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Predicting the ability of elderly diabetes patients to acquire the insulin self-injection technique based on the number of animal names recalled

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ABSTRACT

Aims/Introduction: To our knowledge, no studies have reported that cognitive tests can be used to evaluate whether or not patients can acquire the insulin self-injection technique. We investigated whether or not the number of animal names recalled in 1 min by elderly diabetes patients could be used as a predictor of the patients' ability to acquire the insulin self-injection technique within 1 week.

Materials and Methods: We enrolled 57 inpatients with type 2 diabetes aged >60 years who were starting insulin therapy. We carried out the Mini-Mental State Examination and verbal fluency tests, which included recalling animal names and common nouns starting with the letters 'a,' 'ka' and 'shi' (Japanese letters). We used 12 checkpoints for insulin self-injection to judge the patients' levels of acquisition of the technique. The most predictive cognitive test was determined by multivariate logistic regression analysis.

Results: In the present study, multivariate logistic analysis showed that the number of animal names recalled was the most reliable predictor of the ability to acquire the insulin self-injection technique within 1 week. A figure of 11 animal names predicted a successful acquisition, with a sensitivity of 73% and a specificity of 91% being observed (area under the curve 0.87, 95% confidence interval 0.76–0.97, $P < 0.01$).

Conclusions: The number of animal names recalled in 1 min was the most useful indicator of the ability of elderly diabetes patients to learn to manage insulin self-injection therapy within 1 week. The cut-off value was 11 animal names.

INTRODUCTION

Many elderly patients across the world are diagnosed with type 2 diabetes. In Japan, it is known that 80% of diabetes patients are aged >60 years. Patients with diabetes tend to show cognitive dysfunction to some extent – indeed, type 2 diabetes is a risk factor for dementia[1,2]. It has been reported that diabetes patients achieve worse scores for various cognitive tests than controls without diabetes, even where patients with diabetes without dementia are concerned[3,4]. Taken together, the evidence increasingly shows that patients with type 2 diabetes suffer from cognitive decline.

It is difficult to attain good blood glucose control in elderly diabetes patients with cognitive dysfunction because they are often unable to follow diabetes diets and, frequently, their drug compliance is poor. Therefore, oral hypoglycemic agents are sometimes insufficient for managing the conditions of patients with cognitive impairment. As hyperglycemia is a risk factor for both dementia and diabetic complications[5–7], the Japan Diabetes Society and the American Diabetes Association recommend that a glycated hemoglobin (HbA1c) level <8% is appropriate for elderly patients. Accordingly, insulin therapy

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and inpatient treatment are sometimes required where such patients are concerned.

The purpose of the present study, therefore, was to investigate the use of cognitive tests to evaluate whether or not elderly diabetes patients can acquire the insulin self-injection technique. The semantic fluency test is known to be associated with the function of the parietal lobe[8,9], which is believed to involve the part of the memory that is used in acquiring the insulin self-injection technique. In the present study, we carried out a semantic fluency test, such as recalling animal names. We speculated that the number of animal names recalled by patients would be a useful predictor of the ability to acquire the insulin self-injection technique.

Additionally, in the present study, we referred to a report by Yajima *et al.*[10], who concluded that the semantic fluency test was associated with the property of the insulin self-injection technique that they had learned. However, to our knowledge, there is no report to evaluate cognitive tests for the ability to acquire the insulin self-injection technique.

METHODS

The present study was retrospective, using data from cognitive tests administered before the analysis took place. We enrolled 57 consecutive inpatients aged >60 years with type 2 diabetes, who started insulin therapy for the first time between June 2014 and May 2016 at the Yokohama Sakae Kyosai Hospital, Yokohama, Japan. The exclusion criteria were: (i) stroke patients; (ii) psychiatry patients with depression, schizophrenia, developmental disorders or attention deficit hyperactivity disorders; (iii) patients with diabetic ketoacidosis; (iv) patients with thyroid hormone disorders; and (v) patients who were unable to recall 'places that they have visited' within 1 min during a verbal fluency test. The instruction to recall places visited by the patients was considered to be so easy that patients who were unable or unwilling to respond within 1 min were assumed to be unmotivated to answer further questions.

On admission, the first author administered the Mini-Mental State Examination (MMSE) to all the patients, as well as the following verbal fluency tests: (i) recall places that they have visited; (ii) animal fluency – recall animal names; and (iii) letter fluency – recall common nouns starting with 'a,' 'ka' and 'shi' (Japanese letters), which correspond to 'f,' 'a' and 's' in English. For each of the animal fluency and letter fluency verbal fluency tests, the patients were instructed to recall as many of the terms as possible within 1 min. The total number of responses was noted, excluding any errors and repetitions[11]. The sum of the number of nouns starting with 'a,' 'ka' and 'shi' recalled was considered to represent the total letter fluency responses. The total animal fluency responses were termed the 'animal score,' whereas the total letter fluency responses were named the 'letter score.'

In regard to insulin administration, all of the patients were given prefilled pen-type insulin devices, such as insulin degludec, biphasic insulin aspart 30, 50 or 70 (Novo Nordisk, Bagsvaerd, Denmark) and/or insulin glargine (Sanofi, Paris, France).

All of the patients were taught the insulin self-injection technique by the nurses on the diabetes ward at the Yokohama Sakae Kyosai Hospital one to four times a day, according to necessity. We defined the following points as important details when determining whether or not the patients had acquired the insulin self-injection technique: (i) understanding the effect of the insulin device (for example, realizing that insulin degludec is a long-acting insulin, whereas insulin aspart is a short-acting insulin); (ii) being able to prepare the devices and check the amount of insulin in the cartridge; (iii) learning how to open the cap on the insulin device and how to clean the cartridge attachment; (iv) grasping how to attach the hypodermic needle; (v) learning how to remove bubbles from the cartridge; (vi) knowing how to set up the target dial; (vii) being confident to change the site of the injection; (viii) coping with pricking the skin with the needle; (ix) being able to push the syringe plunger directly and smoothly; (x) being confident to inject the insulin for more than 5 s; (xi) having the ability to check that the dial was at '0' after the injection; and (xii) being capable of removing the needle and closing the cap on the insulin device. The nurses in the ward evaluated the level of insulin self-injection technique acquisition by examining all the checkpoints in relation to each patient, and judged patients who completed all checkpoints at the same time within 1 week as the 'master group,' whereas those who could not complete them were the 'non-master group.'

To evaluate glucose metabolism, overnight fasting blood samples were obtained from all patients on the second day after admission. HbA1c levels were measured using high-performance liquid chromatography (Adams A1c HA-8160; Arkray Inc., Kyoto, Japan). The fasting plasma C-peptide levels were measured at a central clinical laboratory (SRL, Inc., Tokyo, Japan).

All of the statistical analyses were carried out using IBM SPSS 21 Software for Windows (IBM, Armonk, New York, USA). The mean ± standard deviation was reported for continuous variables, and numbers and percentages for categorical variables. Two groups were identified by the results: the 'master group' (those who were able to acquire the technique within 1 week) and the 'non-master group' (those who were unable to acquire the technique within 1 week). Ages, body mass index levels HbA1c levels, fasting plasma C-peptide levels, years of education and verbal fluency test scores for the two groups were compared using the unpaired Student's *t*-test. Duration of diabetes (years), number of times a day insulin self-injection and MMSE scores for the two groups were compared using the Mann–Whitney test. The categorical variables for the two groups were analyzed using the χ^2-test. The predictive factors for the ability to acquire the insulin self-injection technique within 1 week were assessed using univariate and multivariate logistic regression analyses. The correlates for the time taken

(days) to acquire the self-insulin technique were assessed by multiple linear regression analysis. The relationship between animal scores and the time taken to acquire the technique was assessed by univariate linear regression analysis. A receiver operating characteristic curve was used to determine the cut-off value for an independent predicting factor, and to assess the accuracy of the ability to acquire the insulin self-injection technique within 1 week. A *P*-value of <0.05 was considered to be statistically significant. The animal scores and the letter scores for the two groups were compared without adjustments for ages, because these scores have been shown to be consistent for those aged >60 years[12].

This study was approved by the ethics committee at the Yokohama Sakae Kyosai Hospital, and was carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all the participants.

RESULTS

The 'master group' was defined as the group of patients who were able to acquire the insulin self-injection technique within 1 week. The 'non-master group' was the group of patients who could not acquire the technique within the given time frame. Table 1 gives the patient characteristics for the two groups. Both groups showed poor glycemic controls, with HbA1c levels of >10%. Body mass index levels were significantly higher in the 'master group' than in the 'non-master group.' There were no significant differences between the two groups, however, in terms of the insulin self-injection frequency and the number of years of education.

Table 2 gives the results for the cognitive tests for the two groups. The 'master group' showed significantly higher scores for the MMSE and verbal fluency tests compared with the 'non-master group.' Multivariate logistic regression analysis showed that the animal scores and letter scores from the verbal fluency tests could be considered independent factors that were associated with the ability to acquire the insulin self-injection technique within 1 week ($P = 0.02, 0.03$; Table 3).

The mean time taken to acquire the self-injection technique was also examined. A total of 36 patients could acquire it within 1 week, six patients could acquire it until discharge after 1 week (8–14 days) and 15 patients could not acquire it during hospitalization. In all, 42 patients acquired the technique during hospitalization, and the time taken to achieve this was 4.9 ± 3.0 days (1–14 days). The animal score was the only correlate of the time taken to acquire the insulin self-injection technique (Table 4) according to multiple linear regression analysis, and the scatter diagram figure is shown in Figure 1.

From these results, we can state that the animal score was found to be the most reliable factor. The cut-off value and the area under the curve in the receiver operating characteristic curve were determined, therefore, on the basis of the animal score. An animal score of 11 predicted the possibility of acquiring the insulin self-injection technique within 1 week, with a sensitivity of 73% and a specificity of 91% (area under the curve 0.87, 95% CI: 0.76–0.97, $P < 0.01$; Table 5).

DISCUSSION

In the present study, it was found that the number of animals recalled in 1 min by elderly diabetes patients was the most useful predictor of the patients' ability to acquire the insulin self-injection technique within 1 week. Other cognitive tests, such as the MMSE and the letter fluency test, were less useful.

There are three reasons why the number of animal names recalled in 1 min might predict the ability to acquire the insulin self-injection technique better than the other cognitive tests examined here. First of all, the memorization of new things involves the temporoparietal lobe, which contains the hippocampus. The temporoparietal lobe is activated during a semantic fluency task, such as recalling animal names, as shown by functional magnetic resonance imaging[8] and positron emission tomography[9].

The second reason is that temporal lobe lesions are related to impaired performance in sematic fluency tasks[13]. Patients with temporal lobe lesions have been found to have poor

Table 1 | Patient characteristics; acquiring self-insulin injection technique within 1 week is possible (Master group) or impossible (Non-master group)

	Master group ($n = 36$)	Non-master group ($n = 21$)	*P*
Male/female	13/23	11/10	0.648†
Age (years)	71.1 ± 5.6	74.1 ± 6.1	0.307‡
BMI (kg/m^2)	25.7 ± 4.5	22.8 ± 5.7	<0.05‡
HbA1c in the hospital (%)	10.4 ± 1.9	10.6 ± 2.9	0.722‡
Serum CPR, fasting (ng/mL)	1.9 ± 0.8	2.1 ± 1.3	0.913‡
Duration of diabetes (years)	10.6 ± 10.4	14.7 ± 10.2	0.144§
No. years of education	12.7 ± 2.5	10.8 ± 2.5	0.084‡
Times a day of insulin-self injection	2.6 ± 0.9	2.5 ± 1.1	0.880§

Data are expressed as numbers or mean ± standard deviation. As determined by the †χ^2-test. ‡unpaired *t*-test. §Mann–Whitney test. BMI, body mass index; CPR, C-peptide immunoreactivity; HbA1c, glycated hemoglobin; master group, patients for whom acquiring the self-insulin injection technique within 1 week was possible; non-master group, patients for whom acquiring the self-insulin injection technique within 1 week was impossible.

Table 2 | Cognitive test scores of Master group and Non-master group

	Master group (n = 36)	Non-master group (n = 21)	P
MMSE	27.0 ± 2.5	22.1 ± 6.2	<0.01†
Verbal fluency tests			
Animal score	14.8 ± 4.6	7.8 ± 3.5	<0.01‡
Letter score	19.3 ± 8.6	9.3 ± 4.5	<0.01‡

Date are expressed as mean ± standard deviation. As determined by the †Mann-Whitney test and the ‡unpaired t-test. The animal score is the number of animal names recalled in 1 min. The letter score is the total number of common nouns starting with 'a,' 'ka' and 'shi' (Japanese letters) each recalled in 1 min. Master group, patients for whom acquiring the self-insulin injection technique within 1 week was possible; MMSE, Mini-Mental State Examination; non-master group, patients for whom acquiring the self-insulin injection technique within 1 week was impossible.

Table 3 | Predictors for the ability to acquire self-insulin injection technique in 1 week determined by univariate and multivariate logistic regression analyses

	Univariate		Multivariate	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
BMI (kg/m^2)	1.1 (1.0–1.3)	0.05	1.2 (1.0–1.5)	0.05
MMSE	1.4 (1.1–1.7)	<0.01	0.9 (0.7–1.3)	0.66
Verbal fluency tests				
Animal score	1.7 (1.3–2.2)	<0.01	1.4 (1.1–1.9)	0.02
Letter score	1.3 (1.1–1.5)	<0.01	1.3 (1.0–1.5)	0.03

The animal score is the number of animal names recalled in 1 min. The letter score is total number of the common nouns starting with 'a,' 'ka' and 'shi' (Japanese letters) each recalled in 1 min. BMI, body mass index; CI, confidence interval; MMSE, Mini-Mental State Examination.

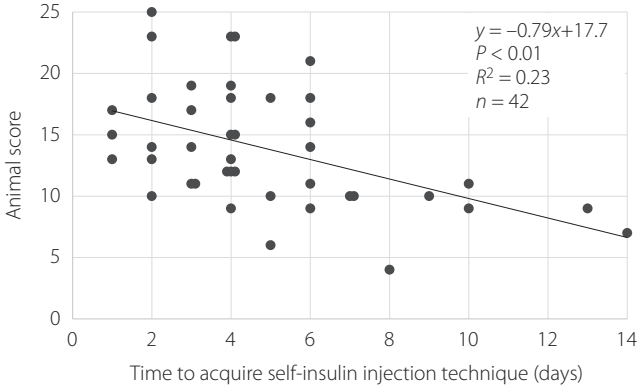

Figure 1 | The relationship between animal scores and the time (days) taken to acquire the self-insulin injection technique. Animal score, the number of animal names recalled in 1 min.

Table 4 | Multiple linear regression analysis correlates of the time (days) taken to acquire self-insulin injection technique

	B (95% CI)	P
BMI (kg/m^2)	0.01 (–0.18 to 0.16)	0.92
MMSE	–0.21 (–0.44 to 0.02)	0.08
Verbal fluency tests		
Animal score	–0.28 (–0.65 to –0.50)	0.01
Letter score	–0.05 (–0.17 to 0.07)	0.40
Adjusted R^2		0.21

The animal score is the number of animal names recalled in 1 min. The letter score is the total number of the common nouns starting with 'a,' 'ka' and 'shi' (Japanese letters) each recalled in 1 min. BMI, body mass index; CI, coinfidence interval; MMSE, Mini-Mental State Examination.

Table 5 | Cut-off value and the area under the curve in the receiver operating characteristics curve with the animal score for acquiring self-insulin injection technique within 1 week

	Cut-off value	AUC (95% CI)	P
Animal score	11	0.87 (0.76–0.97)	<0.01

AUC, area under the curve. The animal score is the number of animal names recalled in 1 min.

memories[14]. We could speculate, therefore, that the patients who recalled fewer animals had worse memories overall.

The final reason that might explain the present findings is that patients with Alzheimer's disease tend to show low scores for semantic fluency tasks, such as the animal names task carried out in the present[15,16]. Patients with Alzheimer's disease have hippocampus atrophies, and develop impaired memories. This means that a low score for the animal names task could be associated with atrophies of the hippocampus and memory disorders – both of which have been linked with diabetes in previous studies[17,18].

In addition, some elements related to phonemic fluency tasks should be considered, when analyzing the present results. These tasks are known to reflect the function of the prefrontal lobe, according to functional magnetic resonance imaging and studies of prefrontal lobe lesions[8,13]. The prefrontal lobe is involved in executive functions, which are sets of mental skills related to attention, inhibitory control and problem solving[19]. In other words, executive functions are supposed to be associated with

controlling one's appetite in patients with type 2 diabetes. Therefore, a phonemic fluency task, such as the 'a,' 'ka,' 'shi' task, is irrelevant in regard to memorizing the procedure for insulin self-injection therapy. This is in direct contrast with the semantic fluency task, which has a relevance to the procedure being examined here.

When considering the relevance of the MMSE, which is the most familiar instrument used here for screening cognitive function and consists of 11 questionnaires on areas such as orientation, registration and recall, it should be noted that not all of the questionnaires could be related to the study at hand. In fact, the 'recall' questionnaire is the only one associated with the memory required to acquire the insulin self-injection technique. By taking this fact into account, it can be assumed that the MMSE is not sufficient to evaluate memory in the manner required by the present study. Indeed, our results showed that some patients with high MMSE scores had low scores for the animal names task and were unable to acquire the insulin self-injection technique (data not shown).

Consequently, it can be stated that the semantic fluency test is the most appropriate test examined here for evaluating the ability of patients to acquire the insulin self-injection technique. A figure of 11 animal names was established as the cut-off score. This cut-off score can be considered appropriate, despite the present study's small sample size, as it accords with the findings of previous research. Yajima *et al.*[10] reported that a score of 10 animal names was able to predict the patients' ability to appropriately carried out insulin self-injection, while Hanyu *et al.*[20] showed that a score of 13 animals discriminated between patients with Alzheimer's disease and controls.

We set a deadline of 1 week to acquire the insulin self-injection technique. The Japanese insurance system recommends a <2-week hospitalization period for glycemic control. Therefore, a new insulin-management strategy needs to be developed if the patients are unable to acquire the self-injection technique in a week. In such situations, the strategy can be altered to suit the patients' home environment. It can be suggested that members of the patients' family and/or a home-visiting nurse should administer insulin to the patients. However, it often takes a long period to arrange home-visiting care, and therefore hospitalization is extended. Accordingly, we believe that a deadline of 1 week is appropriate. If the semantic fluency test predicted the patients' disability to master the insulin self-injection technique within 1 week, we could think of an insulin-management strategy in the early stage. Thus, this trial could shorten the hospitalization period.

The practical data in the present study supported a deadline of 1 week being appropriate. A total of 36 patients in the 'master group' sometimes forgot a part of the insulin self-injection technique, even after mastering it once; however, all the patients could completely master it before discharge. Six of 21 patients in the 'non-master group' managed to master it during hospitalization, and they could carry out it by themselves after discharge. Otherwise, 15 of 21 patients could not master it; therefore, their family members administered the insulin to them in most cases. Most of them chose basal supported oral therapy.

In such situations, the ability to master the insulin self-injection technique affected glycemic control after 1 year. After discharge, in 1 year, 26 of 36 patients in the 'master group' and 15 of 21 patients in the 'non-master group' could be observed. Although there were no severe hypoglycemic events in both groups, the patients in the 'non-master group' had worse glycemic controls than those in the 'master group' (the mean HbA1c level 8.3 ± 2.7 vs 7.0 ± 0.8%, $P < 0.05$, by the unpaired Student's *t*-test). Two patients from the 'non-master group' were hospitalized for glycemic control again within 1 year.

In the present study, we recruited patients aged >60 years, although Yajima *et al.*[10] recruited patients aged >65 years. Cognitive impairment is generally observed in patients aged >65 years, and patients with Alzheimer's disease are generally aged >65 years. However, patients with mild cognitive impairment (i.e., the pre-stage of dementia) are assumed to have difficulties in acquiring the insulin self-injection technique, because the technique is difficult for elderly patients. Half of the patients with mild cognitive impairment were reported to develop Alzheimer's disease in approximately 5 years[21]. Therefore, we recruited patients aged >60 years.

It must be mentioned that there are three key limitations to the present study. The first is the fact that this was a retrospective study. Consequently, the inpatients were taught to manage insulin self-injection therapy by different nurses. The outcomes might have been affected, therefore, by the nurses' ability to teach. The second limitation is that some patients were taught the self-injection technique more times per day than others, according to need. As expected, it was found that the 'master group' was taught the technique more often than the 'non-master group.' Although there were no statistical differences between the mean frequency for each group, the variations might have contributed to the outcomes overall. The third limitation is that we did not evaluate the patients' instrumental activities of daily living. To investigate instrumental activities of daily living skills, we should have evaluated the ability to carry out activities, such as to shop for necessities, prepare meals and utilize transportation. Such skills are supposed to be associated with the ability to master the self-injection technique. Therefore, we should have investigated instrumental activities of daily living skills in addition to cognitive tests.

We calculated our sample size in reference to the report by Yajima *et al.*[10], although the present study was retrospective in nature. Yajima *et al.* found that the mean difference in the animal fluency test scores for patients who could carry out insulin self-injection appropriately and those who could not was 3. Additionally, the standard deviation for each group was approximately 3. If the power was 0.8 and the *P*-value was <0.05, we needed at least 16 patients in each group to make our study feasible. In our experiment, the 'master group'

contained 36 patients and the 'non-master group' contained 21, so it can be said that the number of patients in each group was sufficient.

In conclusion, the number of animal names recalled in 1 min by elderly diabetes patients is a useful predictor of the ability to acquire the insulin self-injection technique within 1 week. The MMSE and the letter fluency test were found to be less useful predictors than the animal fluency test.

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All the authors contributed to the research data and the discussion. The manuscript was also co-written by all the authors.

DISCLOSURE

The authors declare no conflict of interest.

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