O2-09-04 TRAJECTORIES IN GLYCEMIC CONTROL OVER TIME ARE ASSOCIATED WITH COGNITIVE PERFORMANCE IN ELDERLY SUBJECTS WITH TYPE 2 DIABETES

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Project Description: Type 2 Diabetes (T2D) has consistently been demonstrated to be a risk factor for cognitive decline and dementia. However, within T2D, the relationships of long-term glycemic control with cognitive decline are yet unknown. The aim of the present study was to assess the relationship of long-term trajectories of glycemic control with cognitive performance in cognitively normal elderly with T2D. Subjects (n=835) pertain to a diabetes registry (DR) established in 1998 with an average of 18 HbA1c measurements per subject, permitting identification of distinctive trajectory groups of HbA1c and examining their association with cognitive function in five domains: episodic memory, semantic categorization, attention/working memory, executive function, and overall cognition. Analyses of covariance compared cognitive function among the trajectory groups adjusting for age, gender, education, race, and family history of diabetes.

Table 2
Neuropathological findings stratified by glucose exposures

| Glucose Exposure | Average glucose (<100 mg/dL) | Average glucose (100-110 mg/dL) | Average glucose (>110 mg/dL) |
|------------------|-----------------------------|--------------------------------|-----------------------------|
| N                | N%                          | N%                              | N%                          |
| Neuritic plaques | 43                          | 42%                            | 50                          |
| Neurofibrillary tangles | 24                          | 24%                            | 28                          |
| Amyloid angiopathy | 28                          | 28%                            | 27                          |
| Cerebral microinfarcts | ≥3 vs 0-2                  | 12%                            | 13%                          |
|                  | ≥2 vs 0-1                   | 25%                            | 29%                          |
|                  | Any vs. none                | 42%                            | 49%                          |
| Cystic infarcts  | 30                          | 30%                            | 26%                          |
| Atherosclerosis  | 59                          | 60%                            | 61%                          |
| Lewy bodies      | 5                           | 5%                             | 5%                           |
| Frontal or temporal cortex | 13                          | 13%                            | 12%                          |
| Substantia nigra or locus ceruleus | 14                          | 15%                            | 12%                          |
| Amygdala        | 7                           | 7%                             | 5%                           |
| Hippocampal sclerosis | 0                           | 0%                             | 0%                           |

*Neuritic plaques were characterized as intermediate or frequent vs. none or sparse. Neurofibrillary tangles were characterized as Braak and Braak stage VI vs. stage 0-IV. Amyloid angiopathy was characterized as any vs. none. Cystic infarcts were characterized as any vs. none. Atherosclerosis was characterized as moderate or severe vs. none or mild. Lewy bodies were characterized as present vs. absent in each of the regions specified. Hippocampal sclerosis was characterized as present vs. absent.

Amyloid angiopathy data were missing for 1 person with average glucose <100 mg/dL (1%), for 1 person with average glucose 100-110 mg/dL (1%), and for 1 person with average glucose >110 mg/dL (1%).

Cerebral microinfarcts were missing for 2 people with average glucose <100 mg/dL (2%), for 1 person with average glucose 100-110 mg/dL (1%), and for 1 person with average glucose > 110 mg/dL.

Cystic infarct data were missing for 3 people with average glucose <100 mg/dL (3%), for 1 person with average glucose 100-110 mg/dL (1%), and for 4 people with average glucose >110 mg/dL (4%).

Atherosclerosis data were missing for 5 people with average glucose <100 mg/dL (5%), for 4 people with average glucose 100-110 mg/dL (4%), and for 5 people with average glucose >110 mg/dL (5%).

Frontal or temporal cortex Lewy body data were missing for 0 people with average glucose <100 mg/dL, for 1 person with average glucose 100-110 mg/dL (1%), and for 1 person with average glucose >110 mg/dL (1%).

Substantia nigra or locus ceruleus Lewy body data were missing for 0 people with average glucose <100 mg/dL or 100-110 mg/dL, and for 1 person (1%) with average glucose >110 mg/dL.

Amygdala Lewy body data were missing for 9 people with average glucose <100 mg/dL (9%), for 8 people with average glucose 100-110 mg/dL (8%), and for 5 people with average glucose >110 mg/dL (5%).

Hippocampal sclerosis data were missing for 4 people with average glucose <100 mg/dL (3%), for 4 people with average glucose 100-110 mg/dL (4%), and for 2 people with average glucose >110 mg/dL (2%).
Table 1

| Variable                           | Higher Stable*Stable* | Lower Increasing | Higher Stable*Stable* | Lower Decreasing | Higher Stable*Stable* | Lower Decreasing | Higher Stable*Stable* | Lower Decreasing | Total | P value |
|------------------------------------|-----------------------|------------------|-----------------------|------------------|-----------------------|------------------|-----------------------|------------------|-------|---------|
| Years in Diabetes Registry         | 8.35 (2.58)           | 8.35 (2.81)      | 9.36 (2.32)           | 8.88 (2.57)      | 10.13 (1.7)           | 10.95 (0.56)     | 8.70 (2.64)           | <0.0001         |       |         |
| Hba1c at entry into Diabetes Registry | 5.96 (0.67)           | 6.84 (0.94)      | 7.26 (0.84)           | 7.76 (0.95)      | 9.19 (1.4)            | 10.73 (0.97)     | 6.95 (1.32)           | <0.0001         |       |         |
| Mean Hba1c During Follow-Up        | 6.01 (0.28)           | 6.70 (0.23)      | 7.45 (0.23)           | 8.35 (0.34)      | 7.61 (0.36)           | 9.22 (0.45)      | 6.82 (0.77)           | <0.0001         |       |         |
| Current age                        | 72.99 (4.75)          | 72.91 (4.66)     | 72.52 (4.46)          | 70.78 (4.16)     | 73.63 (4.35)          | 72.75 (4.63)     | 70.92 (4.56)          | 0.0027          |       |         |
| Education (years)                  | 13.43 (3.47)          | 13.21 (3.71)     | 13.12 (3.18)          | 12.59 (2.8)      | 12.75 (2.71)          | 12.00 (2.80)     | 13.17 (3.45)          | 0.3857          |       |         |
| HDL                                | 48.39 (11.24)         | 48.06 (10.68)    | 47.93 (11.58)         | 43.97 (8.35)     | 46.75 (8.44)          | 44.98 (11.8)     | 47.76 (10.82)         | 0.1427          |       |         |
| Total cholesterol                  | 179.65 (24.69)        | 182.69 (25.96)   | 180.14 (23.61)        | 182.28 (28.45)   | 172.31 (18.34)        | 167.58 (27.52)   | 180.46 (25.12)        | 0.0184          |       |         |
| Systolic BP                        | 133.4 (8.86)          | 134.88 (9.11)    | 135.45 (9.42)         | 137.70 (9.98)    | 135.38 (12.04)        | 133.99 (8.01)    | 134.74 (9.39)         | 0.0659          |       |         |
| Diastolic BP                       | 76.85 (4.74)          | 77.40 (4.81)     | 76.90 (4.52)          | 77.52 (4.66)     | 75.15 (5.84)          | 76.18 (5.54)     | 77.00 (4.85)          | 0.0319          |       |         |
| GFR                                 | 80.38 (23.87)         | 81.71 (27.13)    | 79.33 (25.98)         | 83.31 (32.5)     | 77.82 (25.73)         | 91.43 (24.42)    | 80.99 (26.29)         | 0.4852          |       |         |
| GDS                                 | 1.00 [0-9]            | 1.00 [0-11]      | 2.00 [0-9]            | 2.00 [0-10]      | 1.00 [0-14]           | 1.00 [0-9]       | 1.00 [0-14]           | 0.3249          |       |         |
| Diabetes medication group          |                       |                  |                       |                  |                       |                  |                       |                  |       |         |
| Oral anti diabetic                 | 164 (72%)             | 324 (89%)        | 103 (84%)             | 25 (54%)         | 45 (76%)              | 2 (13%)          | 663 (79%)             | <0.0001         |       |         |
| Insulin Only                       | 3 (1%)                | 2 (1%)           | 2 (2%)                | 1 (2%)           | 1 (2%)                | 0 (0%)           | 9 (1%)                | <0.0001         |       |         |
| Insulin+oral anti diabetic         | 3 (1%)                | 6 (2%)           | 17 (14%)              | 20 (43%)         | 13 (22%)              | 12 (80%)         | 71 (9%)               | <0.0001         |       |         |
| None                               | 57 (25%)              | 33 (9%)          | 1 (1%)                | 0 (0%)           | 0 (0%)                | 1 (7%)           | 92 (11%)              | <0.0001         |       |         |

p = 0.016 for GM. These associations remained significant even after excluding 28 incident dementia cases (β(SE): 0.0019 (<0.001); p = 0.003 for TBT and 0.0014 (<0.001); p = 0.010 for GM). RBC folate levels had no longitudinal relationship with cerebral volumes. These results indicate that higher plasma concentrations of vitamin B12 are associated with decreased rate of brain volume loss. Randomized controlled trials are needed to determine the impact of vitamin B12 supplementation on preventing cognitive decline in older adults.