N-back task in patients with dementia and depression, compared to patients with only depression: cardiovascular pathology without and with diabetes mellitus

Valentin Bragin [1], Gary Shereshevsky [2], Ilya Bragin [1,3], Elina Slobod [1], Tanya Silenko [1], Gulnara Zaynullina [1], Elina Shkolnik [1].

1. Stress Relief and Memory Training Center, Brooklyn, NY, USA
2. Staten Island University Hospital, Department of Rehabilitation Medicine, Staten Island, NY, USA
3. Saint Luke University Health Network, Bethlehem, PA, USA
Contact email: val11235@gmail.com
www.alzheimers-treatment-today.com

Introduction

It is well known that diabetes mellitus (DM) and cardiovascular pathology are risk factors for development and progression of Alzheimer Dementia (AD) (1, 2). Both diseases affect arteries in the brain, diminish cerebral blood flow, and lead to local cerebral hypoxia, negatively impacting energy metabolism in dementia. In clinical practice most of patients with AD have cardiovascular pathology alone or in combination with diabetes. (3,4)

In our previous study we showed no difference in cognitive performance in patients with dementia, depression, and cardiac disease with DM vs. no DM (5). Since then, to our knowledge, there are no studies that assessed the impact of DM on chronometric performance in dementia and depression patients accompanied by cardiovascular pathology.

This presentation is a continuation of ongoing study with two goals: First is to replicate our previous findings on a larger cohort of patients. Secondly, investigate the impact of DM through more challenging N-back task on cognitive performance in patients with cardiovascular pathology in dementia and depression and additionally in depression without dementia.

Methods

Data were collected from the charts of 472 patients (155 males, 317 females), mean age 77.1 ± 5.98 , education 13.6 ± 3.07 yrs, all with cardiovascular pathology with or without DM, who underwent cognitive testing during their initial visits to the clinic. The number of patients in this presentation is different from the presented abstract due to accumulation of data from new patients. Patients were divided into 2 groups: group 1 - patients with dementia and depression (N=364) and group 2 - patients with depression alone (N=108). Patients in each group were further divided into subgroups of patients with no DM and with DM. In Group 1, 30% of patients had DM and in Group 2, 24% had DM.

The cognitive battery included the MMSE (6), the clock drawing task (CDT), the verbal fluency category (VFC) and letters (VFL) tasks, computerized simple (SRT), complex (CRT- go/no go) reaction time tasks and the N-2 back task with non-verbal stimuli (textures) as targets. Statistical analysis was performed with SPSS v21(7). Wilcoxon signed-rank test was utilized on all variables to compare two subgroups of patients (with and without diabetes).

Results

All patients had depression and memory problems. The length of depression and memory loss was 38.5 ± 23.1 and 36.9 ± 27.1 months, respectively. A significant number of patients had hypertension (83.69 %), high cholesterol (73.52%), CAD (62.5 %), diabetes (29.03%), stroke (10.59%), history of head trauma (19.07%), thyroid disorders (16.10%), anemia (15.04%), history of cancer (11.87%), and COPD (9.96%).

Neuroimaging studies (non contrast MRI) were done for 47.6% of the cohort. Abnormal neuroimaging was found in 100% of this group and consisted of cortical atrophy, lacunar infarcts, ventricular dilation, and white matter microvascular changes alone or in combination with each other.

Significant difference in cognitive performance was seen between patients in Group 1 (Depression and Dementia) and Group 2 (Depression alone) on MMSE (mean MMSE (26±3.4 and 28±1.6, accordingly), p < 0.001), CDT (p=0.02), VFC (p < 0.001) and VFL (p < 0.001). Inside each group, there were no differences between patients with DM and no DM.

There was no significant difference between Group 1 and Group 2 on SRT, CRT and N-back task (performance, reaction time and errors) (Table 1). Inside each group, there were no differences between patients with DM and no DM on SRT and CRT. However, the more challenging WM N-back task with textures as the targets demonstrated a significant difference in processing speed: DM (1202.09), no DM (1030.78), p=0.037.

Table 1. Simple Reaction Time, Complex Reaction Time, and N-back Task

| | Group 1 | | | | Group 2 | | | |
| | Dementia and Depression | | | | Depression | | | |
	N	No DM	N	DM	P-Value	N	No DM	N	DM	P-Value
SRT Performance	253	55.7±7.00	111	56.0±5.40	0.92	82	56.5±7.15	26	57.7±3.12	0.34
SRT Mean (ms)	253	370.7±113.60	111	349.1±94.75	0.24	82	319.2±91.25	26	357.8±119.80	0.07
SRT error	253	3.2±7.25	111	3.1±5.49	0.43	82	2.8±7.26	26	1.3±3.70	0.20
CRT Performance	253	52.1±11.70	111	54.9±8.45	0.86	82	55.7±6.78	26	54.9±8.45	0.71
CRT Mean (ms)	253	488.1±86.22	111	473.8±85.46	0.10	82	467.2±72.08	26	473.8±85.46	0.80
CRT error	253	3.8±5.33	111	3.9±6.58	0.75	82	3.8±5.33	26	3.9±6.58	0.99
N-back Performance	220	6.1±2.77	93	5.9±2.84	0.36	65	6.5±2.26	22	6.0±2.91	0.24
N-back Mean (ms)	220	1239.0±426.30	93	1203.7±629.06	0.07	65	1030.9±224.87	22	1202.1±352.70	**0.04**
N-back Error Total	220	9.7±4.81	93	10.3±5.31	0.44	65	8.9±3.39	22	9.1±3.69	0.75

Abbreviations

SRT – Simple Reaction Time
CRT – Complex Reaction Time – Go/No-Go Task
DM – Diabetes Mellitus

Discussion

Recent attention in neurodegenerative disease and aging has been focused on mental chronometry, in particular investigating decreased speed during different motor tasks (gait, balance, hand movements etc.) (8).The effects of cardiovascular illness and diabetes on development and progression of AD are still actively investigated. (9).

We confirm our previous findings of absent difference in cognitive performance between DM and no DM in mildly demented and depressed individuals. We did not find any differences in the isolated depression group either.

On the N back task we found differences between diabetics and non diabetics only in the depression group. Mean RT was slower in the DM only in the depression group (p= 0.04). This task is likely more informative to demonstrate a difference in processing speed between DM/No DM as it is requires a greater cognitive load.

Interestingly, mildly demented patients with DM have a slower rate of cognitive decline relative to no DM patients (10). We posit that diabetics with dementia may develop more metabolic changes predisposing to higher ketone body utilization by the brain.

In the dementia and depression (group 1), lack of difference in N-back task processing speed in DM and No DM subgroups could possibly be explained by the difference in ketone body utilization, which becomes a valuable source of energy in mild AD (11, 12).

In the depression (group 2), the difference in N-back task processing speed between DM and no DM subgroups could suggest that glucose is still a vital energy source for the brain. Decreased processing speed during N-back task could be a result of compromised glucose metabolism in DM.

We propose that using different energy substrates in dementia with depression vs. depression alone could be helpful for developing dietary recommendations in the future.

Conclusion

For patients with depression, non-verbal N-back task was able to detect differences in processing speed between DM and no DM subgroups.

For patients with dementia and depression, no differences in performance between DM and no DM subgroups were found.

Future research can further explore practical applications of N-back task in patients with dementia and depression, including cognitive remediation.

Acknowledgments

References

1. Kuller, LH, Lopez OL. Cardiovascular disease and dementia risk: an ever growing problem in an aging population, *Expert Review of Cardiovascular Therapy* 2016;14; (7), DOI: 10.1080/14779072.2016.1185366

2. Vagelatos NT, Eslick GD. Type 2 diabetes as a risk factor for Alzheimer's disease: the confounders, interactions, and neuropathology associated with this relationship. *Epidemiol Rev.* 2013;35:152-60. doi: 10.1093/epirev/mxs012.

3. Halter JB, Musi N, McFarland Horne F, et al. Diabetes and Cardiovascular Disease in Older Adults: Current Status and Future Directions. *Diabetes.* 2014;63(8):2578-2589 doi:10.2337/db14-0020.

4. Bangen KJ, Gu Y, Gross AL, et al. Relation of Type 2 Diabetes With Cognitive Change in a Multiethnic Elderly Cohort. *Journal of the American Geriatrics Society.* 2015;63(6):1075-1083. doi:10.1111/jgs.13441.

5. Bragin V, Shereshevsky G, Bragin, et al. Cognitive performance of demented, depressed patients with cardiovascular pathology - without and with diabetes mellitus: a preliminary report of a cross-sectional study. Poster presented at: the Alzheimer's Association International Conference; July 2013; Boston, MA.

6. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 1975; 12, 189-198.

7. SPSS Base 21 Applications Guide, Chicago: SPSS Inc., 2012.

8.Duering M, Gesierich B, Seiler S, et al. Strategic white matter tracts for processing speed deficits in age-related small vessel disease. *Neurology.* 2014;82(22):1946-1950. doi:10.1212/WNL.0000000000000475.) .

9. Paciaroni M, Bogousslavsky J. Connecting Cardiovascular Disease and Dementia: Further Evidence. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease.* 2013;2(6):e000656. doi:10.1161/JAHA.113.000656..)

10. Sanz C, Andrieu S, Sinclair A, Hanaire H, Vellas B. Diabetes is associated with a slower rate of cognitive decline in Alzheimer disease. *Neurology.* 2009 Oct 27;73(17):1359-66. doi: 10.1212/WNL.0b013e3181bd80e9.

11. Castellano CA, Nugent S, Paquet N, et al. Lower brain 18F-fluorodeoxyglucose uptake but normal 11C-acetoacetate metabolism in mild Alzheimer's disease dementia. J. Alzheimers Dis. 2015 43, 1343–1353.

12. Henderson ST, Vogel JL, Barr LJ, et al. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. Nutr Metab (Lond). 2009; 6:31.

Key words : Alzheimer's disease, dementia, depression, diabetes, cardiovascular disease, cognitive testing, MMSE clock drawing, processing speed, reaction time, N-back task