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Association Between Diabetes and Domain-Specific Cognitive Performance in Community-Dwelling Older Adults: A Cross-Sectional Study of the Northern Japanese ORANGE Registry

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Abstract

Background/Objective: Diabetes is associated with cognitive dysfunction in older adults; however, the strength of this association may differ across cognitive domains. This study examined the association between diabetes and multiple cognitive domains in community-dwelling older adults. **Methods**: This cross-sectional study included 1025 community-dwelling adults aged ≥65 years from the ORANGE Registry. Diabetes status was determined based on the participants' self-reported history of diabetes diagnosis. Cognitive performance was assessed using the National Center for Geriatrics and Gerontology Functional Assessment Tool, which measures memory, attention, executive function, and processing speed. Multiple linear regression analyses were used to examine the association between diabetes and each cognitive domain after adjusting for potential confounders. **Results**: Of the 1025 participants, 226 had diabetes and 799 did not. In the unadjusted analyses, participants with diabetes showed poorer performance across all four cognitive domains. After multivariable adjustment, diabetes remained significantly associated with lower attention ($B = -0.157$, 95% CI: −0.299 to −0.016, $p = 0.030$), executive function ($B = -0.190$, 95% CI: −0.329 to −0.052, $p = 0.007$), and processing speed ($B = -0.485$, 95% CI: −0.616 to −0.354, $p < 0.001$). In contrast, the association with memory was attenuated after multivariable adjustment and did not reach statistical significance ($B = -0.132$, 95% CI: −0.271 to 0.008, $p = 0.064$), although a negative association could not be excluded. Additional analyses showed that the negative association between diabetes and processing speed was significantly greater than those for the other three cognitive domains (all $p < 0.001$). After correction for multiple testing using the Holm method, the associations with executive function and processing speed remained statistically significant, whereas the association with attention did not. **Conclusions**: In community-dwelling older adults, self-reported diabetes was associated with poorer executive function and processing speed after multivariable adjustment and correction for multiple testing. The association with processing speed was significantly greater than the corresponding associations with the other three cognitive test outcomes examined. These findings suggest the potential value of multidomain cognitive assessments in older adults with diabetes, although their clinical utility requires further research.

Keywords: diabetes mellitus; cognitive function; processing speed; executive function; older adults; community-dwelling

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Academic Editor: Chrysi Koliaki

Received: 28 September 2026
Revised: 16 November 2026
Accepted: 18 November 2026
Published: 20 November 2026

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1. Introduction

Diabetes mellitus is a common chronic condition among older adults and an important risk factor for cognitive impairment and dementia [1–3]. Cognitive impairment is of particular concern in older adults with diabetes because diabetes management requires complex self-care behaviors, including glucose monitoring, medication management, dietary decision-making, and recognition and management of hypoglycemia [4–6]. Declines in cognitive function may interfere with these activities and compromise the safety and effectiveness of diabetes self-management. Therefore, a more detailed understanding of the relationship between diabetes and cognitive function in older adults is clinically important.

This issue is particularly relevant in Japan, where population aging is advanced. In Akita Prefecture, which has the highest proportion of older adults in Japan, 40.9% of the population was aged 65 years or older in 2026, and households consisting of older adults living alone accounted for 21.7% of all households [7]. In such regions, maintaining cognitive health and supporting independent living among older adults are important public health issues. Therefore, in regions characterized by population aging and a high proportion of older adults living alone, a more detailed understanding of the association between diabetes and cognitive function is important from both clinical and public health perspectives.

Previous research has examined these associations across cognitive domains. Studies that included middle-aged adults have linked type 2 diabetes mellitus (T2DM) to poorer performance across several cognitive domains [8–11]. However, evidence on how the strength of these associations varies across cognitive domains in later life remains limited. For community-dwelling adults aged 65 years or older, analyzing continuous domain scores on a common scale can help determine whether the strength of the adjusted association with diabetes varies across domains.

When examining domain-specific associations, memory, attention, executive function, and processing speed are important cognitive domains relevant to diabetes self-management [12]. The validated National Center for Geriatrics and Gerontology Functional Assessment Tool (NCGG-FAT) assesses all four domains in a single battery [13] and has been used to characterize cognitive performance in older adults in the ORANGE Registry [14].

Accordingly, we examined the associations between self-reported diabetes and performance in these four domains among community-dwelling adults aged 65 years or older in Akita Prefecture. We then explored whether the magnitude of the associations with diabetes differed across the four cognitive domains relevant to diabetes self-management, without a prespecified hypothesis about which domain would show the strongest association.

2. Materials and Methods

2.1. Study Design and Participants

This cross-sectional analysis used baseline data collected between 2018 and 2025 from the Organized Registration for the Assessment of dementia on Nation-wide General consortium toward Effective treatment in Japan (ORANGE Registry), a community-based study of older residents in Akita Prefecture, Japan. Participants were recruited through municipal public announcements inviting residents to undergo community-based cognitive function assessments. Participation was voluntary, and cognitive assessments were conducted for individuals who wished to participate. The community-based assessments included cognitive function testing, physical measurements (height and weight), and questionnaires regarding participants' health status. Eligible participants in the present study were community-dwelling adults aged 65 years or older. For participants who underwent repeated assessments, only data from the first assessment were included. A complete-case analysis was performed, including only participants with complete data on diabetes status, cognitive outcomes, and all covariates required for the fully adjusted model. This approach

was adopted to ensure a consistent analytic sample across all regression models. The research protocol was reviewed and approved by the Certified Clinical Research Review Board, Akita University (Approval No. 2001) and the Research Ethics Review Committee of Akita Prefectural Cerebrospinal and Cardiovascular Center (Approval No. 25-14). All participants provided written informed consent before participating in this study.

2.2. Diabetes and Cognitive Assessments

Diabetes status was determined based on participants' self-reports. Participants were asked, "Have you ever been diagnosed with diabetes?" Those who answered "yes" were classified as having diabetes, whereas those who answered "no" were classified as not having diabetes.

Multidimensional cognitive performance was assessed using the National Center for Geriatrics and Gerontology Functional Assessment Tool (NCGG-FAT), a tablet-based instrument developed and validated for community-dwelling older adults [13]. The NCGG-FAT was administered with assistance from trained examiners, as described previously [14].

Memory was evaluated using a word recognition task, attention using the Trail Making Test Part A, executive function using the Trail Making Test Part B, and processing speed using the Symbol Digit Substitution Task (SDST). The word recognition task consisted of immediate recognition and delayed recognition, and the combined score (range: 0–20) was used as the memory outcome. The Trail Making Test Parts A and B were scored based on completion time in seconds, with shorter times indicating better performance. The Symbol Digit Substitution Task was scored as the number of correct responses within 90 s, with higher scores indicating better performance.

NCGG-FAT-defined cognitive impairment was defined as performance more than 1.5 standard deviations below the age- and education-adjusted reference values in at least one cognitive domain. This operational definition was consistent with that used in a previous study of the ORANGE Registry [15]. This classification was based on cognitive test performance rather than a comprehensive clinical diagnosis of MCI. Assessment of independence in daily living and clinical exclusion criteria for dementia were not incorporated into this cognitive impairment classification. The scores from each subtest were analyzed as separate cognitive outcomes for each participant.

2.3. Covariates and Statistical Analysis

Hypertension and dyslipidemia were determined based on participant self-report. Age, sex, educational attainment, body mass index, hypertension, and dyslipidemia were selected as covariates based on previous evidence identifying demographic and vascular or metabolic factors associated with cognitive impairment and dementia [16,17].

Continuous variables are presented as mean ± standard deviation and categorical variables as numbers and percentages. Participant characteristics were compared between those with and without diabetes using the Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. Effect sizes were calculated as absolute values of r ($|Z|/\sqrt{N}$) for continuous variables and Cramér's V for categorical variables.

Raw scores for each cognitive domain were standardized to z-scores using the mean and standard deviation of the analytic sample. For attention and executive function, the signs of the z-scores were reversed so that higher z-scores consistently indicated better cognitive performance across all domains.

Separate multiple linear regression analyses were performed for each cognitive domain, with the standardized score for the cognitive domain as the dependent variable and diabetes status as the primary explanatory variable. Model 1 included only diabetes status. Model 2 was adjusted for age and sex. Model 3 was additionally adjusted for body mass

index, hypertension, dyslipidemia, and educational attainment. Model fit was evaluated using the coefficient of determination (R^2) and adjusted R^2. Associations are presented as unstandardized regression coefficients (B) with 95% confidence intervals (CIs). Because the dependent variables were standardized, B represents the difference in cognitive performance in standard-deviation units associated with diabetes status.

For the fully adjusted models, residual normality was assessed using histograms and normal P–P plots, and homoscedasticity was assessed using scatterplots of standardized residuals against standardized predicted values. Multicollinearity and influential observations were assessed using variance inflation factors and Cook's distance, respectively. Sensitivity analyses using heteroscedasticity-robust standard errors were conducted for attention and executive function because diagnostic plots suggested possible heteroscedasticity. An additional sensitivity analysis excluded one observation with an extreme standardized residual in the executive function model; this observation was retained in the primary analysis.

All statistical analyses were performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided, and statistical significance was set at $p < 0.05$. To formally compare the associations between diabetes and different cognitive domains, we calculated the differences in standardized cognitive scores between processing speed and each of the other three domains (memory, attention, and executive function) for each participant. Multiple linear regression analyses were then performed using these differences as dependent variables, with adjustment for age, sex, body mass index, hypertension, dyslipidemia, and educational attainment. This approach accounted for within-participant correlations between cognitive outcomes. The Holm method was applied to account for multiple comparisons across the three pairwise tests.

The analyses across the four cognitive domains were considered exploratory. To assess the potential influence of multiple testing, the Holm correction was applied to the four cognitive outcomes in the fully adjusted model as a sensitivity analysis.

3. Results

3.1. Participant Characteristics

Initially, 2932 assessment records were available. Some participants underwent repeated assessments, and only the first assessment was retained for each participant. After excluding 1714 repeated assessment records, 1218 unique participants remained. Of these, 79 participants were excluded due to missing diabetes status, 21 due to missing cognitive outcome data, and 93 due to missing covariate data. Finally, 1025 unique participants were included in the analyses. All the regression models were based on the same 1025 participants. The participant selection process is shown in Figure 1. Of these, 226 had diabetes, and 799 did not. The baseline characteristics according to diabetes status are shown in Table 1. Age and years of education did not differ significantly between the groups. The proportion of women was lower in the diabetes group than in the non-diabetes group (54.0% vs. 68.3%, $p < 0.001$). Participants with diabetes had a higher body mass index and a higher prevalence of hypertension and dyslipidemia than those without diabetes (all $p < 0.001$). NCGG-FAT-defined cognitive impairment was more prevalent in the diabetes group (34.1% vs. 23.0%, $p < 0.001$).

For participants who underwent repeated assessments, only the first assessment was retained. Participants with missing information on diabetes status, cognitive outcomes, or covariates required for the fully adjusted model were excluded from the final analyses.

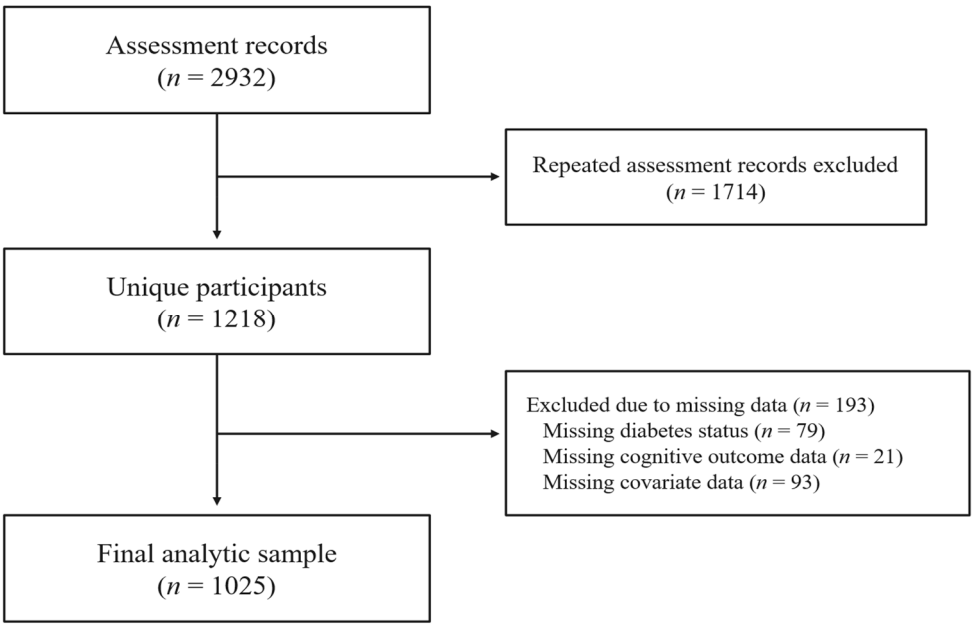


Figure 1. Flowchart of participant selection.

Table 1. Baseline characteristics according to diabetes status.

Variable	Non-Diabetes (n = 799)	Diabetes (n = 226)	p Value	Effect Size
Age, years; mean (SD)	76.5 ± 5.9	76.6 ± 6.5	0.927	0.003
Sex, female; n (%)	546 (68.3)	122 (54.0)	<0.001	0.125
Education, years; mean (SD)	12.1 ± 2.2	11.8 ± 2.3	0.151	0.045
BMI, kg/m^2; mean (SD)	23.5 ± 3.4	24.7 ± 3.6	<0.001	0.124
Hypertension; n (%)	384 (48.1)	167 (73.9)	<0.001	0.215
Dyslipidemia; n (%)	237 (29.7)	121 (53.5)	<0.001	0.208
NCGG-FAT-defined cognitive impairment, n (%)	184 (23.0)	77 (34.1)	<0.001	0.105

BMI, body mass index; NCGG-FAT, National Center for Geriatrics and Gerontology Functional Assessment Tool. Continuous variables are expressed as mean ± standard deviation. p-values were calculated using the Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. Effect sizes are presented as absolute values of r ($|Z|/\sqrt{N}$) for continuous variables and Cramér's V for categorical variables.

3.2. Cognitive Performance According to Diabetes Status

Figure 2 shows the distribution of cognitive domain scores according to diabetes status. Participants with diabetes had significantly lower scores than those without diabetes across all four cognitive domains: memory ($p < 0.01$), attention ($p < 0.05$), executive function ($p < 0.01$), and processing speed ($p < 0.0001$).

3.3. Multivariable Associations Between Diabetes and Cognitive Performance

The associations between diabetes and cognitive domain scores in multiple linear regression analyses are shown in Table 2. In Model 1, diabetes was significantly associated with lower scores in all four cognitive domains. These associations remained significant after adjusting for age and sex in Model 2. In the fully adjusted Model 3, diabetes remained significantly associated with lower attention (B = −0.157, 95% CI: −0.299 to −0.016, $p = 0.030$), executive function (B = −0.190, 95% CI: −0.329 to −0.052, $p = 0.007$), and processing speed (B = −0.485, 95% CI: −0.616 to −0.354, $p < 0.001$). The association with memory was atten-

uated after multivariable adjustment and did not reach statistical significance (B = −0.132, 95% CI: −0.271 to 0.008, $p = 0.064$). In the fully adjusted models, R^2 values ranged from 0.150 for memory to 0.293 for processing speed, with adjusted R^2 values ranging from 0.145 to 0.289 (Table 2). The fully adjusted regression coefficients and 95% CIs are shown in Figure 3. Processing speed showed the largest negative regression coefficient among the four cognitive domains. Additional analyses comparing the regression coefficients across cognitive domains showed that the negative association between diabetes and processing speed was significantly greater than those for memory (B = −0.353, 95% CI: −0.512 to −0.194), attention (B = −0.327, 95% CI: −0.478 to −0.177), and executive function (B = −0.294, 95% CI: −0.445 to −0.143) (all $p < 0.001$). All three comparisons remained statistically significant after correction for multiple comparisons using the Holm method. In a sensitivity analysis applying the Holm correction for multiple testing across the four cognitive domains, the associations with processing speed (adjusted $p < 0.004$) and executive function (adjusted $p = 0.021$) remained statistically significant. However, the association with attention was no longer statistically significant after correction (adjusted $p = 0.060$). The association with memory also remained non-significant (adjusted $p = 0.064$).

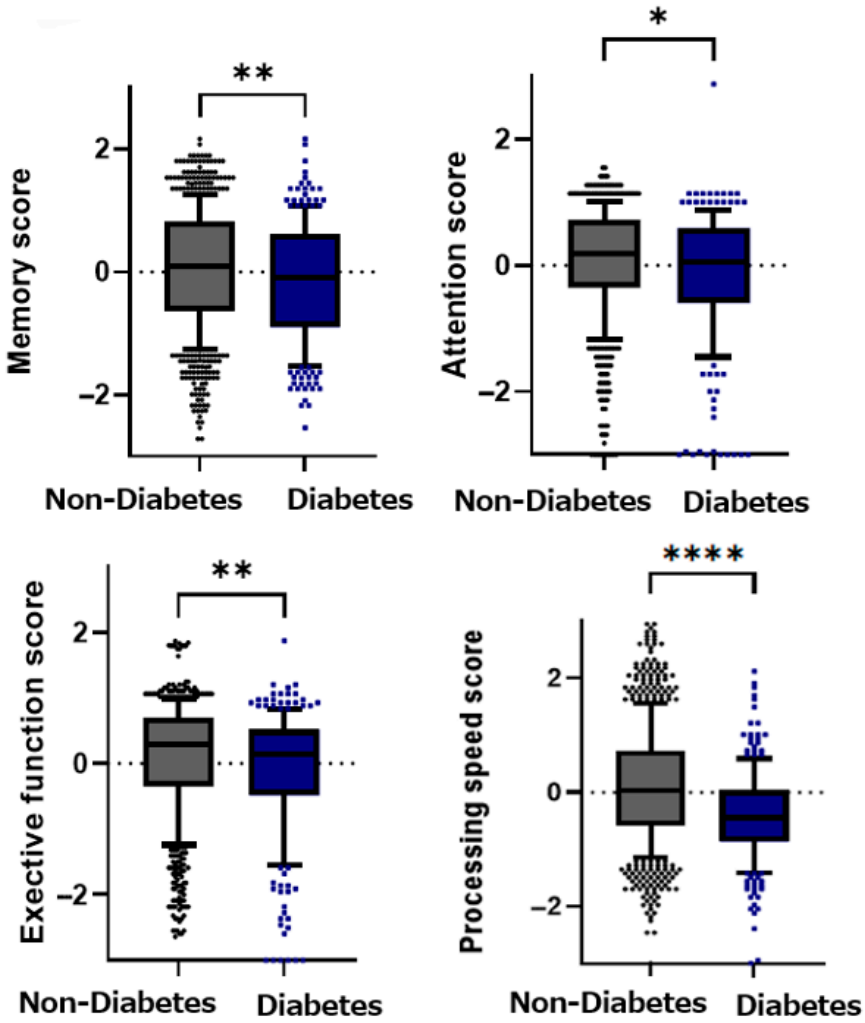


Figure 2. Comparison of cognitive domain scores according to diabetes status. The panels show memory, attention, executive function, and processing speed. Cognitive domain scores were presented as standardized *z*-scores, with higher scores indicating better cognitive performance in all domains. Box plots display the median and interquartile range, with individual observations represented by points. Statistical significance was assessed using the Mann–Whitney U-test. * $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$.

Table 2. Associations between diabetes and cognitive domain scores in multiple linear regression analyses.

Cognitive Domain	Model	B (95% CI)	*p* Value	R^2	Adjusted R^2
Memory	Model 1	−0.190 (−0.333 to −0.047)	0.009	0.007	0.006
	Model 2	−0.170 (−0.304 to −0.036)	0.013	0.137	0.134
	Model 3	−0.132 (−0.271 to 0.008)	0.064	0.150	0.145
Attention	Model 1	−0.224 (−0.372 to −0.077)	0.003	0.009	0.008
	Model 2	−0.197 (−0.333 to −0.061)	0.005	0.169	0.167
	Model 3	−0.157 (−0.299 to −0.016)	0.030	0.183	0.179
Executive function	Model 1	−0.242 (−0.389 to −0.094)	0.001	0.010	0.009
	Model 2	−0.227 (−0.361 to −0.092)	<0.001	0.193	0.191
	Model 3	−0.190 (−0.329 to −0.052)	0.007	0.220	0.216
Processing speed	Model 1	−0.508 (−0.652 to −0.364)	<0.001	0.045	0.044
	Model 2	−0.515 (−0.642 to −0.388)	<0.001	0.270	0.268
	Model 3	−0.485 (−0.616 to −0.354)	<0.001	0.293	0.289

Values are unstandardized regression coefficients (B) with 95% confidence intervals (CIs). Cognitive outcomes were standardized to *z*-scores, with higher scores indicating better cognitive performance. Model 1: Unadjusted. Model 2: Adjusted for age and sex. Model 3: Adjusted for age, sex, body mass index, hypertension, dyslipidemia, and educational attainment. R^2, coefficient of determination; adjusted R^2, adjusted coefficient of determination.

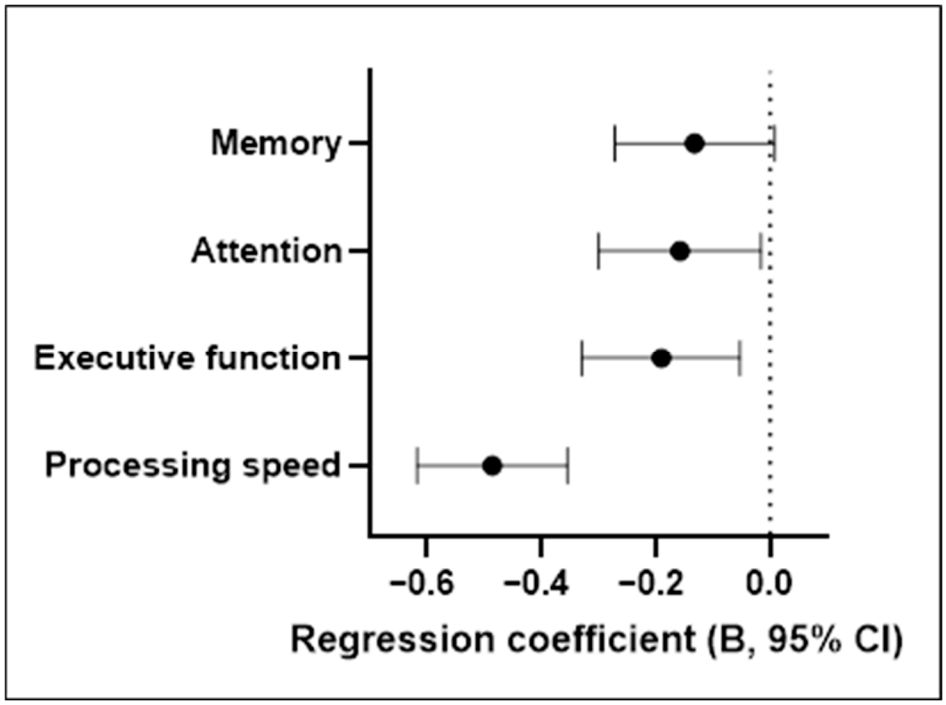


Figure 3. Multivariable-adjusted associations between diabetes and cognitive performance across domains. Forest plot showing unstandardized regression coefficients (B) and 95% confidence intervals for the fully adjusted model. The model was adjusted for age, sex, body mass index, hypertension, dyslipidemia, and education level. Negative B values indicate lower cognitive domain scores in participants with diabetes mellitus.

Regression diagnostics showed that VIFs ranged from 1.067 to 1.157 across the fully adjusted models, indicating no evidence of problematic multicollinearity. Visual inspection

of diagnostic plots did not reveal substantial departures from residual normality or homoscedasticity in the memory and processing speed models, whereas possible deviations were observed in the attention and executive function models. In sensitivity analyses using heteroscedasticity-robust standard errors, the association between diabetes and executive function remained statistically significant (B = −0.190, 95% CI: −0.362 to −0.019, $p = 0.030$). For attention, the coefficient remained unchanged, but the association was no longer statistically significant (B = −0.157, 95% CI: −0.320 to 0.006, $p = 0.058$). After excluding one observation with an extreme standardized residual, the association between diabetes and executive function was attenuated but remained statistically significant ($n = 1024$; B = −0.137, 95% CI: −0.263 to −0.011, $p = 0.033$). All 1025 participants were retained in the primary analyses.

4. Discussion

In this study, we examined the association between self-reported diabetes and multiple cognitive domains in community-dwelling older adults. In the unadjusted analyses, self-reported diabetes was associated with poorer performance across all four cognitive domains. After adjusting for demographic and vascular risk factors, the associations with attention, executive function, and processing speed remained statistically significant, whereas the association with memory was attenuated and did not reach statistical significance. However, the negative regression coefficient and its confidence interval do not exclude the possibility of a negative association between self-reported diabetes and memory performance. After correction for multiple testing, only the associations with executive function and processing speed remained statistically significant, whereas the association with attention was no longer significant. In addition, the association with attention was not statistically significant in the sensitivity analysis using heteroscedasticity-robust standard errors and should therefore be interpreted with caution. In the sensitivity analysis excluding one observation with an extreme standardized residual, the association between diabetes and executive function was attenuated, although it remained statistically significant. This suggests that the estimated magnitude of the association with executive function may be somewhat sensitive to individual observations. Among the cognitive domains examined, processing speed had the largest negative regression coefficient. Furthermore, additional analyses demonstrated that the negative association between self-reported diabetes and processing speed was significantly greater than those observed for memory, attention, and executive function. These findings suggest that the association between diabetes and cognitive performance may differ across cognitive domains, with a particularly pronounced association observed for processing speed. However, these differences were based on standardized scores from specific cognitive tests, and the extent to which they reflect differences in the underlying cognitive functions should be interpreted with caution.

Previous studies have reported impairments across multiple cognitive domains in individuals with T2DM, including memory, attention, executive function, and processing speed, with relatively pronounced deficits in processing speed and executive function, as reported in meta-analyses and longitudinal studies [8–11]. A recent synthesis of systematic reviews reported reductions in processing speed and executive function while highlighting heterogeneity across cognitive domains and studies [2]. A systematic review and meta-analysis of midlife T2DM found that longitudinal studies often reported poorer executive function in later life, whereas findings for later-life memory were inconsistent [18].

The stronger association with processing speed observed in our study is consistent with previous reports of relatively greater deficits in this domain [8–11]. Because diabetes type could not be determined in our study, comparisons with previous studies of T2DM should be interpreted with caution.

White matter abnormalities are one possible explanation for the association with processing speed. Imaging studies have linked T2DM to altered white matter microstructure [19,20] and white matter hyperintensities [21]. Alterations in white matter microstructure have been associated with slower processing speed in community-based samples [22,23]. In adults with T2DM, alterations in white matter microstructure or network organization have also been associated with slower processing speed [19,24]. However, because neuroimaging data were not available in the present study, we could not directly examine white matter abnormalities or determine whether they contributed to the observed association. Therefore, this proposed mechanism remains hypothetical and requires further investigation.

The association between diabetes and poorer processing speed observed in the present study may have clinical relevance for the management of diabetes. Diabetes self-management requires individuals to recognize and process information regarding blood glucose levels and symptoms and select appropriate responses according to the situation. Previous studies have reported that cognitive deficits, including reduced information-processing speed, are associated with difficulties in diabetes self-management, including medication adherence, diet, exercise, appropriate use of health care, and glycemic management [4–6,25,26].

Impairments in executive function have also been linked to difficulties in diabetes self-management [5,6,25,27]. Considering these findings, the associations of diabetes with processing speed and executive function observed in the present study may also be relevant from the perspective of diabetes self-management.

These findings may have implications for the cognitive assessment of older adults with diabetes. The current American Diabetes Association guidelines emphasize the importance of assessing cognitive impairment and self-management capacity in older adults with diabetes and recommend screening for mild cognitive impairment or dementia in adults aged ≥65 years [28]. Our findings raise the possibility that assessing individual cognitive domains, including processing speed, in addition to global cognitive function, may provide additional information about cognitive performance in older adults with diabetes. However, diabetes self-management outcomes were not directly assessed in this study, and the implications of the observed cognitive differences for diabetes self-management remain uncertain. Furthermore, whether domain-specific cognitive assessments improve clinical outcomes requires further investigation.

This study had several strengths. It included a relatively large sample of community-dwelling older adults and assessed multiple cognitive domains using the same multidimensional cognitive assessment system. In addition, each cognitive domain was examined separately after adjusting for several potential confounding factors. Furthermore, the multidimensional cognitive assessment system used in this study has demonstrated test–retest reliability and validity in community-dwelling older adults [13].

This study has several limitations. First, because of the cross-sectional design, the temporal or causal relationship between diabetes and cognitive function could not be determined. Second, diabetes status was determined solely by participant self-report and was not verified using medical records, medication records, or laboratory data. Therefore, potential misclassification of diabetes status cannot be excluded. Furthermore, detailed information regarding glycemic control, diabetes duration, diabetes type, glucose-lowering medications, and history of severe hypoglycemia was unavailable, preventing us from assessing the potential influence of these factors on cognitive performance. Third, several factors, including cerebrovascular disease, cardiovascular disease, depression, physical activity, and smoking history, have been reported to be associated with cognitive function [8,17]. However, these potential confounding factors were not included in the analyses because

of limited data availability or restrictions in variable definitions. In particular, information on the history of cerebrovascular disease, including stroke, was not available for analysis, and the questionnaire item regarding heart disease did not allow cardiovascular disease to be clearly identified. Therefore, residual confounding due to these unmeasured or inadequately assessed factors cannot be excluded. Furthermore, body mass index, hypertension, and dyslipidemia may act not only as potential confounding factors but also as mediators, depending on the underlying causal relationships. Therefore, adjustment for these variables may have resulted in overadjustment. In addition, because multiple cognitive outcomes were examined, the possibility of chance findings due to multiple testing should be considered, particularly for the association with attention, which did not remain statistically significant after correction. Another limitation is that, although the Trail Making Test Parts A and B were used to assess attention and executive function, respectively, these tests involve overlapping cognitive processes, including visual scanning and processing speed. Therefore, differences in the regression coefficients across cognitive domains should not be interpreted as definitive evidence of differences in the associations between diabetes and the underlying cognitive functions. Furthermore, the use of complete-case analysis may have introduced selection bias, particularly if participants with missing data differed systematically from those included in the analyses. Because baseline information was incomplete for many excluded participants, a comprehensive comparison of their characteristics with those of included participants was not feasible.

Finally, participants were recruited from a single region in Japan, which may limit the generalizability of the findings to other populations. In addition, voluntary participation in community-based cognitive assessments may have introduced selection bias, as older adults with relatively preserved mobility and greater motivation to participate may have been more likely to attend the assessments. Consequently, individuals with substantial mobility limitations or more severe cognitive impairment may have been underrepresented.

5. Conclusions

In community-dwelling older adults, self-reported diabetes was associated with poorer processing speed and executive function after multivariable adjustment and correction for multiple testing. The adjusted association with processing speed was stronger than the corresponding associations with the other three cognitive test outcomes examined. However, these findings should be interpreted with caution, as the comparisons were based on standardized scores from specific cognitive tests.

Longitudinal studies with clinically verified diabetes status and repeated cognitive assessments are needed to clarify how diabetes relates to changes in domain-specific performance over time. Measuring diabetes self-management in these studies would help clarify the clinical relevance of those changes.

Author Contributions: Conceptualization, K.S. and H.O.; Methodology, K.S. and H.O.; Formal Analysis, K.S.; Investigation, K.S., T.O. and A.K.; Writing—Original Draft Preparation, K.S.; Writing—Review and Editing, T.O., A.K. and H.O.; Supervision, H.O.; Project Administration, H.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Certified Clinical Research Review Board, Akita University (Approval No. 2001; 1 October 2018) and the Research Ethics Review Committee of Akita Prefectural Cerebrospinal and Cardiovascular Center (Approval No. 25-14; 14 July 2025).

Informed Consent Statement: Written informed consent was obtained from all the participants involved in the study.

Data Availability Statement: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request, subject to institutional data-sharing agreements.

Acknowledgments: The authors thank all participants in this survey. We also thank the staff of the Akita Prefectural Government and the participating municipalities for their assistance with the assessments.

Conflicts of Interest: The authors declare no conflict of interest.

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