent

Exclusion criteria

Patients with

- Hypertension
- Obese
- Smokers
- Cerebrovascular disorders,
- Cardiovascular disorders,
- Neuropathy, and
- Chronic renal disorders,
- Deformities of the spine, joints or bones

Groups

Group 1: comprised of randomly chosen 40 diagnosed cases of Type 2 DM at least 2 years of duration.

Group 2: comprised of 40 age and gender-matched controls.

Methodology

General check-up of pulse, blood pressure, height, weight, food habits were recorded. 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.

Technique

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 21.0 statistical software. 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

As per Table 1, there was no significant difference in age in cases and controls. The mean age of Type 2 DM group was 45.7 years, and the control group was 43.6 years. There was a significant statistical difference between weight and BMI. Tables 2 and 3 show a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls. These RTs further increased during mental stress in diabetes. Table 4 shows that 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.

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

Variables	Diabetes n=40	Controls n=40	t value	P value
Age	45.7±5.3	43.6±4.6	1.172	0.12
Weight	66.5±7.7	61.4±8.4	1.651	0.13
BMI	23.8±2.7	23.2±3.8	0.735	0.42
SBP	123.7±5.1	122.8±4	2.591	0.01
DBP	80.9±4.3	79.8±2.2	1.111	0.34

* $P < 0.05$, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Visual and auditory reaction times in type 2 diabetes mellitus and controls during rest

Variables	Diabetes n=40	Controls n=40	t value	P value
VRTS	420.4±74.2	244.2±46.2	11.138	0.000*
VRTC	452.6±98.2	276.4±49.6	8.864	0.000*
ARTS	347.3±81.5	216±43	7.861	0.000*
ARTC	379.5±104.7	290±60.3	4.155	0.000*

* $P < 0.05$, S: Simple, C: Choice

Table 3: Visual and auditory reaction times in type 2 diabetes mellitus and controls during mental stress

Variables	Diabetes n=40	Controls n=40	t value	P value
VRTSS [†]	524.4±105.8	288.3±55.7	10.904	0.000*
VRTCS [†]	547.6±115.4	317.9±81.3	8.924	0.000*
ARTSS [†]	460.5±96.7	300.1±93.2	6.639	0.000*
ARTCS [†]	498.4±119.2	340.7±55.9	6.658	0.000*

*P<0.05, S: Simple, C: Choice, S[†]: Mental stress

Table 4: Visual and auditory reaction times in type 2 diabetes mellitus and controls during resting and mental stress

Reaction times	Diabetes n=40		Controls n=40	
VRTS	420.4±74.2	-6.556	244.2±46.2	-4.976
VRTSS [†]	524.4±105.8	0.000	288.3±55.7	0.000
VRTC	452.6±98.2	-3.760	276.4±49.6	-3.457
VRTCS [†]	547.8±115.4	0.001	317.9±81.3	0.002
ARTS	347.3±81.5	-7.725	216±43.9	-6.784
ARTSS [†]	460.5±96.7	0.000	300.1±93.2	0.000
ARTC	379.5±104.7	-5.719	290±60.3	-5.629
ARTCS [†]	498.4±119.2	0.000	340.7±55.9	0.000

*P<0.05, S: Simple, C: Choice, S[†]: Mental stress

Discussion

In this case-control study, we observed that there was a significant difference in ART and VRT, both simple and choice in Type 2 DM and controls and these RTs further increased during mental stress in Type 2 DM than in controls. We observed 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 and require skilled individuals to assess. On the other side, RTs can be easily recorded on an outpatient department basis. They can prove sensitive indicators of cognitive function, particularly attention and psychomotor speed. Therefore, the strength of this study was that RTs can be a screening tool for early detection of cognitive dysfunction. Many studies have shown Type 2 DM even affects middle-aged too. In our study, we did involve the younger population. Subjection to various forms of stress is a common daily observation in the living of most individuals now, which can affect

brain function in a positive way or negative way. The cumulative effect of stress is strongly influenced by the duration and type of stressor. In the acute form, stress may be essential in the adaptive mechanism for survival and leads to transient changes within the CNS. In our study, we tried to assess the transient effect on RT in Type 2 DM as a secondary effect of stress on cognition.

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[9,10]. 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[11,12]. 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. There are different stress-inducing techniques which have been used previously such as Stroop color-word test[13], mental arithmetic task[14], public speaking task, isometric handgrip test[15], cold pressor test[16], and computer work[17]. Among all, mental stress testing is easier to administer and can be precisely regulated by the investigator. Although Mensa test, Stroop color-word 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.

Limitations

There are one or two limitations of our study. Although controls were age- and gender-matched, their BMI differed. It is implied that BMI affects cognition[18]. Another limitation of the study was that we did not perform the benchmark test that could identify a cognitive function where we could contrast our observation and assess the sensitivity and specificity of our test. However, these batteries of tests are time-devouring.

Conclusion

From this study, we can conclude 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 suggest that cognition is affected in Type 2 DM patients and mental stress further deteriorates cognition.

Reference

1. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001;414(6865): 782–7.
2. Arvanitakis Z, Wilson RS, Schneider JA, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and progression of rigidity and gait disturbance in older persons. *Neurology* 2004;63(6):996–1001.
3. Ott A, Stolk RP, Hofman A, van Harskamp F, Grobbee DE, Breteler MMB. Association of diabetes mellitus and dementia: the Rotterdam study. *Diabetologia* 1996;39(11):1392–7.
4. Kodl CT, Seaquist ER. Cognitive dysfunction and diabetes mellitus. *Endocr Rev* 2008;29(4):494–511.

5. Richardson JTE. Cognitive function in diabetes mellitus. *Neurosci Biobehav Rev* 1990;14(4):385–8.
6. Biessels GJ, Kappelle AC, Bravenboer B, Erkelens DW, Gispen WH. Cerebral function in diabetes mellitus. *Diabetologia* 1994;37(7):643–50.
7. Chiaravalloti ND, Christodoulou C, Demaree HA, DeLuca J. Differentiating simple versus complex processing speed: Influence on new learning and memory performance. *J Clin Exp Neuropsychol* 2003; 25:489-501.
8. 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; 66:222-9.
9. Nordlund A, Pålsson L, Holmberg C, Lind K, Wallin A. The cognitive assessment battery (CAB): A rapid test of cognitive domains. *Int Psychogeriatr* 2011; 7:1144-51.
10. 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; 50:1039-52.
11. Lee AK, Rawlings AM, Lee CJ, Gross AL, Huang ES, Sharrett AR, *et al.* 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; 9:1956-65.
12. Zilliox LA, Chadrasekaran K, Kwan JY, Russell JW. Diabetes and cognitive impairment. *Curr Diab Rep* 2016; 16:87.
13. Scarpina F, Tagini S. The stroop color and word test. *Front Psychol* 2017; 8:557.
14. Fonkoue IT, Schwartz CE, Wang M, Carter JR. Sympathetic neural reactivity to mental stress differs in black and non- hispanic white adults. *J Appl Physiol (1985)* 2018; 124:201-7.
15. Vijayalakshmi P, Madanmohan T, Bhavanani AB, Patil A, Babu K. Modulation of stress induced by isometric handgrip test in hypertensive patients following yogic relaxation training. *Indian J Physiol Pharmacol* 2004; 48:59-64.
16. Silverthorn DU, Michael J. Cold stress and the cold pressor test. *Adv Physiol Educ* 2013; 37:93-6.
17. Larsman P, Thorn S, Sjøgaard K, Sandsjö L, Sjøgaard G, Kadefors R. Work related perceived stress and muscle activity during standardized computer work among female computer users. *Work* 2009; 32:189-99.
18. Steenbergen L, Colzato LS. Overweight and cognitive performance: High body mass index is associated with impairment in reactive control during task switching. *Front Nutr* 2017; 4:51.