Table 4
NSFQ total scores, total sexual dysfunction (%), and plasma prolactin levels (ng/ml) in each antipsychotic treatment group.

Males				
			Total sexual dysfunction	
Drug	Prolactin level a	NSFQ	≥3 (from mild to severe) n (%)	≥4 (moderate and severe) n (%)
Aripiprazole	5.2 ± 7.6	13.4 ± 5.0	11 (78.6)	5 (35.7)
Olanzapine	10.6 ± 7.4	13.1 ± 5.0	10 (66.7)	8 (53.3)
Polytherapy	23.2 ± 15.6	12.7 ± 6.1	29 (64.4)	15 (33.3)
Risperidone	29.8 ± 16.4	12.7 ± 5.4	27 (64.3)	19 (45.2)
Others	4.2 ± 0.4	8.0 ± 4.2	1 (33.3)	0 (0)

Females				
			Total sexual dysfunction	
Drug	Prolactin level f e	NSFQ	≥3 (from mild to severe) n (%)	≥4 (moderate and severe) n (%)
Aripiprazole	6.7 ± 7.6	13.5 ± 5.4	14 (82.4)	10 (58.8)
Olanzapine	23.4 ± 7.9	13.2 ± 3.2	5 (55.6)	3 (33.3)
Polytherapy	51.5 ± 45.2	12.7 ± 6.1	15 (83.3)	13 (72.2)
Risperidone	79.9 ± 48.9	13.9 ± 4.6	25 (92.6)	18 (66.7)
Others	17.6 ± 18.1	10.6 ± 6.1	3 (42.9)	2 (28.6)

There were significant differences in the prolactin levels among the antipsychotic groups of aripiprazole, olanzapine, polytherapy and risperidone in males ($F=13.251$, $df=114$, $p<0.001$, $^{a}p<0.001$, $^{b}p<0.001$, $^{c}p<0.026$, $^{d}p<0.001$) and females ($F=14.107$, $df=70$, $p<0.001$, $^{e}p<0.01$, $^{f}p<0.001$, $^{g}p<0.01$) subjects. The total NSFQ scores were not significantly different among the groups of aripiprazole, olanzapine polytherapy, and risperidone in males ($F=0.075$, $df=114$, $p=0.973$) and females ($F=1.537$, $df=70$, $p=0.213$). There was no significant difference in the frequency of total sexual dysfunction among the groups receiving aripiprazole, olanzapine polytherapy, and risperidone (males, from mild to severe, chi square 1.5508 $p=0.82$; moderate and severe, chi square 4.3366 $p=0.36$; females, from mild to severe, chi square 9.0318 $p=0.06$; moderate and severe, chi square 7.6454 $p=0.11$).

Smith et al., 2002). Third, noradrenergic and histaminergic effects are also suggested to change aspects of sexual performance (Meston and Frohlich, 2000). Fourth, the influence of the primary disease, treatment duration, age, and gender make it even more difficult to interpret the data (Smith et al., 2002). Finally, the different methodologies used to reveal sexual dysfunction likely lead to a major underestimation of the frequency of sexual dysfunction (Peuskens et al., 1998) Thus, clinicians should take these facts into account and pay attention to symptoms of sexual dysfunction in the presence or absence of hyperprolactinemia.

Previous studies suggested that the prolactin-raising drugs (e.g., risperidone) provoke significantly higher rates of sexual problems (40–60%) compared with prolactin-sparing drugs (e.g., quetiapine, ziprasidone, and aripiprazol) (<30%) (Knegtering et al., 2004, 2006; Montejo Gonzalez et al., 2005; Montejo and Rico-Villademoros, 2008a; Montejo et al., 2010a, 2010b; Serretti and Chiesa, 2011; Baggaley, 2008), whereas both our findings and those of Fujii et al. (2010) did not reveal any difference in the prevalence of sexual dysfunction among different medications in Japanese schizophrenic patients. The inconsistency between previous studies and the present study may be related to: (1) the small number of subjects on monotherapy and different numbers of subjects in the drug groups in our study, (2) the use of different rating scales (NSFQ ascertains information about sexual concerns indirectly, whereas the similar items on other scales are ascertained in a more direct manner. As a consequence, NSFQ may not be a strong instrument to detect such differences.), (3) different demographic data (the duration and treatment of illness in this study were more than 200 months, so there were many chronic patients in this study.), and (4) ethnic or cultural differences, (5) no baseline data (e.g., previous sexual functioning, sexual life, partner) before treatment with antipsychotics. However, our study revealed that patients taking antipsychotics reported to induce less sexual dysfunction have just as much sexual dysfunction as patients taking antipsychotics reported to induce more sexual dysfunction, suggesting that clinicians should pay attention to the clinical signs of sexual dysfunction regardless of the drugs patients are taking.

Our study has several limitations. First, sexual dysfunction was evaluated at only single time point, and this study was a cross-sectional study using a small clinical sample which composed of many chronic patients. So other factors but drug could have impact on the result of

this study, and it was difficult to comprehend the factor of drug perceptively. Moreover the number of patients on monotherapy was small and differed among the antipsychotic groups. However, our sample had adequate statistical power to effectively accept or reject the null hypothesis (males, $F = 13.251$, $p < 0.01$, power of test = 1.00; females, $F = 14.107$, $p < 0.01$, power of test = 1.00). Therefore, the current study could detect differences of prolactin level among drug groups accurately. Although we collected data regarding patients' ages, duration of illness, and duration of medication, no baseline data (e.g., previous sexual functioning, sexual life, partner) before treatment with antipsychotics were available and no inclusion and exclusion criteria were used in this study. These limitations might have impact on the results in this study different from prior studies. Sexual life could be influenced by many different factors that methodology may need to be quite strict. In addition, NSFQ may not be sufficient for assessing the orgasm, satisfaction and arousal due to the specific cultural aspects related to the Asian population and the further studies using other instruments should be performed in order to address this issue.

To clarify the relationship between prolactin levels and sexual dysfunction, an interventional study that investigates the effect of lowering prolactin levels on sexual dysfunction by switching antipsychotics is needed. Second, we have no data on other characteristics that might influence sexual dysfunction, including smoking status and other endocrinologic factors (such as testosterone and estradiol levels) and metabolic parameters like obesity or diabetes (Bhasin et al., 2007). Considering the important role of endocrinologic and metabolic factors in sexual dysfunction, further studies are needed to evaluate the impact of these factors (Wu et al., 2010). Third, although the patients who participated in the study were in stable condition, the impact of the disease itself on sexual dysfunction was not assessed. This factor should be included in a future study. Fourth arousal disturbances and orgasmic dysfunction are very relevant in the investigation of sexual functioning and these results are needed to obtain and clarify accurate sexual information, but these factors were not asked directly at NSFQ (There is item of sexual arousal in female NSFQ). We think that this fourth limitation might be a strong limitation and have impact on the result in this study. In order to address these issues, we are planning to conduct study of sexual function using SALSEX or other scale together with NSFQ and in order to improve performance of NSFQ.

5. Conclusion

This study is the first survey using NSFQ to estimate sexual dysfunction. Results showed a high prevalence of sexual dysfunction and hyperprolactinemia in Japanese schizophrenic patients, as with previous studies. Clinicians should pay careful attention to patients' sexual dysfunction to improve their QOL and adherence to therapy.

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Table 1. Clinical Characteristics Associated with 3-Month Mortality in 429 Elderly Adults Admitted to the Emergency Department for Infection

Clinical Characteristics	Participants/ Deaths, n/n	Relative Risk (95% Confidence Interval)	
		Crude	Adjusted[a]
Barthel Index before admission (30–60)	357/125	3.7 (1.8–7.8)	–
Barthel Index major change (>30)	297/113	3.2 (1.9–5.4)	1.8 (1.1–3.1)
Acute Physiology and Chronic Health Evaluation II Acute Physiology Subscore ≥13	79/42	3.2 (1.9–5.3)	1.5 (1.0–2.4)
Dehydration (blood urea nitrogen:creatinine >60)	140/56	1.9 (1.2–3.1)	1.5 (1.0–2.2)
Mini-Mental State Examination score <18	96/47	3.9 (2.4–6.3)	2.8 (1.8–4.3)
Delirium	100/47	2.5 (1.5–3.9)	–
Active cancer (with or without metastasis)	49/31	4.6 (2.5–8.6)	3.6 (2.2–5.8)
Charlson Index ≥4	121/53	2.2 (1.4–3.4)	–
More than nine drugs	154/67	2.3 (1.4–3.5)	1.7 (1.1–2.6)
C-reactive protein ≥10	152/62	1.9 (1.3–2.9)	1.5 (1.0–2.3)
Serum albumin ≤3.5 g/dL	287/104	2.1 (1.3–3.4)	–
Serum cholesterol <140 mg/dL	124/47	1.6 (1.0–2.5)	–
Male	217/69	1.1 (0.7–1.6)	–
Aged >80	224/79	1.5 (0.9–2.4)	–

[a]Adjusted for all variables associated with mortality in crude univariate analyses.

bility or instability, homeostasis, in the context of an ill older adult goes back to the concept of frailty. The greater the severity of the infection, the greater the risk of functional decline, but it can also be inferred that the greater the functional decline the greater the frailty (functional status can be evaluated as a risk factor for infectious disease or as an outcome of interest after specific interventions using well-validated instruments).[10] When an acute disease such as infection produces a functional impairment, this condition becomes an index of outcome and should be detected to predict poor clinical course.

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EFFECTS OF MILD COGNITIVE IMPAIRMENT ON DRIVING PERFORMANCE IN OLDER DRIVERS

To the Editor: It has been suggested that cognitive dysfunction caused by some neurodegenerative disorders is associated with risk of traffic accidents,[1,2] but studies have reported inconsistent results for individuals in the prodromal stages of dementia who were diagnosed with mild cognitive impairment (MCI), with Clinical Dementia Rating Scale (CDR)[3] scores of 0.5 to 1.0, and few studies have directly examined the effects of MCI on driving performances of older adults who continue driving.

Recently, it was reported that MCI had a limited effect on driving performance on a driving simulator (DS),[4] but it is not clear which cognitive characteristics of individuals with MCI contribute to safer driving performance and which do not. To address this, a case–control study was designed to compare the driving performance of adults with the clinical amnestic subtype of MCI (aMCI), older adults with normal cognition, and younger adults with normal cognition, using a DS.

METHODS

Active drivers were recruited: 19 younger adults with normal cognition (NYA; aged 39.3 ± 6.5), 26 older adults with normal cognition (NOA; aged 70.0 ± 6.1), and 12 older adults with aMCI (aged 71.8 ± 7.6). The NYA and

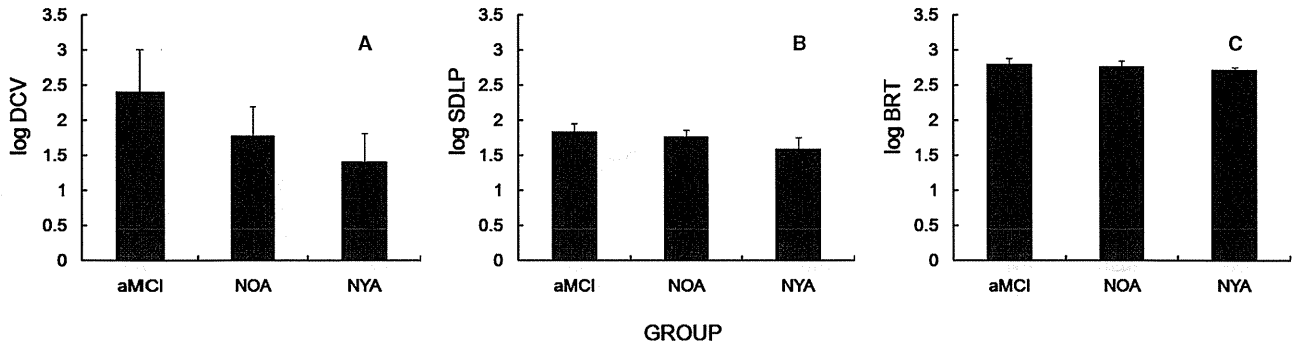

Figure 1. Means for driving task performances for each group. (A) Car-following task. (B) Road-tracking task. (C) Harsh-braking task. DCV, distance coefficient of variation; SDLP, standard deviation of the lateral position; BRT, brake reaction time; aMCI, amnestic type of mild cognitive impairment; NOA, older adults without cognitive impairment; NYA, young adults without cognitive impairment.

NOA had no impairment in activities of daily living and no evidence of cognitive decline on an enrollment screening questionnaire. The individuals with aMCI were diagnosed according to the criteria for MCI (CDR = 0.5).[5] The confirmation of amnesia was identified using psychometric methods, and all showed memory decline and preservation of general cognitive state. Additional neuropsychological measures including the Digit Span Test, the Trail Making Test (TMT) Parts A and B, the Clock Drawing Test, and the modified Stroop Test (mST), which have been used in previous studies related to complex driving tasks,[2] were also used for analyses.

The driving evaluation using a DS was performed after the neuropsychological testing was completed. Before starting the evaluation, each driver was familiarized with the DS in three practice driving trials.[6] Daily driving skills associated with traffic accidents were measured: a road-tracking, a car-following, and a harsh-braking task. These tasks were run on a DS manufactured by Toyota Central R&D Labs., Inc. (Nagakute, Japan).[7]

RESULTS

Figure 1 displays the groups' mean performance for each driving task. The aMCI group demonstrated significantly poorer performance on the car-following and road-tracking tasks than the NYA group and significantly poorer performance than the NOA group only on the car-following task. There were no significant differences between the three groups on the harsh-braking task.

Correlational Analyses

In the older group (NOA and aMCI), there were significant positive correlations between the car-following task and TMT-A, TMT-B, and mST. Multiple linear regression analyses were conducted to confirm whether these variables predicted the car-following performance better than just memory impairment did. The results showed that TMT-B score significantly predicted performance after adjusting for severity level of amnesia (β = 0.395, correlation coefficient = 0.629, adjusted coefficient of determination = 0.359).

DISCUSSION

The present study provides the first evidence of difference in driving ability between older adults with symptomatic memory impairments and age-matched cognitively normal controls. A significant difference between the two groups was observed only on the car-following task. The results indicate that there may be effects of cognitive decline on driving performances other than those of normal aging.

This finding does not correspond exactly to those of the previous study.[4] The difference may be due to the DS scenario, the characteristics of participants with MCI, or the grouping that additionally takes normal aging into account. It is not clear why driving deficits in the participants with aMCI were found only on the car-following task. Although the reason may be sought in a task difficulty or a task characteristic, it may be that drivers need the flexibility of visual attention and executive function, assessed by the TMT-B, that significantly predicted performance on the car-following task. Therefore, the TMT-B may be a useful tool for determining whether older drivers would pass or fail the actual car-following task. The results also suggest that persons with aMCI not only have memory impairment, but may require close supervision when driving because of lack of gathering and processing information.

CONCLUSION

The present study indicated a clear difference in driving ability between older adults with symptomatic memory impairment and those with age-matched normal cognition. The difference may be associated with flexibility of visual attention and executive function.

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STUDY OF DAILY DRIVING CHARACTERISTICS OF INDIVIDUALS WITH DEMENTIA USING VIDEO-RECORDING DRIVING RECORDERS

To the Editor: In recent years, there have been concerns about an increase in serious accidents and various other problems with the increase in the number of drivers who have dementia,[1–3] and urgent countermeasures are required. An objective method of measuring the driving ability of older people with dementia has not been established,[4,5] but there are few reliable and valid techniques that are appropriate for evaluating driving ability in older people and drivers with dementia who are engaged in unsafe driving. The difference in driving characteristics between individuals with and without dementia were investigated using video images recorded using a driving recorder, an in-car device that stores images taken before and after an impact.

The subjects were 28 Japanese who drive daily (18 without and 10 with dementia) (Table 1). The test was conducted from October 2007 to October 2009. The Mini-Mental State Examination[6] was administered to consenting participants, and their daily driving (~2 weeks) under typical driving conditions was recorded using the driving recorder (Witness Plus, Nihon Kotsu-jiko Kanshiki Kenkyu-jo, Ibaraki, Japan) installed in their cars. This study was performed after receiving approval from the ethics review committee at Fujita Health University School of Medicine. Researchers tabulated the incidence of potentially serious events during daily driving from foreground scenes recorded through full-time video recording. Because the number of events varied with driving time, the number was divided by the total driving time to derive the number of events per unit of driving time for each participants. The numbers derived were then compared between the two groups. In this study, events were defined as lack of attention to oncoming cars, not stopping at a stop sign, and neglect of traffic signals.

Disorders in the group with dementia consisted of Alzheimer's disease (n = 7), Alzheimer's disease plus vascular dementia (n = 2), Alzheimer's disease (frontal variant)[7,8] (n = 1). The median number of events per unit of time during daily driving was 7.9/hour in the group with dementia and 3.0/hour in the group without (P = .01). According to event type, the occurrence of not stopping at a stop sign was the most frequent event in both groups, and the group with dementia was significantly more likely not to stop at a stop sign and to neglect traffic signals (Table 1).

The American Academy of Neurology offers assessment criteria,[9] but there are no worldwide uniform criteria. A test using a car is deemed to be the most reliable in the United States, a car-dependent society.[1,9] Accordingly, a car was used for examination in the current study, but few tests have been developed to examine daily driving characteristics using a driving recorder, as in the present study. This method retains data as full-time video records of driving, which is different from recall-based surveys in which drivers recall scenes that they felt were dangerous, as in conventional analysis of occurrence of potentially serious events. Hence, this method is useful for detecting

SHORT COMMUNICATIONS

Slower adaptation to driving simulator and simulator sickness in older adults

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ABSTRACT. ***Background and aims:*** *Methods of assessing driving abilities in the elderly are urgently needed. Although the driving simulator (DS) appears to be a safe and cost-effective method of objectively evaluating driving performance, it may pose adaptation problems for elderly adults. In this study, we examined age-related adaptation deficits on the DS.* ***Methods:*** *Healthy young adults (n=15) and healthy elderly persons (n=17) completed some neuropsychological tests, and then performed a road-tracking task with the DS, which was repeated four times (Trials 1-4).* ***Results:*** *After simulated driving in DS, simulator sickness (SS) was observed in 18.8% of participants. The frequency of SS was 29.4% in elderly adults and 6.7% in young adults, and 17.6% of the elderly participants dropped out of the experiment. Performance on the Necker cube copying task was significantly correlated with the onset of SS. Driving performance also showed a significant interaction between group and trial, for both driving accuracy and vehicle speed. In addition, the performance of elderly adults significantly improved between trials 1 and 4, reaching a plateau in trial 4, whereas that of young adults did not change across trials.* ***Conclusion:*** *This study provides preliminary evidence of slower adaptation to a DS-based driving task by older adults, which was associated with cognitive aging. Age affected driving accuracy and velocity when a road-tracking task was simply repeated. It is concluded that the capacity of elderly people to adapt to DS environments should be taken into consideration when evaluating their performance on DS tasks.*
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INTRODUCTION

The proportion of licensed drivers over the age of 65 has increased with respect to two or three decades ago, and this number is expected to increase even further over the next few decades. It has been established that age-related decline, in both cognitive and perceptual and physical abilities, is associated with an increased risk of being involved in a traffic accident (1, 2). Identifying unsafe elderly drivers is therefore a critical issue in terms of individual and public safety (3, 4), and geriatric clinicians have been faced with the task of categorizing senior citizens into "safe" *vs* "unsafe" drivers (5). Valid methods for assessing the driving abilities of elderly people are urgently required.

While many consider road testing to be the gold standard by which to evaluate driving competence, road tests are costly and may be dangerous if the driver is incompetent. Although the driving simulator (DS) appears to be a safe and cost-effective method for objective evaluation of driving performance (6-9), DS applications are not without limitations, particularly when elderly adults are concerned. One important problem concerns the slower adaptation to simulation environments observed in elderly persons. When using a DS to evaluate the driving performance of elderly adults, it is necessary to discriminate between true driving abilities and age-related adaptation deficits specific to the simulator environment.

Simulator sickness (SS), or simulator adaptation syndrome, has been defined as a set of symptoms similar to those experienced after exposure to virtual interfaces, as well as to flight and driving simulators. Symptoms include headache, sweating, dry mouth, drowsiness, disorientation, vertigo, nausea, dizziness, and vomiting (10). One expla-

Key words: Driving simulator, elderly drivers, simulator sickness, learning effect, slow adaptation.

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nation is that symptoms are caused by a mismatch between visually perceived movements and the sense of movement perceived by the vestibular system, what is called the sensory conflict theory (10). Although SS is caused by several factors, aging is known to be one of them. Some studies have reported that older participants experience more SS in driving simulators than younger participants (10, 11). Cognitive variables may also play a certain role in SS; however, systematic studies have not investigated the relationship between SS and these variables, which is hindering the use of DS as an assessment tool for elderly persons with cognitive impairment.

In order to examine whether age-related adaptation deficits affect DS performance, we asked both elderly adults and young adults (controls) to drive a DS on four separate occasions, one immediately after the other, and compared the adaptation process between the two groups. In the present study, we focused on two specific markers of adaptation: the influence of simple repetition on task performance, and the occurrence frequency of SS. We also carried out a preliminary search to identify cognitive functions related to SS in elderly persons.

METHODS

Participants

We recruited 15 healthy young adults and 17 healthy elderly persons over 60 years of age. The participants were naïve with regard to this study, and were paid for their participation. They all had normal or corrected-to-normal vision, and reported no history of any psychotropic medication use, head injury with loss of consciousness, secondary neurological disorders, or drug intoxication.

None of the elderly participants showed any signs of general cognitive decline. Medical histories (including stabilograph assessment results and MRI scans) were obtained and carefully reviewed, to exclude any individuals with neuropsychiatric disease. Elderly participants with a diagnosis of dementia, and/or those with Mini-Mental State Examination (MMSE) (12) scores of 23 or less, and/or a Logical Memory delayed recall subtest score of 12 or lower on the Wechsler Memory Scale-Revised (WMS-R) (13) were excluded.

The ethics committee of the Nagoya University School of Medicine approved this study, and written informed consent was obtained from each subject prior to participation.

Tasks

Driving performance. Daily driving skills associated with traffic accidents were measured by a road-tracking task, which required participants to drive at a constant speed of 100 km/h while maintaining their vehicles at the center of a gently winding road. According to Park et al., SS emerges at a high rate in this type of DS situation, which includes high speed and multiple turns (14).

The standard deviation of the lateral position (SDLP; in cm), which indicates weaving, and the velocity (km/h) of the vehicle were used as performance measures. Recordings were made every 20 ms during the test, which lasted for 5 minutes. Details regarding the DS (manufactured by Toyota Central R&D Labs., Inc.) configuration and driving tasks used are available elsewhere (9, 15).

Evaluation of driving with the simulator was performed after neuropsychological testing was complete. Before starting the test, each driver was familiarized with the simulator by driving for a maximum of 5 minutes on a two-lane highway with no other traffic. The driving task was then repeated four times by each participant (trials 1-4).

Cognitive functions. Cognitive functions were assessed by structured performance tests selected to represent a broad range of cognitive domains, including those measured in previous studies related to complex driving tasks (16). To assess attention and executive function, the forward and backward digit span subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (17) and the paper-based Stroop Test (18) were completed. The Clock Drawing Test (CDT) (19) and Necker cube copying task (20) were completed to assess visuospatial function in elderly adults. An experienced psychologist examined all participants by the above test battery.

RESULTS

Participants were healthy young adults (n=15, 5 women and 10 men; age range, 29-43 years) and healthy elderly persons (n=17, 7 women and 10 men; age range, 60-79 years). SS was observed in 18.75% (6/32) of participants after simulated driving. The frequency of SS was 29.41% (5/17) in elderly adults and 6.67% (1/15) in young adults. This difference was not statistically significant (p=0.229, Fisher's exact test). Three elderly adults failed to complete the trials due to SS, and the data from one younger adult were excluded from following analyses, due to a mechanical problem. One-way Analysis of Variance (ANOVAs) were conducted for each neuropsychological task. The demographic characteristics of participants are listed in Table 1. The main effect of group was significant for the Stroop test ($F_{(1,26)}$=18.70, p=0.002), whereas no main effects were found for the WAIS-R digit span forward and backward tasks. Differences in cognitive functions between age groups are listed in Table 2.

In order to identify cognitive functions related to the onset of SS in elderly participants, the correlation between SS and each cognitive task score in the elderly group was analyzed. The results of Spearman's rank correlation method indicated that only the performance of the Necker cube copying test was significantly associated with the onset of SS ($\rho_{(15)}$= -0.68, p=0.002). SS was also associated with dropping out of the task (ρ(15)= -0.49,

Table 1 - *Demographic data of each age group: means ± standard deviations.*

	Elderly adults (n=14)	Young adults (n=14)
Female/male	5/9	5/9
Age (years)	66.6±4.7	35.2±5.0
Education (years)	15.1±3.0	16.0±0.0
Duration of holding a driving license (years)	43.7±7.2	15.1±5.4
Cognitive characteristics		
Mini-Mental State Examination	28.1±1.9	
WMS-R Logical Memory: immediate recall	21.2±5.9	
WMS-R Logical Memory: delayed recall	19.3±7.0	

WMS-R: Wechsler Memory Scale-Revised.

p=0.030). Table 3 lists the association between SS and each cognitive task score in the elderly group.

Figure 1 shows task performance trends from baseline to each time-point after repeating. To examine whether age-related adaptation deficits could be observed on the DS task, 2 (Group: young adults, elderly adults) × 4 (Trial: 1 to 4) factorial ANOVAs were carried out on driving performance measures. The results are summarized in Figure 1. For SDLP, the analysis revealed the main effects of group and trial ($F_{(1,26)}$=11.85, p=0.002; $F_{(3,78)}$=8.37, p=0.001). The interaction between group and trial was also significant ($F_{(3,78)}$=3.41, p=0.038). Following-up this interaction, we found a significant simple effect of group in all trials ($F_{(1,26)}$=11.09, p=0.003; $F_{(1,26)}$=13.87, p=0.001; $F_{(1,26)}$=8.50, p=0.007; $F_{(1,26)}$=5.41, p=0.028) and also a significant simple trial effect in elderly adults ($F_{(3,24)}$=8.03, p=0.001), but no such effect in young adults. Multiple comparisons with the Bonferroni adjustment were performed, and significant differences were found between trial 1 and 2 and trial 4 in the elderly group (p=0.001; p=0.001).

As regards velocity, analysis revealed the main effects of group and trial ($F_{(1,26)}$=15.95, p=0.001; $F_{(3,78)}$=15.07, p<0.001). The interaction between group and trial was also significant ($F_{(3,78)}$=11.72, p<0.001). Following up this interaction, a significant simple effect of group was found in all trials ($F_{(1,26)}$=21.86, p<0.001; $F_{(1,26)}$=12.85, p=0.001; $F_{(1,26)}$=9.62, p=0.005; $F_{(1,26)}$=7.70, p=0.010), together with a significant simple trial effect in elderly adults ($F_{(3,24)}$=12.67, p<0.001), but no such effect in young adults. Multiple comparisons with the Bonferroni adjustment were performed, and significant differences were found between trial 1 and 2 and trial 4 in the elderly group (p<0.001; p=0.044). These results showed that the performance of elderly adults improved from trial 1 to trial 4, whereas that of young adults did not change across trials. Moreover, by trial 4, the performance of the elderly group had reached a plateau.

Correlational analyses were conducted to examine the relationship between the road-tracking task trial and the neuropsychological task performance of each group. In the elderly group, there were significant negative correlations between SDLP values in the trial 3 and 4 and scores on the WAIS-R backward digit span subtest ($r_{(12)}$= -0.77, p=0.001; $r_{(12)}$= -0.60, p=0.023), and significant positive correlations between driving performance in trial 2, 3 and 4 and performance on the Stroop test ($r_{(12)}$=0.54, p=0.047; $r_{(12)}$=0.59, p=0.025; $r_{(12)}$=0.59, p=0.027). In the young group, there were significant positive correlations between SDLP values in trial 2 and scores on the WAIS-R forward digit span subtest ($r_{(12)}$=0.59, p=0.035), as well as significant negative correlations between SDLP values in trial 3 and performance on the Stroop test ($r_{(12)}$= -0.62, p=0.024). No sig-

Table 2 - *Neuropsychological scores of each age group: means ± standard deviations.*

	Elderly adults (n=14)	Young adults (n=14)	*p* (one-way ANOVA)
Clock Drawing Test	8.5±1.2		
Necker cube copying (correct/any distortion)	9/5		
WAIS-R: digit span forward	6.9±2.6	7.8±2.5	0.159
WAIS-R: digit span backward	7.4±2.5	6.7±2.0	0.667
Stroop Test (sec)	13.1±6.3	5.8±4.3	0.002

WAIS-R: Wechsler Adult Intelligence Scale-Revised.

Table 3 - *Association between occurrence of simulator sickness (SS) and cognitive functions in elderly group.*

	Simulator sickness			
	Onset SS (frequency of SS: 5/17)		SS in drop-outs (frequency of SS: 3/17)	
	Spearman's ρ	p	Spearman's ρ	p
Cognitive functions				
Clock Drawing Test	-0.34	0.142	-0.04	0.845
Necker cube copying	-0.68	0.002	-0.49	0.030
WAIS-R: digit span forward	-0.29	0.197	0.09	0.700
WAIS-R: digit span backward	-0.26	0.241	-0.17	0.445
Stroop Test	0.40	0.058	0.21	0.314

WAIS-R: Wechsler Adult Intelligence Scale-Revised.

nificant correlations were detected in the elderly group for velocity. In the young group, there were significant negative correlations between speed in trial 2 and scores on the WAIS-R forward digit span subtest ($r_{(12)}$= -0.62, p=0.022), as well as significant positive correlations between speed in trial 2 and performance on the Stroop test ($r_{(12)}$= -0.57, p=0.043).

DISCUSSION

Human behavior is dependent on dynamic interactions between people and their environment. The effects of normal aging on adaptation to the environment are controversial. Specifically, some studies have found no age-related adaptation deficits (21, 22), whereas others suggest that aging results in both slower adaptation and a reduced ability to adapt (23, 24). The present study demonstrates that aging affects both the occurrence of SS and the influence of simply repeating tasks on performance. Our results point toward the limitations of a DS to screen for unsafe elderly drivers. Protocols specifically designed to test the driving ability of senior citizens should be developed.

Our findings indicate that SS was typically observed in elderly adults. In addition, as 17.6% of our elderly drivers dropped out of the study because of SS, this result corroborates previous research (10, 11, 14). Brooks et al. speculated that one explanation of SS is the increased balance and dizziness problems experienced with aging (10). However, our older participants had no neuropsychiatric history and had normal stabilographic assessment results. This study demonstrates an association between SS onset and visuospatial function as measured by the Necker cube copying test, indicating that the increased SS in elderly people is caused by cognitive aging associated with visuospatial cognition. This finding suggests that people with compromised visuospatial cognition, such as patients with Alzheimer's disease, are more vulnerable to SS than normal elderly people.

Our study also demonstrates that the low driving accuracy of elderly persons is correlated with a decline in attention markers on later trials. Conversely, such a simple linear pattern was not found in younger adults. Rather, on the middle trials (2, 3), low driving accuracy and low velocity were correlated with high performance on attention tasks. These results suggest that variations in DS performance due to age-related adaptation deficits disappear across repeated tasks, and that DS performance directly reflects individual differences in attention and executive function. As the effects of aging on adaptive visuomotor mechanisms are a potential confounding factor (21-23, 25), the driving ability of elderly persons should be evaluated after they have reached a DS performance plateau. Repeating the driving task three times is an effective technique for adaptation to this type of DS. In addition, young adults had a different link between cognitive characteristics and adaptation to the DS in comparison with elderly adults.

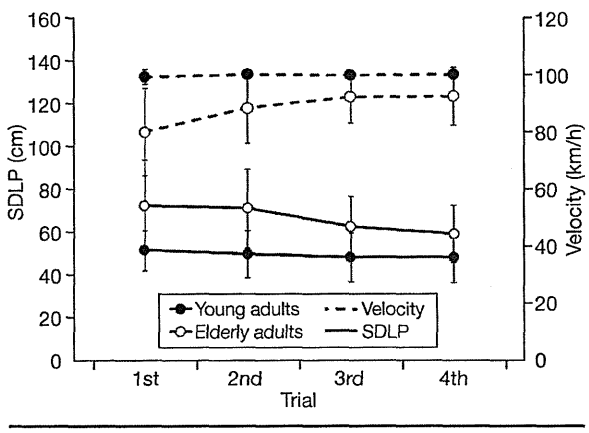

Fig. 1 - *Trends of task performances from baseline to each time point after task repetition.*

This study has several limitations. The first is that the degree of SS was not quantified. However, drop-outs who experienced severe SS were all elderly, which supports the hypothesis that SS is an age-related adaptation deficit. A second limitation was the small sample size, which should be taken into consideration when interpreting the results. Lastly, no dementia patients participated in this study.

In conclusion, this study provides preliminary evidence concerning the slower adaptation to DS-based driving tasks associated with cognitive aging in older adults. Age affected driving accuracy and velocity when a simple road-tracking task was repeated. It is concluded that DS assessment of driving skills must be performed after a certain level of practice. The external validity of DS should also be further investigated. In order to standardize DS tasks as assessment tools, further research is needed on the effects of SS on simulator performance.

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reports suggest that the 5-HT1A agonists buspirone and tandospirone are efficacious in the treatment of SSRI-induced abnormal movements, especially bruxism.[2,3]

Aripiprazole is a partial agonist/antagonist at dopamine D2 and D3 and serotonin 5-HT1A receptors and antagonist at the 5-HT2A receptors. We hypothesize that its beneficial effect on a patient's orofacial and buccal dystonia is attributable to its partial-agonist activity on dopamine receptors and above all to its partial-antagonist action on 5-HT1A receptors, jointly overwhelming its antagonism of the 5-HT2A receptors. Although anecdotal, our case suggests that low-dose aripiprazole might be a promising new treatment modality of sub-acute SSRI-induced abnormal movements.

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What is a rational antidepressant treatment for major depression in patients with Parkinson's disease?

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ABOUT 50% OF PARKINSON'S disease (PD) patients suffer from depression.[1] As the quality of life (QOL) impairment in PD patients is partly caused by psychiatric symptomatology, the treatment for depression in PD is clinically important. Although a meta-analysis raises questions about the efficacy of selective serotonin reuptake inhibitors (SSRI) for treatment of depression in PD patients,[2] SSRI are often the first choice for treatment of these patients. A recent study suggested that the efficacy of SSRI may be inferior to that of tricyclic antidepressants (TCA) for depression in PD. SSRI have the potential to worsen parkinsonian motor function and TCA have a strong anticholinergic effect and impair cardiac conduction, causing poor tolerability. Here, we describe a PD patient with depression successfully treated with mirtazapine and consider the optimal treatment strategy for depression comorbid with PD, which remains a matter of debate.

The patient is a 62-year-old woman with mild dilated cardiomyopathy. At age 61, she was diagnosed with major depression based on the symptoms of psychomotor retardation and prescribed milnacipran 75 mg/day without improvement of the symptoms. Four months later, she was diagnosed with PD by a neurologist after developing motor symptoms, including resting tremor, rigidity, and gait disturbance. Although parkinsonian symptoms were well controlled with levodopa 300 mg/day and pramipexole 1.5 mg/day during 6 months, she had gradually developed insomnia, severe appetite and weight loss, loss of interest and suicidal ideation. She was sent by a neurologist to our outpatient department of psychiatric service, diagnosed as having major depression comorbid with PD, and subsequently hospitalized. Milnacipran 75 mg/day was switched to mirtazapine 30 mg/day over 2 weeks while keeping her anti-parkinsonian medication unchanged. After fixing mirtazapine 30 mg/day, her depressive symptoms were improved without the exacerbation of parkinsonian symptoms. She was discharged home and remained in remission at 1 month after hospitalization.

Dopamine agonists (DA) are first-line therapy for motor symptoms and effective for depression in PD as well. DA can cause nausea and appetite loss by stimulating dopamine D_2 receptor in the chemoreceptor trigger zone, thus DA are not suitable for patients who have digestive symptoms. The blockade of serotonin $(5\text{-HT})_3$ receptor in the same region (e.g. by mirtazapine), can reduce DA-induced digestive symptoms. Furthermore, the worsening of extrapyramidal symptoms involving SSRI is attributed to an agonistic effect on the 5-HT_{2A} receptor at the dopaminergic nerve terminal in the *substantia nigra* and inhibition of dopamine release.[3] The blockade of 5-HT_{2A} receptor with mirtazapine might reduce this risk. According to these pharmacological profiles, mirtazapine appears to be a rational treatment option for depression in PD patients. Randomized clinical trials are warranted to confirm the effectiveness of mirtazapine in PD patients with depression.

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Valproic acid augmentation in clozapine-associated hand-washing compulsion

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OBSESSIVE–COMPULSIVE SYMPTOMS (OCS) are frequent in patients with schizophrenia.[1] This association

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has become prominent since the introduction of atypical antipsychotics for the treatment of schizophrenia, mainly clozapine.[2] Although clozapine has been reported to induce or exacerbate OCS, there is not enough data on the management of these symptoms.

We report the case of a schizophrenia patient without a history of OCS who developed clozapine-induced OCS that responded to valproic acid augmentation.

Mr S, a 51-year-old male patient, first developed paranoid delusions and auditory and visual hallucinations at the age of 23, fulfilling the diagnostic criteria of DSM-IV for schizophrenia. He had been in remission with clozapine 500 mg/day for approximately 1 year before relapse occurred as a result of treatment non-compliance. In April 2011, he was admitted with exacerbation of positive symptoms and was hospitalized. He was started on clozapine 50 mg/day and titrated up to 500 mg/day. A significant improvement was observed in positive symptoms. However, Mr S developed compulsive hand-washing behavior in the 3rd week of the treatment. He had been spending 5–8 h/day washing his hands. He did not have a history of obsessive–compulsive disorder. We assumed clozapine-induced OCS (meeting DSM-IV criteria) and gradually decreased the dosage of clozapine which resulted in aggravation of positive symptoms and elevated mood. Therefore, valproic acid 1000 mg/day was added to the regimen of clozapine 500 mg/day. Two weeks after starting valproic acid (serum level 77.8 mg/L), Mr S's positive symptoms and elevated mood were significantly reduced and his compulsive hand-washing had disappeared. During 3 months of follow up, he remained well under a combined treatment with clozapine (500 mg/day) and valproic acid (1000 mg/day) and there was no reemergence of his compulsion.

Our patient developed hand-washing compulsion during treatment with clozapine which disappeared after augmentation of valproic acid. Although the exact mechanism is not known, the development of OCS associated with clozapine use has been explained by the central serotonergic receptor blocking effects of this drug.[1]

Although a few case reports have mentioned the efficacy of valproic acid in the treatment of OCD in the literature,[3] there is only one case report showing alleviation of clozapine-induced OCD symptoms with valproic acid augmentation in a patient with schizophrenia.[4]

We suggest that valproic acid may be a choice when treating OCS, which may appear as the adverse effect of atypical antipsychotics in patients with schizophrenia. Randomized controlled trials are required to establish the efficacy of valproic acid in the treatment of antipsychotic-induced OCS before definitive conclusions can be reached.

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Risperidone augmentation with amisulpride: The blue-tongue sign

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THE BLUE-TONGUE SIGN is a strikingly blue tongue due to selective D2 dopamine antagonism. The blue-tongue sign occurs rarely in young women treated with metoclopramide; blue tongues have been anecdotally associated with haloperidol therapy.[1] We would like to report an uncommon and disturbing side-effect of risperidone augmentation with amisulpride. Our case is at variance with the traditional view that abnormal skin pigmentation is irreversible or only partially reversible.[2,3]

A 23-year-old man was admitted to a psychiatric closed ward because of aggravated psychotic symptoms. His chief complaints were auditory hallucination and paranoid delusions. Brain magnetic resonance imaging, electroencephalography, and laboratory examination were done to evaluate organic causes. He was diagnosed with schizophrenia after mental status examination. Medication for him was started with risperidone 6 mg and increased to 8 mg. On 6 weeks of admission, risperidone was augmented with amisulpride 200 mg for relieving the persisting nominal psychotic symptoms. From 7 weeks of admission, his psychotic symptoms were relieved with risperidone 6 mg augmentation with amisulpride 600 mg. During the follow up in the outpatient clinic, he complained of abnormal tongue pigmentation at 3 weeks of discharge. His tongue resumed its normal color after a 2-week observation without antipsychotics discontinuation or replacement of other neuroleptics.

This case indicates that risperidone augmentation with amisulpride-induced abnormal tongue pigmentation would be completely reversible without antipsychotics discontinuation or replacement of other neuroleptics. Also the blue-tongue sign could be the crossroad for understanding the pathophysiological mechanism of dopamine pathway in which most neuroleptics are involved for treating psychotic symptoms.

L-3,4-dihydroxyphenylalanine (L-DOPA) from tyrosine is converted to dopamine by the dopa decarboxylase enzyme. Simultaneously, DOPA from tyrosine will be changed to dopaquinone. This dopaquinone is sequentially converted to three kinds of melanin (pheomelanin, eumelanin, and neuromelanin). An explanatory hypothesis for the abnormal

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Reliability and validity of a new sexual function questionnaire (Nagoya Sexual Function Questionnaire) for schizophrenic patients taking antipsychotics

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Objective This study aims to validate a new user-friendly sexual function questionnaire (Nagoya Sexual Function Questionnaire [NSFQ]) for schizophrenic patients taking antipsychotics.
Methods Schizophrenic outpatients (men = 30, women = 30) were asked to fill out the NSFQ at initial entry into the research program ($Time_1$) and again 1 to 2 weeks later ($Time_2$). To assess the convergent validity of the NSFQ, at $Time_1$, subjects were asked to fill out the Japanese version of the Udvalg for Kliniske Undersogekser Side Effect Rating Scale (UKU). To assess the discriminant validity of the NSFQ, at $Time_1$, subjects were also asked to fill out the Japanese version of Epworth Sleepiness Scale.
Results Results from Cronbach's alpha analysis indicated that the NSFQ demonstrated excellent internal consistency and scale reliability. The NSFQ also demonstrated strong test–retest reliability. The NSFQ total score was highly correlated with the UKU total score. The NSFQ was shown to have good convergent validity with the UKU. The NSFQ total score was not correlated with the Japanese version of Epworth Sleepiness Scale total score.
Conclusions This study revealed the internal consistency, test–retest reliability, and convergent and discriminant validities of the NSFQ.

KEY WORDS—sexual dysfunction; rating scale; antipsychotic agents; validation; schizophrenia

INTRODUCTION

Despite the fact that several lines of evidence have shown that sexual dysfunction is a common symptom in patients with schizophrenia (Kotin *et al.*, 1976; Ghadirian *et al.*, 1982; Smith *et al.*, 2002; Cutler, 2003), physicians usually tend to overlook or disregard sexual dysfunction during the psychiatric evaluation of psychotic patients. For example, Ghadirian *et al.* (1982) reported that more than 50% of men and 30% of women experience some sort of sexual dysfunction during conventional antipsychotic treatment. Furthermore, Fakhoury *et al.* (2001) showed that discomfort associated with sexual dysfunction is common among patients and is more frequent in men (68%) than in women (49%). Moreover, Segraves (1989) demonstrated that men taking traditional antipsychotics were more likely to experience side effects affecting the reproductive system (30–60%), and the main problems were related to erection and ejaculation.

Sexual dysfunction in such patients may be due to various factors, including the symptoms of schizophrenia (Aizenberg *et al.*, 1995), the secondary effects of living with a severe and chronic mental health condition, or the adverse effects of the antipsychotics or other medications (Smith *et al.*, 2002). Knegtering *et al.* and Montejo Gonzales *et al.* reported that prolactin-raising drugs (e.g., risperidone) provoke significantly higher rates of sexual dysfunction (40–60%) in comparison with prolactin-sparing drugs (quetiapine, ziprasidone, and aripiprazol) (<30%) (Knegtering *et al.*, 2004; Montejo Gonzalez *et al.*, 2005; Knegtering *et al.*, 2006; Montejo *et al.*, 2008a, 2008c, 2010a, 2010b). These results have also been confirmed in a meta-analysis (Serretti and Chiesa, 2011).

The previously mentioned studies presented data that showed a relatively high rate of sexual dysfunction in patients with schizophrenia, and the prolactin-raising drugs provoke significantly higher rates of sexual dysfunction than prolactin-sparing drugs. From the

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clinical point of view, it is important to be aware of sexual dysfunction in patients with schizophrenia and apply the knowledge of sexual dysfunction to the treatment of schizophrenia, because this symptomatology is relatively common among patients and may contribute to poor quality of life and poor adherence with therapy (Olfson *et al.*, 2005; Gopalakrishnan *et al.*, 2006). The prevalence of sexual concerns differs in healthy individuals according to ethnicity. The situation is complicated by the reluctance of psychiatric staff (i.e., psychiatrists, nurses) to discuss sexual concerns with patients (Wolfe and Menninger, 1973; Withersty, 1976). This problem is more pronounced in far eastern countries, perhaps due to socio-cultural reasons (Moreira *et al.*, 2005, 2006). Therefore, it is very difficult to evaluate sexual dysfunction of schizophrenic patients on the basis of clinical samples collected in Asian populations. Conversely, in developed countries, there are many instruments intended to be used for the assessment of sexual dysfunction (e.g., the Arizona Sexual Experience Scale [ASEX] (McGahuey *et al.*, 2000), the sexual part of Udvalg for Kliniske Undersogekser Side Effect Rating Scale [UKU] (Lingjaerde *et al.*, 1987), Psychometric properties of the Psychotropic-Related Sexual Dysfunction Questionnaire [SALSEX] (Montejo *et al.*, 2000, 2008b), and the Changes in Sexual Functioning Questionnaire [CSFQ] (Clayton *et al.*, 1997)). Although most instruments are very useful, some of them are rather long (CSFQ has 36 items for men and 35 items for women), intrusive (particularly for Asian patients and clinicians, who feel very embarrassed about discussing sexual concerns; the contents of ASEX, UKU, and SALSEX include vaginal dryness, vaginal lubrication, and orgasmic dysfunction), and difficult to use (UKU involves a semi-structured interview).

The problems of existing sexual dysfunction questionnaires can be divided into three categories: (i) the scales are complicated, and the items are not always straightforward so that schizophrenic patients may not be able to answer correctly because of their cognitive deficit (CSFQ); (ii) for some patients and clinicians who feel very embarrassed about discussing sexual concerns (Asian people in particular), it may be difficult to use such scales because the scale items are related to very private issues (ASEX, UKU, and SALSEX); and (iii) because the scale is not user friendly or brief, clinicians are not willing to use it in their routine work (CSFQ and UKU).

Thus, in order to address the problem of evaluation of sexual dysfunction in schizophrenic patients, we designed a brief, seven-question instrument called the Nagoya Sexual Function Questionnaire (NSFQ) (Appendix). The NSFQ is designed to be short, minimally intrusive, and self-administered, regardless of the availability of a sexual partner. We also tested the internal consistency, test–retest reliability, and convergent and discriminant validities of the NSFQ in assessing sexual dysfunction among schizophrenic patients taking antipsychotics.

METHODS

Development of the measure

The NSFQ is a self-administered sexual function scale. The NSFQ was developed through the collaborative effort of specialists in psychiatry and in urology. The NSFQ consists of seven items. Each item is evaluated on a five-point scale: (1) = not at all; (2) = almost never; (3) = sometimes; (4) = often; (5) = always; and (6) = unsure. As mentioned previously, some patients and clinicians, especially those with an Asian background, feel very embarrassed about discussing sexual concerns. Some of them may refuse to address intrusive questions. Although we did not want to insist that patients answer, we wanted to avoid missing values. Therefore, we included the answer "(6) = unsure" as a possible answer for intrusive items, such as sexual interest, sexual confidence, erection, ejaculation, and sexual arousal. We think that the answer "(6) = unsure" is useful for patients and clinicians who feel embarrassed about discussing sexual concerns, especially among the Japanese population. Answers of (1) through (5) are assigned scores of 1 to 5 points, respectively, and (6) is assigned 1 point. Finally, the clinician calculates the total score. The items for men are (1) = pulsating sensation in the breast/mammary area; (2) = galactorrhea; (3) = interest in women; (4) = sexual interest; (5) = sexual self-confidence; (6) = erectile dysfunction; and (7) = ejaculatory dysfunction. The items for women are (1) = menstrual irregularity; (2) = pulsating sensation in the breast/mammary area; (3) = galactorrhea; (4) = interest in men; (5) = sexual interest; (6) = sexual self-confidence; and (7) = sexual arousal. Subjects were asked to answer questions 6 and 7 if they gave scores of (2)–(5) for questions 1–5.

With respect to the development of items for the NSFQ, the following were considered. Galactorrhea is rare in men, but 11% of men developed both galactorrhea and gynecomastia during prolactin-raising drug treatment (risperidone) (Kelly and Conley, 2006). Additionally, because men are especially reluctant to discuss galactorrhea, items 1 and 2 might be useful for

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further research on this side effect. Furthermore, patients and clinicians who feel embarrassed to talk about sexual concerns (Asian people in particular) may feel discomfort when discussing female orgasm. For the previously mentioned reason, we include sexual arousal as a substitute for orgasmic dysfunction. Moreover, from the evidence about the association between hyperprolactinemia and sexual dysfunction (Haddad and Wieck, 2004), we include not only sexual dysfunction but also side effects related to the reproductive system, which are related to increased prolactin levels, as items of the NSFQ.

Subjects

Data were collected from October 2009 to August 2010. The subjects' demographic characteristics are presented in Table 1. The subjects were consecutive, stable outpatients with a diagnosis of schizophrenic disorder according to Diagnostic and Statistical Manual of Mental Disorders Fourth Edition criteria who had been stabilized on antipsychotic medication for at least 2 months. Subject recruitment was carried out by approaching all patients during the study period. The subjects were assured that their responses would be both confidential and anonymous. All subjects were provided with a written description of the study and its objectives. The subjects gave their informed consent to participate, and the study was approved by the Ethics Committee of the Nagoya University School of Medicine.

Procedures

The subjects were asked to fill out the NSFQ at initial entry into the research program ($Time_1$) and again 1 to 2 weeks later ($Time_2$). To assess the convergent validity of the NSFQ, at $Time_1$, the subjects were asked to fill out the Japanese version of the UKU Side Effect Rating Scale. Because only the UKU has been translated into Japanese and validated in Japanese patients (Itoh *et al.*, 2010), the UKU was chosen. The UKU, which is administered by a semi-structured interview, consists of the following items: sexual dysfunction side effects (increased or diminished sexual desire; erectile, ejaculatory, or orgasmic dysfunction; and vaginal dryness) and somatic side effects related to the reproductive system (menorrhagia, amenorrhea, galactorrhea, and gynecomastia). As in the original version of the UKU, each item was scored on a four-point scale: 0 = none or doubtful; 1 = present to a mild degree; 2 = present to a moderate degree; and 3 = present to a severe degree. The UKU consists of six items for men (gynecomastia, increased or diminished sexual desire, and erectile, ejaculatory, or orgasmic dysfunction) and seven for women (menorrhagia, amenorrhea, galactorrhea, increased or diminished sexual desire, orgasmic dysfunction, and vaginal dryness). To assess the discriminant validity of the NSFQ, at $Time_1$, the subjects were also asked to fill out the Japanese version of the Epworth Sleepiness Scale (JESS), which is a scale for sleepiness (Johns, 1991).

Statistical methods

Internal consistency of the NSFQ scale, a measure of scale reliability, was assessed using Cronbach's alpha analysis. Cronbach's alpha is an index of correlation among items on a scale. To determine the test–retest reliability of the NSFQ, bivariate correlations were performed of total NSFQ scores obtained at the initial administration ($Time_1$) and then again 1 to 2 weeks later ($Time_2$). In order to assess the convergent validity of the NSFQ, bivariate correlations were performed between the NSFQ total score and the UKU total score. Discriminant validity of the NSFQ was assessed by performing bivariate correlations between NSFQ total scores and JESS total scores. All analyses were performed using JMP version 5.1.2 (SAS Institute, Inc., Cary, NC). Spearman's rank correlation coefficient was calculated for categorical variables. A p-value less than 0.05 was considered significant.

RESULTS

Results

The total score of each scale is summarized in Table 2. The number of patients with NSFQ item scores of three or higher and four or higher and UKU item scores of one or higher and two or higher are summarized in Table 3.

Table 1. Characteristics of patients

Sex	*N*	Age	Dose (mean mg/day ± SD, CP equivalent)	Duration of illness (mean months ± SD)	Duration of treatment (mean months ± SD)
Male	30	34.9 ± 7.5 (17–45)	621.0 ± 369.9	116.7 ± 96.7	135.8 ± 97.6
Female	30	36.1 ± 7.7 (17–45)	598.5 ± 309.0	146.4 ± 183.1	122.4 ± 90.2

SD, standard deviation; CP, chlorpromazine.

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Table 2. Total scale score

	NSFQ ($Time_1$)	NSFQ ($Time_2$)	UKU	JESS
Male	12.2±4.89	10.9±4.66	2±2.71	6.17±4.75
Female	15.5±6.16	15.47±6.25	2.29±2.49	7.17±3.86

NSFQ, Nagoya Sexual Function Questionnaire; UKU, Udvalg for Kliniske Undersogekser Side Effect Rating Scale; JESS, Japanese version of the Epworth Sleepiness Scale.

Table 3. Number of patients with sexual dysfunction on the Nagoya Sexual Function Questionnaire and the Udvalg for Kliniske Undersogekser Side Effect Rating Scale

	NSFQ: <3	UKU: <1	NSFQ: <4	UKU: <2
Male	16 (53.3%)	17 (56.7%)	6 (20%)	8 (26.7%)
Female	21 (70%)	22 (73.3%)	13 (43.3%)	14 (46.7%)

NSFQ, Nagoya Sexual Function Questionnaire; UKU, Udvalg for Kliniske Undersogekser Side Effect Rating Scale.

Reliability

Results from Cronbach's alpha analysis indicated that the NSFQ demonstrated excellent internal consistency and scale reliability (men, alpha = 0.764; women, alpha = 0.7918). The NSFQ also demonstrated strong test–retest reliability (men, $r = 0.92$, $p < 0.001$; women, $r = 0.92$, $p < 0.001$).

Validity

To assess the convergent validity of the NSFQ, bivariate correlations were performed between the NSFQ total score and the UKU total score. The NSFQ total score was highly correlated with the UKU total score (men, $r = 0.69$, $p < 0.001$; women, $r = 0.85$, $p < 0.001$). The NSFQ was shown to have good convergent validity with the UKU. The discriminant validity of the NSFQ was assessed by performing bivariate correlations between the NSFQ total score and the JESS total score. The NSFQ total score was not correlated with the JESS total score (men, $r = 0.45$, $p = 0.01$; women, $r = 0.16$, $p < 0.4$). Thus, the NSFQ has been validated.

DISCUSSION

The results of the current study demonstrate that the NSFQ has internal consistency and is a reliable, valid tool for measuring sexual dysfunction. The NSFQ is shorter and less intrusive than other sexual function instruments, and it is self-administered (Table 4). Thus, the NSFQ can be easily, conveniently, and repeatedly administered. Furthermore, NSFQ items include not only sexual dysfunction (sexual interest, erectile dysfunction, and ejaculatory dysfunction) but also side effects related to the reproductive system (gynecomastia, menstrual irregularity). Thus, the NSFQ can be used to evaluate the degree of male and female general dysfunction and assess sexual function and somatic effects separately. As shown in Table 4, the number of patients with sexual dysfunction indicated by the UKU (UKU item score of one or higher and two or higher) and the number of patients with sexual dysfunction according to the NSFQ (NSFQ item score of three or higher and four or higher) were almost the same. Accordingly, the NSFQ is as good as the UKU for identifying sexual dysfunction. Fujii *et al.* (2010) researched the prevalence of sexual dysfunction in Japanese schizophrenic patients by using the UKU. The rates of male sexual dysfunction among patients were the same for the current study and Fujii's study, whereas the rate of female sexual dysfunction in the current study was higher than in Fujii's study (men: UKU ≥ 1, 105 [59.3%]; UKU ≥ 2, 58 [32.8%]; women: UKU ≥ 1, 86 [49.1%]; UKU ≥ 2, 55 [31.4%]).

Several limitations of this study should be considered when interpreting the results. First, the sample size was relatively small, but it is important to note that major sexual function scales such as ASEX and SALSEX were validated using the same or even smaller sample sizes (ASEX, men = 23, women = 35;

Table 4. Comparison among sexual dysfunction scales

	NSFQ	SALSEX	ASEX	UKU	CSFQ
Number of questions	7	7	5	M: 6, F: 7	M: 36, F: 35
Intrusive or not	Not	Intrusive	Intrusive	Intrusive	Intrusive
Including question of sexual dysfunction	Yes	Yes	Yes	Yes	Yes
Including question of reproductive side effect	Yes	No	No	Yes	No
Self or clinician administered?	Self	Clinician	Self or clinician	Clinician	Self or clinician
Semi-structured interview	No	No	No	Yes	No

NSFQ, Nagoya Sexual Function Questionnaire; SALSEX, Psychometric properties of the Psychotropic-Related Sexual Dysfunction Questionnaire; ASEX, Arizona Sexual Experience Scale; UKU, Udvalg for Kliniske Undersogekser Side Effect Rating Scale; CSFQ, Changes in Sexual Functioning Questionnaire.

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SALSEX, men = 37, women = 8); however, the present sample may not be representative of schizophrenic patients in general. For example, subjects younger than 17 years and those older than 45 years were not tested. Future studies should be conducted in untreated schizophrenic patients, healthy subjects, and patients in other cultures and countries, healthy controls, and patients with other mental disorders including mood disorders. Specifically, if future studies validate the NSFQ in different population settings, the NSFQ could be used for patients who are embarrassed to discuss sexual dysfunction openly, not only in Japan but also in other countries.

The second limitation of this study is that only high NSFQ scores were initially considered to reflect sexual dysfunction. However, we subsequently realized that subjects suffering from premature ejaculation or spontaneous orgasm (reflected in extremely low NSFQ scores) could also be considered to have sexual dysfunction. In the future, analyses should focus both on extremely low and extremely high NSFQ scores, given that sexual dysfunction can involve both hyperfunction and hypofunction.

The third limitation of the current study is that the NSFQ evaluation of sexual dysfunction is based on subjective interpretation of the symptoms. A lack of sexual activity, for example, is not always perceived as sexual dysfunction, because personal views (i.e., religious or other) can often give a specific color to the topic that is sometimes considered to be a "taboo." Who ultimately decides when sexual dysfunction is present? Is the patient's self-report the deciding factor, or should it be left up to the clinician or a score on a questionnaire? Clearer guidelines defining the boundaries of sexual dysfunction for use in clinical and research studies should be developed.

The fourth limitation of this study is that the Japanese version of UKU was chosen for convergent validity of the NSFQ. In future research, we hope that the NSFQ will be validated by considering convergent validity with SALSEX, ASEX, or other sexual function scales.

CONCLUSIONS

The current study developed a new sexual function questionnaire that is short and easier to answer than other traditional scales, and its high validity and reliability were confirmed. The NSFQ may be used widely as a measure of sexual dysfunction, which patients hesitate to discuss, and contribute to helping patients and clinicians discuss sexual dysfunction with each other, with the goal of improving psychiatric patients' quality of life and adherence with therapy.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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APPENDIX A: NAGOYA SEXUAL FUNCTION QESTIONNAIRE (NSFQ)—MALE VERSION. SYMPTOMS OF PSYCHIATRIC DISEASE OR THE SIDE EFFECTS OF DRUGS A PATIENT IS TAKING SOMETIMES AFFECT HIS OR HER SEXUAL LIFE, SUCH AS MENSTRUAL IRREGULARITY IN THE CASE OF A FEMALE PATIENT.

The questions in the following paragraphs are related to a situation that may be related or lead to sexual activity. For each item, please indicate your *overall* level for *one month*, including *today*.

(1) How often do you feel a pulsating sensation in the breast area?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(2) Have you noticed a milky discharge from your nipples?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(3) How often do you notice a loss of sexual interest in women as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(4) How often do you feel less interested in sexual matters as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(5) How often do you feel less confident sexually as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

If you gave responses of (2)–(5) for questions 1–5, please answer questions 6 and 7.

(6) How often do you feel that you are experiencing more problems related to erection as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

(7) How often do you feel that you are experiencing more problems with ejaculation as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

NAGOYA SEXUAL FUNCTION QESTIONNAIRE (NSFQ)—FEMALE VERSION. SYMPTOMS OF PSYCHIATRIC DISEASE OR THE SIDE EFFECTS OF DRUGS A PATIENT IS TAKING SOMETIMES AFFECT HIS OR HER SEXUAL LIFE, SUCH AS MENSTRUAL IRREGULARITY IN THE CASE OF A FEMALE PATIENT.

The questions below are related to a situation that may be related or lead to sexual activity. For each item, please indicate your *overall* level for *one month*, including *today*.

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(1) How often do you experience menstrual cycle irregularities?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(2) How often do you feel a pulsating sensation in the breast area?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(3) Have you noticed a milky discharge from your nipples?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(4) How often do you notice a loss of sexual interest in men as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always.

(5) How often do you feel less interested in sexual matters as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

If you gave responses of (2)–(5) for questions 1–5, please answer questions 6 and 7.

(6) How often do you feel less confident sexually as compared with before?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

(7) How often do you find yourself not being sexually aroused when in fact you thought you would be?

(1) = Not at all, (2) = almost never, (3) = sometimes, (4) = often, (5) = always, (6) = unsure.

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