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Research Article

Relationships between Urination Dysfunction (UD) and Brain Functions of Middle and Upper-Middle Aged Community Dwellers: Evidence from the Yakumo Study

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ABSTRACT

Aim: To compare the cognitive and physical abilities between upper-middle aged participants who have experienced Urination Dysfunction (UD) during last 4 weeks and intact control participants.

Methods: In total 694 upper-middle aged participants (age ranged from 40 to 89 years old) were given a questionnaire for UD, cognitive tests (Digit Cancellation Test: D-CAT, and Logical Memory Test: LMT) and physical ability tests (Timed-get-Up and Go test: TUG and postural tremor test), individually.

Results: We compared cognitive and physical abilities test performances between UD and Intact control group participants.

Conclusion: The performance in a cognitive test, D-CAT, assessing prefrontal cortex function, and performance in tests of physical abilities including agility (TUG), were inferior in UD participants compared to the control group. However, there were no group differences in tests of LMT, physical balance, or BMI. These results strongly suggest that brain function is a risk factor for UD and health promotion staff of local governments should prepare proper measures to delay the onset of UD.

Keywords: Urination dysfunction; Prefrontal function; Physical agility; Aged community dwellers; Body mass index

INTRODUCTION

Urination dysfunction (UD), such as urinary urgency (UU), pollakiuria, Urinary Inconsistent (UI), is a cardinal geriatric syndrome. Its prevalence increases with advancing age, and it is more prominent in women than in men [1,2]. The UD is a problem not only to older adults in nursing homes but also to upper-middle aged non-disabled people in their daily life [3,4]. Therefore, measures to prevent problems associated with UD from middle age are an important issue in an aging society.

Studies on the brain mechanisms of mainly on UI have accumulated [5,6]. Smith et al. reported that all potential correlates of UI, including sociodemographic characteristics, BMI, smoking history, physical activity medical comorbidity, physical performance, activities of daily living impairment, use of ambulatory assistive devices, physical and mental Health-Related Quality Of Life (HRQoL), and depressive symptoms, have been investigated [7]. Evidence has accumulated that neural circuits in the frontal areas controlling behavior, including those involved in decision-making, attention processes, and integration of extrinsic input, also participate in urinary control. Buschbeck et al. reported that the supplementary motor area, midcingulate cortex, insula, frontal operculum, and right prefrontal cortex were consistently more active when the desire to void was enhanced compared to engaging in a baseline task when bladder sensations were suppressed [8]. Moreover, the right anterior insula and midbrain Periaquaeductal Grey (PAG) are more active at higher than at lower bladder volumes. Sakakibara reported that an overactive bladder reflects damage to the prefrontal

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cortex, cingulate cortex, and other areas regulating the micturition reflex [9]. Furthermore, the influence of higher cortical areas other than the involvement of the peripheral and basal ganglia has also been discussed. Therefore, neuroimaging studies have shown that frontal cortical regions are involved in controlling the micturition. These pioneering studies suggested a link between UI and frontal lobe dysfunction.

Nevertheless, there are only such studies and mainly limited to studies conducted by urologists, and the results are not readily available to local government health-promoting officials and public health nurses. Furthermore, urologists that examined the relationship between UI and cognitive function have not necessarily relied on the latest neuropsychological research methods.

A previous study conducted by Hatta, et al., suggested a substantial relationship between UI and the decline of prefrontal cortex function [10]. However, this our previous study had several shortcomings describe later. Furthermore, Huang et al. failed to find a significant association between cognitive decline and UI [11]. As a result, the relationship between UI and the decline of cognitive function remains controversial.

The current study was designed to address the weaknesses of previous studies by using a strict definition of UD based on standardized test, a larger sample, and add physical performance tests. In short, main purpose of this study was to replicate or validate the finding of strong relationship between UD and frontal lobe dysfunction of our previous studies from a different cohort to demonstrate the relationships between UD (including not only UI but pollakiuria and UU) and frontal lobe dysfunction.

Hatta et al. provided empirical evidence of the relationship between UI and cognitive decline based on the working model of Circuit 1 in Griffth by using the Nagoya University Neuropsychological Assessment Battery (NU-CAB) [6,10]. The comparison between UI and Control groups showed no group differences in the Money Road Test or LMT. However, the UI group was significantly inferior to the control irrespective of sex in D-CAT and letter fluency tests. These results supported the working model that the UI group had frontal lobe function problems.

Moreover, several recent studies have reported a strong association between physical activity and urinary tract symptoms in middle-aged women [12]. However, relationships between UI and physical abilities have not been examined to date. In addition, BMI is regarded as one of the essential factors in urinary and erectile functions in many western societies [13]. Nevertheless, the effects of BMI (Body Mass Index) on Japanese UD participants have not been investigated to date.

Then, we are trying to replicate our previous findings using different learger cohort than before considering to compensate for weaknesses of previous studies and newly investigate therelationshiops between UD and brain functions from a cognitive and a physical perspective. Additionally, we aimed to examine the effect of physical motor functions and BMI on UD. It is expected that the findings would provide lead to guidelines for local government health promotion staff on how to delay the onset of UD, which is expected to reduce the financial and social burden in contemporary aged society.

MATERIALS AND METHODS

Participants

Participants were 694 community dwellers who participated in the Yakumo Study during from 2012 to 2014. The Yakumo study is an on-going cohort study that was inaugurated in 1981. Researchers from various fields, such as epidemiology, internal medicine, orthopedics, urology, ophthalmology, otolaryngology, and neuropsychology, have participated in the Yakumo Study [14]. The data for the current study were obtained from three sections of the Yakumo study; neuropsychology, orthopedics, and urology. Participation in the study was voluntary, and all the participants could manage their everyday life by themselves. Some participated annually, whereas others participated just once or twice. The first year's data were used for the analysis in the case of these participants.

The participants were selected by the following criteria; responding to the questionnaire without missing items, who were examined in the neuropsychology, orthopedics, and urology departments, and were over 40 years of age. The participants showed no signs of serious frailty syndromes such as metastasized neoplastic diseases, psychiatric illnesses, or signs of dementia. Informed consent was obtained from all the participants. Participants whose MMSE scores were below 26, as calculated by NU-CAB, were excluded from the data analysis. The basic characteristics of the participants are shown in Table 1.

Group		Urinary dysfunction	Intact control
Number of participants	Women	177	206
	Men	79	232
Age	Women	64.81 (9.93)	61.29 (9.85)
	Men	69.94 (8.21)	64.56 (9.54)
Years of Education	Women	11.04 (2.20)	11.66 (2.48)
	Men	11.61 (1.93)	11.84 (2.50)

Table 1: Demographic data of participants.

Measures of UD

The UD was assessed by the questionnnair Overactive Bladder Symptom Score (OABSS) followed by Honma, Yoshida, Ohara, et al. [15]. This was created based on Japanese cases with symptoms specific to overactive bladder and consists of four questions: daytime urination, nocturia, urgency, and urge incontinence. The questionnaire asks about the symptoms for the past 4 weeks for 4 items and calculates the total score. It is distributed from 0 to 15 points, 5 points or less is mild, 6-11

points is moderate, 12 points or more is severe. It is a diagnostic criterion to judge. The OABSS was distributed to all participants about 3 weeks before the Yakumo-Town health checkup project, and this is part of the survey item "Minna no Kenko", a questionnaire that required submission at the checkup venue. The staff individually checked for omissions at the admission desk of the health checkup venue. In this study, participants with OABSS 0 points were in the Intact control group, and participants with 6 points or more were in the UD group.

Cognitive assessment

The NU-CAB was employed to assess the participants' cognitive abilities. The NU-CAB is mainly used for the assessment of an individual's frontal cortex related abilities, such as attention, language, memory, working memory, and executive functions. The reliability and validity of the NU-CAB have been reported elsewhere [16]. The NU-CAB consists of several sections such as a Word Recall Test (WRT), a Logical Memory Test (LMT), a Digit Cancelation Test (D-CAT1 and D-CAT3), the Money Road-Map Test (MRT), Stroop test, Letter Fluency Test (LFT) and Semantic Fluency Test (SFT). As described earlier, our previous study has demonstrated significant differences between UI and a control group in the D-CAT1, whereas no differences were indicated in the LMT. Therefore, to address the aim of the present study, we analyzed the same indices, D-CAT1 and LMT.

The D-CAT1 assesses the information processing speed, focusing on attention, and sustained concentration, which is related to the executive function in Baddeley's theory of working memory. The D-CAT is a paper and pencil screening test of attention. This test is based on Sohlberg and Matter's attention model consisting of five hierarchical classifications, in which each component of the hierarchy requires the effective functioning of the preceding component. As people's capacity for paying attention to daily activities is crucial for the successful completion of everyday tasks, there are several kinds of target cancellation test in a limited period, types, the used D-CAT test sheet consisted of 12 rows of 50 digits. Each row contains five sets of numbers ranging from 0-9 that are arranged in random order. Participants are instructed to search for target numbers (6) and delete each target number with a slash, as fast and accurately as possible until the experimenter gives a signal to stop. In the current study, the experimenter stressed that all the target numbers should be canceled without any omissions. The LMT was also used as the measure primarily reflecting the temporal and frontal functions. This LMT was the Japanese version of the Wechsler Memory Scale. In the LMT, the examiner reads a short story consisting of 25 segments twice. The participants were asked to recall the story immediately. Each segment that was correctly recalled were assigned a score of 1-point, such that the total score ranged from 0 to 25 points.

Assessment of physical activity

Orthopedic surgeons examined the participants for the presence or the absence of morphological abnormalities of the knees, hips, and the spine based on radiography and also assessed a range of muscle movements, as well as bone density, among others. They also conducted the individual timed-get-up and go (TUG) tests, and a balance test by using a stabilometer. In this study, we employed the TUG index as an indicator of physical and motor agility and the stabilometer index as an indicator of balance.

The TUG is a well-known mobility test for older adults that assess the time taken to complete a task [17]. In the TUG, the examiner asks participants to do a series of tasks, such as standing up from a seated position, walk straight 3 m, turn, stop, and sit down. In the current study, the examiner measured the time required to complete the above tasks twice by using a stopwatch. To assess the balancing ability, the postural tremor was measured by using a stabilometer (Anima GW 5000, Anima Co.,Tokyo). In the current study, two examiners, an orthopedic surgeon, and an assistant measured the postural tremor of each participant. First, the participant stood still for 60 seconds with their eyes open; then, an eye mask was used to cover their eyes, and they were again asked to stand still for 60 seconds. The participants placed their feet on the foot shapes of the device and stood upright with both arms at their side, observing a fixation point 2 meters ahead. The oscillation of the center of gravity during this time was measured. In this study, the ENV AREA score in the open eye condition was used as a fundamental parameter of the body balancing ability while standing.

BMI (Body Mass Index)

The BMI was calculated from the height and weight measured on the day of the screening based on the formula, weight/height 2.

RESULTS

Mean performance, performance ranges and SDs of cognitive and physical activity tests are shown in Table 2. Performance score transformed into Z scores to conduct statistical analyses and it is shown in Table 3.

Statistical analyses using Z scores were conducted by t-tests. The results indicated a significant group difference between UD and Control groups in D-CAT1 and TUG scores, with the performance of the UD group being inferior to that of the Control group. However, there were no significant between-group differences in the LMT, ENV AREA, or BMI. Figure 1 shows group differences in these measures. These results suggest that not only prefrontal cortex related cognitive functions but also brain areas related to physical agility have deteriorated in UD compared to control participants.

	Range	Mean	SD
D-CAT1	Sep-48	26.72	6.8
LMT	0- 25	16.16	4.79
TUG	2.77 - 35.45	6.4	1.66
ENV area	0.51 - 13.11	2.69	1.5

BMI	14.00 - 43.70	23.77	3.49

Table 2: Mean performances and rage of measures.

	UD group (N=256)		Intact control group (N=438)		Statistic results	
	Mean	SD	Mean	SD	t score	p score
D-CAT1	-0.21	0.97	0.12	1	4.244	0
LMT	-0.02	0.92	0.02	1.04	0.482	0.63
TUG	0.12	0.77	-0.12	0.63	4.466	0
ENV area	0	0.96	0	1.03	0.037	0.97
BMI	0.07	0.95	-0.04	1.03	1.504	0.133

Table 3: Mean Z scores and SDs of the measures in urination dysfunction (UD) and intact control groups.

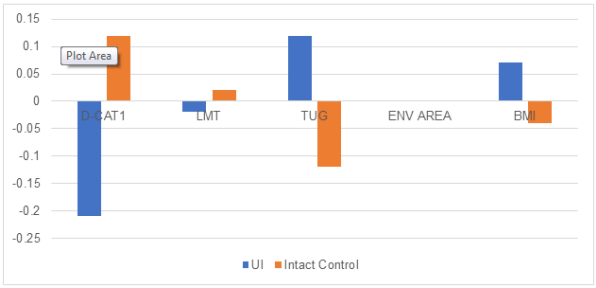

Figure 1: Mean Z scores of measures in Urination Dysfunction and Intact Control groups.

DISCUSSION

The purpose of this study was to replicate our previous findings using different larger cohort than before considering weaknesses of previous studies and to investigate newly the relationships between UD and brain functions not only cognitive but also physical abilities perspective. This aim based upon the requests from the local government health-promoting staff to provide reliable and robust evidences for successful health promotion activity.

For elderly people, in addition to UD, hypertension is typically associated with aging. The association between blood pressure and cerebral dysfunction of older adults has a history of nearly 50 years. Since then, ample research has clarified the relationship between hypertension and cognitive decline. These studies have pointed out, for example, that continuing to eat a low salt diet and exercise habits are effective for preventing hypertension. However, human beings cannot sustain action based on knowledge alone, even if they understand that the information is correct. Recently, cognitive behavior therapy has played a substantial role in addressing this issue. However, the efficacy of cognitive-behavioral therapy depends on participants' understanding of neuropsychological mechanisms that are modified by the treatment. The evidence regarding UD and cognitive decline mediated by aging remains paltry compared to the evidence of the link between hypertension and cognitive decline. Therefore, researchers must provide robust scientific evidence regarding the link between UD and cognitive decline to local government health-promoting officers and public health nurses.

The results of this study coincidences with previous our findings by indicating that the performance of the UD group in the D-CAT test was inferior to that of the control groups, whereas there were no group differences in LMT performance. This suggests that the decline in prefrontal cortex function of the UD group compared to the control is a robust finding that supports the model of brain functioning 6. Moreover, this study indicated that TUG performance was inferior in the UD group compared to the control group, which was not the case with ENV AREA performances, suggesting that in the domain of physical functions, agility is related to UD, but not to balance. Generally, balance is considered to be a function of the phylogenetically old parts of the brain, including the cerebellum-basal ganglia, whereas agility is a function of the prefrontal cortex and the motor area. Therefore, the findings of significant group differences in TUG, in the absence of group difference in balance, also suggest a strong link between UD and hypofunction of the prefrontal cortex [18-20].

There were no group differences in BMI between UD and control. Pedersen et al. reported that German and Danish women with a BMI less over 35 tended to have problems related to UI and concluded that UI was significantly associated with BMI as a potential risk factor [21]. Bedoya-Ronga and Currie also reported that high BMI was a significant risk factor for women in the UK [13]. According to the World Health Organization recommendations, a BMI of 18.50–24.99 is classified as normal 25.00-29.99 as pre-obese, 30.00-34.99 as obese Class I, 35.00-39.99 as Obese class II and 40+ as obese Class III. As apparent from Table 2, the mean BMI of the sample of this study was 23.8, and almost none of the participants were obese. Therefore, the BMI might not be as significant in Japan as compared to Europe and the United States. It is conceivable that the effects of the BMI on UD in Japanese people are negligible.

What information of this study can provide to local government health-promoting officials and public health nurses? Firstly, UD is strongly associated with the deterioration of the frontal lobe function. Therefore, health-promoting officials and public health nurses should take measures to maintain the frontal cortex function of middle-aged community-dwelling people. Several previous studies have pointed out the crucial role of maintaining opportunities for interpersonal communication as well as continuing intellectual activities for delaying frontal cortex deterioration associated with aging [22]. Moreover, Hatta, Ito, and Hasegawa proposed that intellectual skills acquired at a later stage of human development, such as writing, and writing lyrics, among others, start to deteriorate earlier than skills acquired in childhood [23]. Therefore, it is essential to maintain

cognitive abilities acquired later in human development for slowing the deterioration of frontal lobe function.

Secondly, reduced agility in the physical domain closely related to the onset of UD. Therefore, it is crucial to maintain the habit of physical exercise after the middle age, as has been suggested by numerous [23-25]. Our previous intervention study had two conditions, letter exchanging and aerobic exercise, and results indicated that the former was more effective for maintaining prefrontal cortex function. Most people are aware of the efficacy of maintaining an appropriate lifestyle (eg., intellectual activities, and physical exercise) on preserving brain function. Nevertheless, it is difficult for ordinary adults to continue exercising over many years. A longitudinal study indicated that only 6 of 104 healthy community dwellers succeeded in continuing to exercise for 11 years (from 65 to 75 years old) as recommended by health leaders.

CONCLUSION

Almost elderly people tend to quit from exercise habit that have been recommended frequently by health promotion staffs though they have not physical difficulty of continuing. Being bored is one of the proper characteristics that humans have in common. How to overcome such traits of being bored of people is a crucially important issue to reduce the waste of social capital. There is no simple road to achieving this goal. However, one effective method is to obtain and present scientific evidence to community dwellers and wait for them to change their behavior.

CONFLICT AND INTEREST STATEMENT

The authors have no conflicts of interest to declare the findings of this study.

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