Usefulness of the Touch Panel-type Dementia Assessment Scale (TDAS) and Evaluation of Correlation between Hemoglobin A1c and TDAS in Middle-Aged and Older Women

Hiromi IKEDA[1], Fumiko ISHIZAKI[1], Toshihide HARADA[1,*], Satomi AOI[1], Tadayuki IIDA[2], Noriko TAMURA[1], Chiho CHIKAMURA[1], Yumiko NITTA[3] and Kohsaku NITTA[4]

1) *Faculty of Health and Welfare, Prefectural University of Hiroshima, 1-1 Gakuen-machi, Mihara, Hiroshima 723-0053, Japan*
2) *Department of Public Health, Fujita Health University School of Medicine, 1-98 Dengakugakubu, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan*
3) *Suzugamine Women's College, 4-6-18 Inokuchi, Nishi-ku, Hiroshima 733-8623, Japan*
4) *Shiraki-no-sato, 230 Shiraki-cho Kogoshi, Asakita-ku, Hiroshima 739-1412, Japan*

ABSTRACT

There is a suspected relationship between glycometabolism and cognitive function in non-diabetic women. In this study, we aimed to give further evidence of a correlation between glycometabolism and cognitive function with the use of a new computer-based rating scale for Alzheimer's disease, TDAS. The subjects were 174 non-diabetic, middle-aged, older women. The levels of hemoglobin A1c (HbA1c, the Japan Diabetes Society (JDS)), TDAS and Revised Hasegawa's Dementia Rating Scale (HDS-R) were measured. Mean value of HbA1c, score of TDAS, time of TDAS and HDS-R were 5.2 ± 0.3 (n = 169), 0.9 ± 1.4 n = 173), 13.0 ± 1.4 min (n = 173) and 29.4 ± 1.0 (n = 174), respectively. The coefficient of the correlation (r) between age and HbA1c was 0.31, that between age and HDS-R was -0.21, that between age and score of TDAS was 0.33, and that between age and time of TDAS was 0.43. The correlations were significant. There was no correlation between HbA1c and HDS-R. The coefficient of the correlation (r) between HbA1c and score of TDAS was 0.16 (p = 0.042), and that between HbA1c and time of TDAS was 0.17 (p =0.027). The correlations between HbA1c and score of TDAS and between HbA1c and time of TDAS were significant.

These results suggest that TDAS is very useful for evaluation of cognitive function and that there is a correlation between glycometabolism and cognitive function in non-diabetic middle-aged and older women, even if their cognitive function is within normal limits.

Key words: *Glycometabolism, TDAS, HDS-R, Mild cognitive impairment*

In the Japanese clinical setting, HDS-R is widely used as a simple mental function test for cognitive impairment. The test takes about 10 min per person, and it puts a heavy burden on medical staff. As a result, new methods for assessing cognitive function have been sought. In recent years, for the screening of mild cognitive impairment, Urakami developed a new computer-based rating scale for Alzheimer's disease, TDAS[6,7,11]. The results of evaluation by TDAS were significantly correlated with those using HDS-R and with the mini-mental state examination (MMSE) of our previous study[11,12]. The TDAS is intended as a substitute for the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog), and is specifically designed to rate cognitive dysfunction in just 20 min without examiner-related differences.

Diabetes is associated with cognitive impairment[1,2,4,9,10]. Diabetes predominantly affects hippocampal-based declarative memory performance. Insulin resistance itself, before the onset of overt diabetes with its associated hyperglycemia, is accompanied by cognitive impairment[3-5,8]. Elevated insulin levels among non-diabetic individuals have been linked to lower global cognitive performance, possibly suggesting that the early effects of the metabolic dysregulation associated with insulin resistance may contribute to the cognitive impairment prior to hyperglycemia[1,2,13,14].

The purpose of this study was to measure TDAS, compare HDS-R and to evaluate correlations between HbA1c and TDAS in middle-aged and older women.

---

*Address correspondence to: Dr. Toshihide Harada
E-mail: hartoshi@pu-hiroshima.ac.jp

SUBJECTS AND METHOD

The subjects were 174 non-diabetic middle-aged and older women. Mean age at examination was 62.0 ± 6.8 years (54-77 years in distribution). All individuals had fasting glucose levels below 100 mg/dl and HbA1c below 6.1%. None of the participants showed evidence of neurological, medical (other than dyslipidemia, or hypertension), or psychiatric (including depression and alcohol or other substance abuse) signs and symptoms. None of the participants were being treated with hypoglycemic medications. The study content and method were sufficiently explained to all subjects, and written consent was obtained before the study. This study was conducted in accordance with the Declaration of Helsinki.

In this study, we used a new computer-based rating scale for Alzheimer's disease (Nihon Kohden Corp., Tokyo, Japan) named the TDAS. The hardware for the TDAS comprises a 14-inch touch panel display and computer devices built into one case. The TDAS runs on Windows OS and was bundled with a custom program made with reference to the ADAS-cog. The levels of HbA1c, TDAS and HDS-R were measured. Probability values of 0.5 or lower were regarded as statistically significant in all tests. Statistical analysis was performed using SPSS16.0J software (SPSS Japan Inc., Tokyo, Japan).

RESULTS

Mean value of HbA1c, score of TDAS, time of TDAS and HDS-R were 5.2 ± 0.3 (n = 169), 0.9 ± 1.4 (n = 173), 13.0 ± 1.4 min (n = 173) and 29.4 ± 1.0 (n = 174), respectively. The coefficient of the correlation (r) between age and HbA1c was 0.31,

that between age and HDS-R was -0.21, that between age and score of TDAS was 0.33, and that between age and time of TDAS was 0.43. The correlations were significant. There was no relationship between HbA1c and HDS-R. The coefficient of the correlation (r) between HbA1c and TDAS score was 0.16 (p = 0.042, Fig. 1), and that between HbA1c and time of TDAS was 0.17 (p = 0.027, Fig. 2). The correlations between HbA1c and score of TDAS and between HbA1c and time of TDAS were significant.

DISCUSSION

The Alzheimer's Disease Assessment Scale was designed as a rating scale for the severity of dysfunction in cognitive and non-cognitive behaviors. Its subscale, the ADAS-cog, is a cognitive testing instrument most widely used to measure the impact of the disease. However, the ADAS-cog takes more than 45 min to administer. A more comprehensive rating battery is therefore required. Urakami developed a new computer-based rating scale for Alzheimer's disease named the TDAS, which was intended to substitute for the ADAS-cog and specifically designed to rate cognitive dysfunction in about 20 min[6,7,11,12]. Regarding the present status of insurance-based medicine in Japan, it is difficult to provide long consultation times even in specialized medical institutions. For this reason, too, Urakami argued the necessity for simple screening methods such as TDAS in "outpatient clinics specializing in memory impairment" [6,7,12].

Urakami also claimed that TDAS causes only slight psychological stress and is noninvasive because examinees answer questions asked by a computer and not by a person. It also produces no
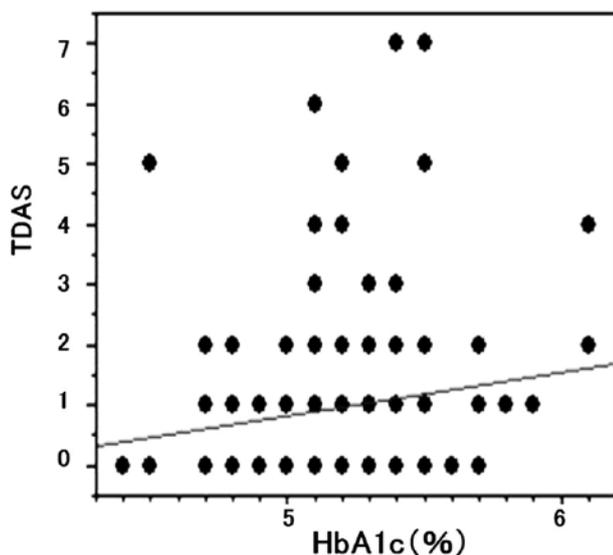
Fig. 1. Correlation between HbA1c and TDAS score
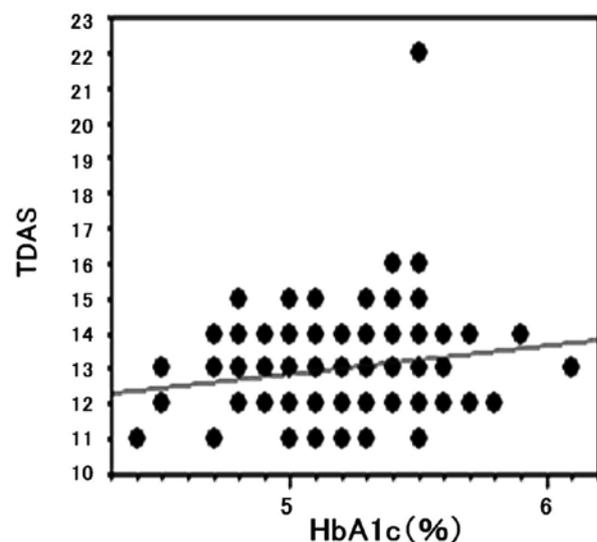
Fig. 2. Correlation between HbA1c and time of TDAS (min)

differences among raters because of the absence of differences among examiners. In the present study, the TDAS could be individually performed, and results excluding examiner-related bias were obtained. These are the merits of using TDAS.

The contents are questions regarding the immediate recognition of words, orientation to time and date, delayed recognition of words, and spatial cognitive function by the selection of pictures showing a cube and triangular prism[6]. Examinees answer questions asked by the computer (spoken and visualised on the screen). Scores $\geqq 14$ indicate cognitive impairment. Therefore, the TDAS score of our subjects (0.9 ± 1.4 (n = 173)) was within normal limits. The score of HDS-R (29.4 ± 1.0 (n = 174)) supported that result. The results of evaluation by TDAS significantly correlated with those obtained using HDS-R and MMSE in our previous study[11]. Urakami performed cognitive impairment screening using TDAS in subjects diagnosed as normal by specialists, and observed cognitive impairment in 38.9% of them[6,7,12]. In the present study, the scores of both TDAS and HDS-R were within normal limits, but TDAS was very useful for the evaluation of cognitive function and was correlated with the levels of HbA1c. We concluded that TDAS was more useful and sensitive than HDS-R.

The study by Mogi suggests that Japanese elderly DM subjects, especially those undergoing insulin treatment, have poor cognitive function[8]. In the present study, TDAS revealed that there was a relationship between glycometabolism and cognitive function in non-diabetic middle-aged and older women. This indicates that TDAS is a simple, sensitive and very useful means for detecting cognitive function. These results also suggest that there is a relationship between glycometabolism and cognitive function in non-diabetic middle-aged and older women, even if their cognitive function is within normal limits. When Bruehl examined insulin resistance simultaneously with other biomedical indicators with which it co-occurs, only insulin resistance itself was associated with declarative memory, while HbA1c was associated with executive functioning and working memory[1]. Bruehl suggests that otherwise healthy middle-aged and older individuals with insulin resistance have subtle cognitive impairments similar to those observed in well-controlled diabetes, namely decreases in declarative memory and executive function. Those abnormalities likely reflect the damaging effects of insulin resistance on the hippocampal formation and frontal lobe. It appears that prior to the onset of diabetes and sustained hyperglycemia, the effects of insulin resistance put the brain at risk for damage, possibly via subtle vascular abnormalities including endothelial dysfunction and even

possible alterations in insulin receptor functioning. Because insulin resistance itself is a silent condition, middle-aged and older women are likely to be unaware that they are at risk for negative health consequences prior to the onset of diabetes. Nevertheless, TDAS is a simple screening test of cognitive function and evaluation of its severity using only TDAS is ill-advised. We consider that TDAS requires comprehensive evaluation, including the evaluation of behavior, neurological findings, and findings of diagnostic imaging, and that the final diagnosis of cognitive function should be performed by medical specialists. In the present study, there is a relationship between age and TDAS score and between time of TDAS and HbA1c. In middle-aged and older women, the number of patients with cognitive impairment has been increasing. Insulin resistance may also develop with aging. This study is limited by its modest sample size and its restriction to non-diabetic middle-aged and older women, which does not allow a thorough investigation of possible gender effects. In addition, the cross-sectional design of the study limits our ability to make more causal inferences. Further study will be needed to clarify that insulin resistance itself, before the onset of overt diabetes with its associated hyperglycemia, is accompanied by a reduction of cognitive function, and that the effects of metabolic dysregulation associated with insulin resistance may contribute to the decline of cognitive function prior to hyperglycemia.

REFERENCES

1. **Bruehl, H., Sweat, V., Hassenstab, J., Polyakov, V. and Convit, A.** 2010. Cognitive impairment in nondiabetic middle-aged and older adults is associated with insulin resistance. J. Clin. Exp. Neuropsychol. **32**: 487-493.
2. **Cheng, W., Harada, T., Ishizaki, F., Yin, H.N., Wang, Q.W., Ma, L., Nitta, Y. and Nitta, K.** 2005. Changes of plasma IL-13 in patients with acute cerebral infarction. International Medical Journal **12**: 33-35.
3. **Harada, T., Ishizaki, F., Murakami, I., Tachiki, N., Horie, N. and Nitta, K.** 2002. Age-related changes in P300 event-related potentials in Japanese normal volunteers. International Medical Journal **9**: 41- 43.
4. **Harada, T., Ishizaki, F., Nitta, Y., Nitta, K., Shimohara, A., Tsukue, I., Wu, X. and Cheng, W.** 2008. Microchips will decrease the burden on the family of elderly people with wandering dementia. International Medical Journal **15**: 25-28.
5. **Harada, T., Ishizaki, F., Horie, N., Katsuoka, H., Nitta, Y., Yamada, T., Nitta, K. and Ito, M.** 2011. Alcohol-induced persistent mild cognitive impairment with successful withdrawal from alcohol

dependence-a case report. Hiroshima J. Med. Sci. **60**: 11-13.

6. **Inoue, M., Meshitsuka, S., Yoshioka, S. and Kawahara, R.** 2000. Development of computerized screening system for dementia and its preliminary field test. Comput. Methods Programs Biomed. **61**: 151-155.

7. **Inoue, M., Jimbo, D., Taniguchi, M. and Urakami, K.** 2011. Touch panel-type dementia assessment scale: a new computer-based rating scale for Alzheimer's disease. Psychogeriatrics **11**: 28-33.

8. **Mogi, N., Umegaki, H. and Hattori, A.** 2004. Cognitive function in Japanese elderly with type 2 diabetes mellitus. J. Diabetes Complict. **18**: 42-46.

9. **Nitta, Y., Shigeyoshi, Y., Nakagata, N., Kaneko, T., Nitta, K., Harada, T., Ishizaki, F. and Townsend, J.** 2009. Kinetics of blood glucose in mice carrying hemizygous pax6. Exp. Anim. **58**: 105-112.

10. **Tomioka, M., Adachi, T. and Suzuki, H.** 2006. The insulin/Pl 3-kinase pathway regulates salt chemo-taxis learning in caenorhabditis elegans. Neuron **51**: 613-625.

11. **Tsuboi, K., Harada, T., Ishii, T., Ishizaki, F., Nitta, Y. and Nitta, K.** 2009. Evaluation of correlations between a simple touch-panel method and conventional methods for dementia screening in the elderly. International Medical Journal **16**: 175-179.

12. **Tsuboi, K., Harada, T., Ishii, T., Morishita, H., Ohtani, H. and Ishizaki, F.** 2009. Evaluation of the usefulness of a simple touch-panel method for the screening of dementia. Hiroshima J. Med. Sci. **58**: 49-53.

13. **Wu, S., Harada, T., Cheng, W., Ishizaki, F., Nitta, Y., Nitta, K. and Yan, L.** 2009. The experimental study of Alzheimer's disease model. International Medical Journal **16**: 67-70.

14. **Yin, H.N., Cheng, W.P., Harada, T., Ishizaki, F., Nitta, Y., Nitta, K. and Ohtani, H.** 2004. An analysis of apolipoprotein E polymorphism in aged patient with vascular dementia. International Medical Journal **11**: 291-293.