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Cognitive Processes and Functions in Patients with Type 2 Diabetes in Comparison to Pre-diabetic Patients

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ABSTRACT

Background: Type 2 diabetes is an important risk factor for cognitive decline in diabetic patients. The main goal of this study was the assessment of memory, attention and visuospatial ability dysfunctions in patients with type 2 diabetes in comparison to pre-diabetic patients and normal subjects in Endocrine and Metabolism Center of Isfahan City from April 2011 to July 2011.

Methods: The sample comprised of 32 patients with type 2 diabetes, 28 pre-diabetic patients and 30 healthy individuals. Memory, attention and visuospatial ability were assessed by Rey Complex Figure Test (RCFT), Paced Auditory Serial Addition Test (PASAT) and sub tests of Wechsler Adult Intelligence Scale-Revised (WAIS-R).

Results: The pair wise comparisons of cognitive functions among three groups, suggesting a significant difference between diabetic and normal groups in PASAT3″. PASAT2″, RCFT (recall trial) and Symbol coding (P=0.003, P=0.009, P=0.010, and P<0.001, respectively). But there was no difference in copy trial of RCFT and block design between two groups (P=0.170, P=0.490). There was significant difference between pre-diabetic group and normal group in recall trial of RCFT (P=0.020), as well as significant difference between diabetes type 2 and pre-diabetic group in symbol coding (P=0.001).

Conclusion: There were significant differences in cognitive functions in patient with type2 diabetes, pre-diabetic patients and normal individuals. Thus monitoring neuropsychological status besides controlling levels of blood sugar in these patients is important.

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Introduction

Type 2 diabetes is associated with cognitive decline [1,2,3]and is thought an important risk factor of dementia and Alzheimer disease [4,5,6,7]. The risk effect is stronger when diabetes occurs at mid life than in late life [8]. Numerous cross-sectional studies have shown decrements in memory, attention and visuospatial ability performances in patients with type 2 diabetes [9,10,11], and a few recent studies have reported on neuropsychological functioning in the early stage of type 2 diabetes [12]. There is a decrement in cognitive functioning in patients with type 2 diabetes and pre-diabetic patients [13,14,15,16] This decrement in cognitive functioning is associated with brain atrophy [17,18], and was thought to be modulated by insulin [19,20]. The stage of that decrement was not manifested and may be started in pre-diabetic stage.

The present study provides evidence on the relationship between cognitive and neuropsychological functioning with type 2 diabetes and pre-diabetic patients.

Methods

We conducted a cross-sectional study between April and July 2011 in Endocrine and Metabolism Center of

Isfahan City, central Iran. The sample size was 32 for diabetes, 28 for pre-diabetes, and 30 for normal subjects respectively. Diabetic and pre-diabetic patients were selected after the diagnosis made by a specialist according to American Diabetes Association criteria for diagnosis, and also according to their clinical data recorded in their files. Correlation coefficients between the research variable and the demographic variables including age, sex and academic status were controlled by the researcher.

The inclusion criteria were being diabetic or pre-diabetic according to the diagnosis made by a specialist, age range between 35 to 60 years, being educated (from grade 9 and up), having no deficits in visual and auditory abilities and in using the hands, and finally having no depression. The control group was matched with the experimental groups, and was selected from personnel of University of Isfahan, and personnel of some elementary schools. The patients were selected randomly according to the research criteria. The criteria for diagnosis of diabetes according to American Diabetes Association is fasting plasma glucose (FPG) at or above 126 mg/dl(7.0 mmol/l), at 2-h value in an oral tolerance test (OGGT) at or above 200 mg/dL(11.1 mmol/l) and if plasma glucose test greater than 100 mg/dl but less than 126 mg/dl, one may have impaired fasting glucose (IFG). Some people also impaired glucose tolerance (IGT), a condition in which blood glucose levels are higher than normal(140 mg/dl but less than199 mg/dl) 2 hours after the start of an oral glucose tolerance test (GTT), if you have IFG and or IGT, one may be diagnosed with pre-diabetes [21].

Written consent was given from each patient, and they were interviewed by the researcher for not being clinically depressed. Then all of the three groups were assessed by neuropsychological tests. Other clinical and demographic data was obtained from each patient's files.

Statistical Analysis

Shapiro - Wilk and Kolmogorov Smirnov were used to tests of normality for data, and in some data the Kruskal-Wallis test was used instead of parametric statistical tests. In addition, Leavene's test was used to test the equality of variances. There was equality of variances for the results of Rey Complex Figure Test (RCFT) (recall trial) test, symbol coding and block design; however, there was not equality of variances for Paced Auditory Serial Addition Test (PASAT), and RCFT(copy trial) test, therefore in addition to ANCOVA, the non parametric tests was also done for the data.

Since the authors have used analysis of covariance for the data, first of all the correlations between cognitive functions and demographic variables were calculated, and then those variables with significant effects were controlled; and finally the analysis of covariance was used in order to find possible differences between cognitive functions in three groups.

Neuropsychological assessment

1. Tests of Block Design and Symbol Coding from the Wechsler Adult Intelligence Scales-Revised test battery [22]. Test –retest reliability of the test, 0.90 is reported [23].
2. Rey Complex Figure Test. This test is composed of copy trials, immediate and delayed recall, as well as recognition [24].The validity of this test was 0.50 and test-retest reliability of this test is about 0/90 has been reported [25].
3. Paced Auditory Serial Addition Test. This test is a serial addition task used to assess capacity and rate attention and sustained and divided attention [26]. The reliability of this test was 0.90. The reliability of the test was calculated by the authors of this article. The calculated Cronbach's alpha was 0.74.

The neuropsychological assessment consisted of 6 verbal and non-verbal tasks, administered in fixed order that took about 30 min for each patient. The tasks were divided into 3 cognitive domains. The domain of memory performance was assessed by symbol coding of Wechsler Adult Intelligence Revised [22], and Rey Complex Figure Test. This test composed of a copy trial and an immediate and a delayed recall trial, as well as recognition test. Attention was assessed by Paced Auditory Serial Addition Test, and symbol coding of Wechsler Adult Intelligence Revised and visuospatial ability was assessed by block design of Wechsler Adult Intelligence Revised, and copy trial of Rey Complex Figure Test.

Results

According to Table 1 there was a significant difference among three groups, after controlling the variables of age, sex and academic status (P<0.001). Eta square shows that 19% of the difference in cognitive functions can be due to the difference among three groups.

Table 1: Results of multivariate analysis of variance in patient with type 2 diabetes, pre-diabetes and control group

Statistical index	Wilkslambda	F	*P* value	PartialEta Squared	Observed Power
Age	0.87	1.88	0.093	0.12	0.66
Gender	0.77	3.91	0.002	0.22	0.95
Education	0.60	8.45	0.001	0.39	1.00
Group	0.65	3.11	0.001	0.19	0.99

According to Table 2 the difference in cognitive functions among three groups were statistically significant for PASAT3″ (P=0.012), PASAT2″ (P=0.033), RCFT (recall trial) (P=0.022), and symbol coding (P=0.001) respectively, but not for RCFT (copy trial) (P=0.401) and block designing (P=0.028).

Table 3 shows the pair wise comparisons of cognitive functions among three groups, suggesting a significant difference between diabetic and normal groups in PASAT3″. PASAT2″, RCFT (recall trial) and Symbol cod-

ing (*P*= 0.003, *P*=0.009, *P*=0.010, and *P*=0.001, respectively). But there was no difference in copy trial of RCFT and block design between two groups (*P*=0.179 and *P*=0.491 respectively). There was significant difference between pre-diabetic group and normal group in recall trial of RCFT (*P*=0.026), as well as significant difference between diabetes type 2 and pre-diabetic group in symbol coding (*P*=0.001).

As seen in Figure 1, the mean-adjusted indicated that the scores of control group in memory (Rey Complex Figure Test and Symbol Coding), attention (Paced Auditory Serial Addition Test) and visuospatial abilities (block design and Rey Complex Figure Test) are significantly more and higher than both diabetic and pre-diabetic patients.

Table 2: Results of multivariate analysis of covariate in patient with type 2 diabetes, pre-diabetes and control group

Variable	Sum of square	df	*P* value	Partial Eta squared	Observed power
PASAT3″	705.78	2	0.012	0.10	0.77
PASAT2″	399.62	2	0.033	0.07	0.64
RCFT(copy trial)	8.42	2	0.401	0.02	0.20
RCFT(recall trial)	192.06	2	0.022	0.08	0.70
Symbol coding	1865.52	2	0.001	0.24	0.99
Block design	76.19	2	0.279	0.03	0.27

Table3: Results of pairwise comparisons in patients with type 2 diabetes, pre-diabetes and normal group

Dependent variable	Groups	Subgroups	Mean	Std. error	*P* value
PASAT3″	Type 2 diabetes	Pre-diabetic	-4.01	2.26	0.073
		Normal	-7.13	2.35	0.003
	Pre-diabetes	Normal	-3.01	2.34	0.201
PASAT2″	Type 2 diabetes	Pre-diabetic	-2.30	1.95	0.241
		Normal	-5.40	2.03	0.009
	Pre-diabetes	Normal	-3.09	2.02	0.129
RCFT(copy trial)	Type 2 diabetes	Pre-diabetic	-0.03	0.55	0.575
		Normal	-0.78	0.57	0.179
	Pre-diabetes	Normal	-0.47	0.57	0.417
RCFT(recall trial)	Type 2 diabetes	Pre-diabetic	-0.52	1.27	0.683
		Normal	-3.05	1.32	0.010
	Pre-diabetes	Normal	-2.98	1.32	0.026
Symbol coding	Type 2 diabetes	Pre-diabetic	-7.39	2.16	0.001
		Normal	-11.44	2.24	0.0001
	Pre-diabetes	Normal	-4.04	2.22	0.074
Block design	Type 2 diabetes	Pre-diabetic	-2.27	1.14	0.112
		Normal	-1.02	1.46	0.491
	Pre-diabetes	Normal	1.25	1.46	0.392

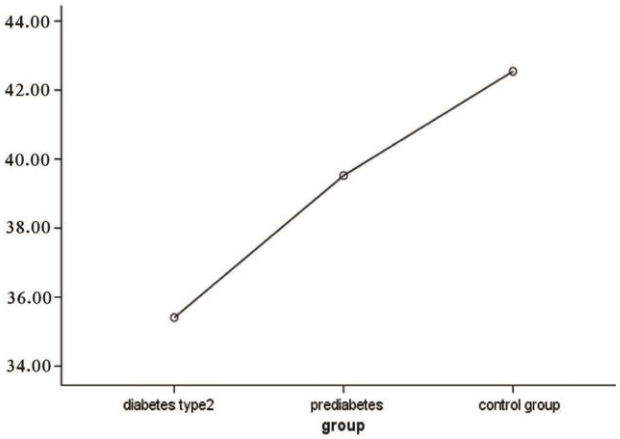
Discussion

There was a significant difference among normal, diabetic and pre-diabetic groups in Andre Rey figure test. This finding is concordant with the reports of Arvantakis et al. [27] and Brundel et al. [17]. Ruis et al. [28] in their study reported that there was a significant difference between diabetics and control groups in their cognitive functions, which was similar to the results of this study. Also the findings of this study is concordant with those of Yeung et al. [29] and Berg et al. [9], suggesting that type 2 diabetics show a decrement in the speed of their cognitive abilities. Cooray et al. [11]reported that there was a significant difference in word fluency and visuospatial ability in the baseline of diabetic patients; however, after start of therapy and controlling the glycemic of the patients this difference was disappeared. This finding is also similar to the results of present research.

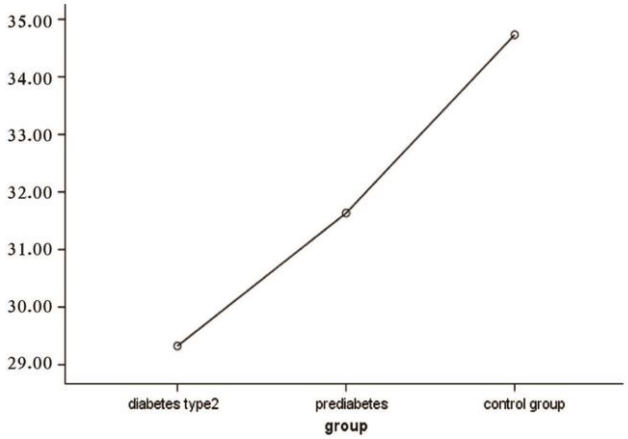
One of the important findings of this study was that both diabetic and pre-diabetic patients shown a significant difference in memory function, in comparison to normal group; however, there was no difference among them in the speed of cognitive processing. The similarity between our results, and those of Ruis et al. [28], again emphasizes on the cognitive deficits which is evident, even in per-diabetic period of illness. As some recent researches have shown there is a possibility of a relationship between Alzheimer disease and diabetes [2], and even between pre-diabetics and Alzheimer as well [5],[28]. Baker et al. [7] reported that there might be a relationship between insulin resistance and deterioration of an Alzheimer type. All of these studies shown that the possible link between cognitive deterioration and diabetes might be serious, and future researches should open a new way in our understanding of the possible related factors.

The prominent innovative of this study was that, it was carried out on a sample of pre diabetic patients for the first time. The second importance of this study was

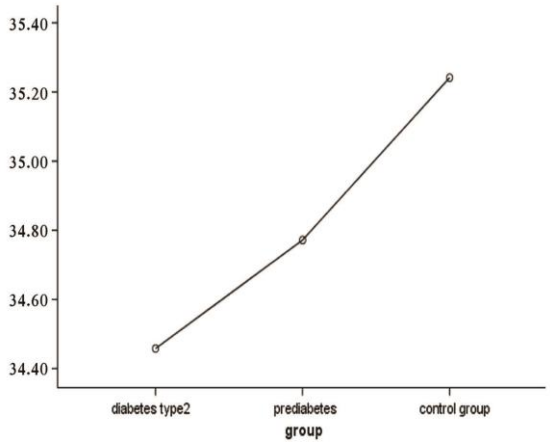
that for the first time the Iranian norm for some research tools was calculated and applied by the authors. Several limitation of the present study should be considered. First our study did not analyze the effects of duration of diabetes type 2 and pre-diabetes. The second limitation of this study was that the level of literacy of the patients was supposed to be more than second year of secondary school, however, the literacy of some patients were lower than that.



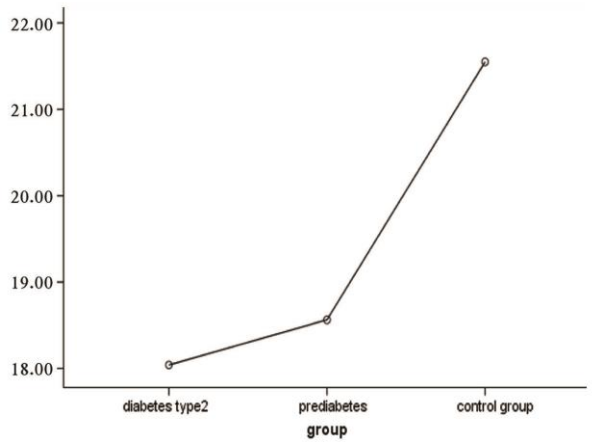
A: Estimated marginal means of PASAT 3



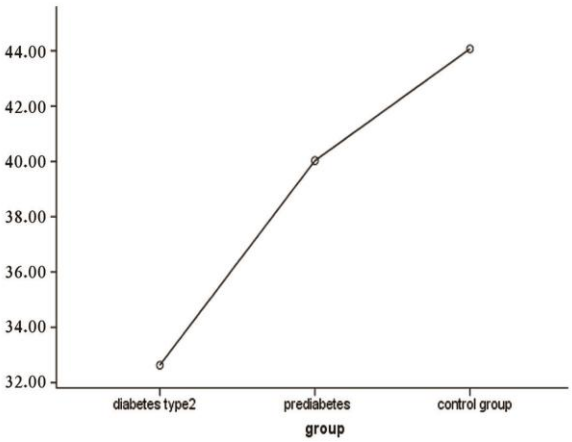
B: Estimated marginal means of PASAT 2



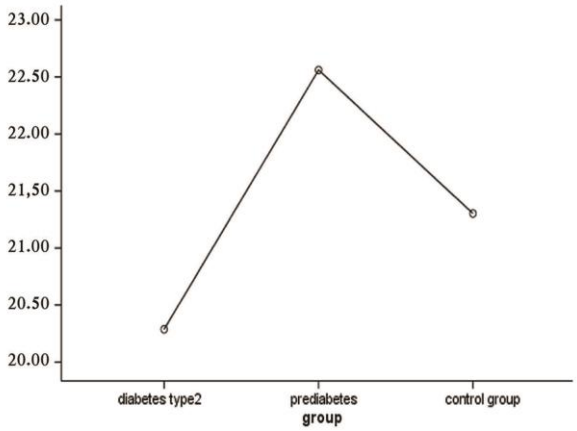
C: Estimated marginal means of RCFT copy



D: Estimated marginal means of RCFT recall



E: Estimated marginal means of symbol coding



F: Estimated marginal means of block design

Figure 1: Estimate marginal of neuropsychological functioning (PASAT: Paced Auditory Serial Addition Test; RCFT: Rey Complex Figure Test)

Conclusion

These findings suggest that diabetic and pre- diabetic patients experience decline in cognitive functioning. Thus monitoring neuropsychological status besides controlling levels of blood sugar in these patients is important.

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Conflict of interest statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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References

1. Allen KV, Frier BM, Strachan MWJ. The relationship between type 2 diabetes and cognitive dysfunction: longitudinal studies and cognitive dysfunction studies and their methodological limitations. *Eur J Pharmacol.* 2004;490:169-175.
2. Eldern SGC, Roos A, Westendrop RGJ, Blauw GJ, Jukema JW, Bollen ELEM, et al. Progression of brain atrophy and cognitive decline in diabetes of mellitus: a 3 years follow-up. *Neurology*. 2010;75:997-1002.
3. Hazari MAH, Reddy BR, Uzma N, Kumar BS. Cognitive impairment in type 2 diabetes mellitus. *Int J Diabetes Mellit*. 2011; In press.
4. Akomolafe A, Baiser A, Meigs JB, Roda Au, Green CR, Farrer AL, et al. Diabetes mellitus and risk of developing Alzheimer disease. *Arch Neural.* 2006;631:1551-1555.
5. Xu W, Qui C, Winbland B, Fratigioni L. The effect of borderline diabetes on the risk of dementia and Alzheimer disease. *Diabetes.* 2007:56;211-216.
6. Rasgon NL, Kenna HA, Wroolie TE, Kelley R, Silverman D, Brooks J, et al. Insulin resistance and hippocampal volume in women at risk for Alzheimer disease. *Neurobiol Aging*. 2011;32:1942-1948.
7. Baker LD, Cross DJ, Minoshima S, Belongia D, Watson GS, Craft S. Insulin resistance and Alzheimer-like reduction cerebral glucose metabolism for cognitively normal adults with pre-diabetes or early type diabetes. *Arch Neurol*. 2011;68(1):51-57
8. Xu W, Qui C, Gatz M, Pedersen NL, Johansson B, Faratilglioni L. Mid-and late-life diabetes in relation to risk of dementia. *Diabetes*. 2009:58,71-77.
9. Berg EVD, Reijimer D, Bresser JD, Kesseles RPC, Kapplle LJ, Biessels GJ. A four year follow up study of cognitive functioning in patient with type 2 diabetes mellitus. *Diabetologia*. 2010;53:58-65.
10. Awad N, Gangnon M, Messier C. The relationship between impaired glucose tolerance, type 2 diabetes, and cognitive function. *J Cline Neuropsychological.* 2004;26:1044-1080.
11. Cooray G, Nilsson E, Wahlin A, Laukka EJ, Brismar K, Brismar K, et al. Effects of intensified metabolic control on CNS function in type 2 diabetes. *Psychoneuroendocrinology*, 2011;36(1):77-86.
12. Razay G, Vreughdehil A, Wilcok G. The metabolic syndrome and Alzheimer disease. *Arch Neurol*. 2007;64:93-96.
13. Biessels Gj, Kerssen A, De Haan E, Kappelle LJ. Cognitive dysfunction and diabetes: Implication for primary care. *Prim Care Diabetes*. 2007;1:187-193.
14. Berg EVD, Kloppendborg RP, Kessels RPC, Kappelle LJ, Biessels GJ. Type 2 diabetes mellitus, hypertention, dyslipidemia and obesity: A systematic comparison of their impact on cognition. *Biochimica et Biophsica Acta*. 2009;1792:470-481.
15. Roriz FJS, Roriz MS, Rosset I, Camozzato AL, Santos AC, Chaves MLF, et al. Pre diabetes, brain aging and cognition. *Biochimica et Biophysica Acta*. 2009;1792:432-443.
16. Marchasson IB, Laper E, Laksir H, Puget E. Insulin resistance, diabetes and cognitive function: consequences for preventative strategies. *Diabetes and Metab*. 2010;36:173-187.
17. Brundel M, Heuvel MVD,Bresser JD, Kapplle LJ, Biessels GJ. Cerebral cortical thickness in patients with type 2 diabetes. *J Neurol Silenc*. 2010;299(1-2):126-130.
18. Rasgon NL, Kenna HA, Wroolie TE, Kelley R, Silverman D, Brooks J, et al. Insulin resistance and hippocampal volume in women at risk for Alzheimer disease. *Neurobiol Aging*. 2011;32:1942-1948.
19. Plastino M, Fava A, Pirritano D, Cotronei P, Sacco N, Sperli T, et al. Effects of insulin therapy on cognitive impairment in patient with Alzheimer disease and diabetes mellitus type 2. *J Neurol Sci*. 2010:288,112-116.
20. McNay EC, Ong CT, Maccrimon RJ, Cresswell J, Bogan JS. Hippocampal memory processes are modulated by insulin and high-fat-induced insulin resistance. *Neurobiology of Learning and Memory*.2010:93:546-553.
21. American Diabetes Association. *Complete guide to diabetes:The ultimate home reference from the diabetes experts*. 4th ed. Virginia: American Diabetes Association; 2005.
22. Marnat GG.*Handbook of psychological assessment*. 4thed. New Jersey: John Willy & sons; 2003.
23. Abedi MR, Omidi A, Rezayat A. A preliminary study of validity and reliability of the revised Wechsler Adult. Iranian norm [MSc thesis]. Tehran: Iran University of Medical Sciences, 1995.
24. Munshi M, Grande L, Ayres D, Suhi E, Caplson R, Lin S, et al. Cognitive dysfunction is associated with poor diabetes control in older adult. *Diabetes Care*. 2006:29,1794-1799.
25. Nazeri MM. Standardization of Andre Rey Figure Test [MSC Thesis]. Tehran: Islamic Azad University of Rodehen; 2004.
26. Otfried S, Esther S. *Compendium of neuropsychological tests, a: administration, norms, and commentary*. 2nd ed. Auckland: Oxford University Press; 1998.
27. Arvantakis Z, Willson RS, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and risk of Alzheimer disease and decline in cognition function. *Arch Neurol*. 2004;61:661-666.

28. Ruis C, Donk MVD, Biessels GJ, Kapplle LJ, Gortter KJ, RuttenGEHM. Cognition in the early stage of type 2 diabetes. *Diabetes Care*. 2009:32,1261-1265.

29. Yeung SE, Fisher AL, Dixon R. Exploring effects of type 2 diabetes on cognition functioning in older adults. *Neuropsychol*. 2009;23:1-9.