



## Research paper

## Cognitive function in Japanese women with posttraumatic stress disorder: Association with exercise habits

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## ABSTRACT

**Background:** Posttraumatic stress disorder (PTSD) has been associated with cognitive impairments, yet little is documented on the cognitive function of PTSD patients in Asian countries. It is shown that regular exercise can reduce PTSD symptoms, while no study has investigated the association between exercise and cognition in PTSD patients. This study aimed to examine cognitive functions of Japanese women with PTSD, and to explore the association between regular exercise and cognitive functions.

**Methods:** Forty-two women with DSM-IV PTSD and 66 demographically matched healthy control women participated in this study. Most of the patients developed PTSD after experiencing interpersonal violence. Cognitive functions were assessed by the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Regular exercise habit was assessed by a self-reported questionnaire.

**Results:** Compared to controls, PTSD patients performed significantly more poorly in all cognitive domains examined, including immediate memory, visuospatial construction, language, attention, delayed memory, as well as the total score of RBANS (all  $p < 0.001$ ). Compared to PTSD patients without the habit of exercise, those who habitually exercised showed significantly better performance on delayed memory ( $p = 0.006$ ), which survived after controlling for potentially confounding variables in a multiple regression model.

**Limitations:** The cross-sectional design and relatively small sample size limited our findings.

**Conclusions:** PTSD in Japanese women is associated with pervasively impaired cognitive functions, including notable impairments in verbal memory. Such memory deficits might be improved by regular exercise, although further studies are needed to investigate the causal relationship between exercise and cognition in PTSD.

## 1. Introduction

Posttraumatic stress disorder (PTSD) is a debilitating psychiatric condition that can develop after a major traumatic event. Lifetime prevalence of PTSD in the Japanese population is estimated at around 1.3% (Kawakami et al., 2014). Core symptoms of PTSD include re-experience (intrusive symptoms), avoidance, hyperarousal, and negative mood and cognition. People with PTSD exhibit these symptoms for more than a month, with severe distress and functional impairment.

Besides these defining symptoms, PTSD has been shown to be

associated with compromised cognitive functioning in several key domains, including verbal learning/memory, working memory, attention, and executive functions (Scott et al., 2015). Importantly, such cognitive dysfunction in PTSD can be a significant predictor of low social functioning (Geuze et al., 2009) and poor responsiveness to cognitive behavioral therapy (Wild and Gur, 2008). Furthermore, it is reported that people with PTSD are at greater risk of developing dementia (Yaffe et al., 2010).

Studies showing these cognitive impairments in PTSD have mostly been conducted in western countries, with their focus on combat-

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related trauma in male patients (reviewed in Scott et al., 2015). Several studies have also examined cognitive function in civilian, female patients with PTSD, demonstrating similar findings to what has been shown in the male veteran patients (Scott et al., 2015). However, little is documented on the cognitive function of PTSD patients in Asian countries, except for one study in Korea (Shin et al., 2015). Thus, more should be done to characterize the cognitive functions of PTSD patients in these countries.

Another line of evidence suggests that people with PTSD have higher rates of physical comorbidity, such as cardiovascular disease, diabetes, dyslipidemia, and obesity, all of which could contribute to premature mortality. In line with this, studies have investigated the potentially beneficial effects of health-promoting behaviors, including exercise and dietary habits, in the treatment of PTSD (Hall et al., 2015; Rosenbaum et al., 2015; Uemura et al., 2016). Notably, physical activity has been shown to reduce core symptoms of PTSD (for meta-analysis, see Rosenbaum et al., 2015), and has thus become a promising treatment option for PTSD. However, cognitive function has not been included as an outcome in these studies, and there has been no study to our knowledge that has examined the association between physical activity and cognitive function in PTSD patients. On the other hand, studies have also shown that exercise can improve cognition in individuals with mild cognitive impairment (Zheng et al., 2016) and those with dementia (Groot et al., 2016). Furthermore, a recent study demonstrated that treadmill exercise improved spatial memory in a rat model of PTSD (Shafia et al., 2017). These findings suggest that physical exercise may ameliorate cognitive dysfunction in patients with PTSD as well.

In this study we firstly examined cognitive functions in women with PTSD in a Japanese population, and secondly explored the association between regular exercise and cognitive functions in the same sample. We hypothesized that our PTSD patients would show impaired functioning across a wide-range of cognitive domains compared to healthy control subjects and that regular exercise would be associated with less impairment in patients' cognitive functions.

## 2. Methods

### 2.1. Participants and procedure

The present study was conducted at 3 institutes: National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan, Tokyo Women's Medical University Hospital, and Nagoya City University Hospital. This study was approved by the ethics committee of each institute, and was conducted in accordance with the Declaration of Helsinki. After description of the study, written informed consent was obtained from each participant.

All participants, both patients and controls, were Japanese women. They were consecutively recruited at the 3 institutes and their affiliated hospitals/clinics in Tokyo and Nagoya (2 metropolitan areas in Japan).

A total of 42 patients with PTSD (age range: 21–59 years) were enrolled in this study. Experience of traumatic events and diagnosis of PTSD were initially evaluated by an expert clinician and then confirmed by the Japanese version (Nagae et al., 2007) of the Posttraumatic Diagnostic Scale (PDS; Foa, 1995). The Japanese version (Otsubo et al., 2005) of the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) was also administered to identify any other Axis-I disorders as well as PTSD.

Sixty-six healthy volunteers (age range: 20–64 years) were recruited through advertisements in free local magazines and on our website and by word of mouth. They were evaluated by M.I.N.I. and PDS, and only those who had no current psychiatric disorders or traumatic experiences were enrolled.

Additionally, both patients and controls were excluded if they had severe physical illness, schizophrenia, remarkable manic episodes of bipolar disorder, or intellectual disability, or were non-native Japanese

speakers.

### 2.2. Psychological assessment

Psychological characteristics of the participants were assessed by 4 self-reported questionnaires, including the PDS, the Impact of Event Scale-Revised (IES-R; Weiss and Marmar, 1997), the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and the Sheehan Disability Scale (SDISS; Sheehan et al., 1996).

The Posttraumatic Diagnostic Scale (PDS; Foa, 1995) is a well-established self-report questionnaire created in accordance with the diagnostic criteria of PTSD in DSM-IV (Foa, 1995; Foa et al., 1997). The PDS comprises 4 parts that evaluate traumatic experiences reflecting Criteria A of the DSM-IV (Part 1 & 2), PTSD severity during the past month reflecting Criteria B-D (Part 3), and functional impairments associated with the PTSD symptoms (Part 4). The assessment of PTSD severity in Part 3 consists of 17 items, each scored on a 4-point Likert scale of symptom frequency, with higher scores indicating greater symptoms. The Japanese version of PDS has demonstrated good reliability and validity (Itoh et al., 2017; Nagae et al., 2007). In this study, Part 1 & 2 was administered to all participants to determine the presence/absence of traumatic experiences, and if present, Part 3 & 4 was administered for the assessment of diagnosis and severity of PTSD.

PTSD severity of the patients was also assessed with the validated Japanese version (Asukai et al., 2002) of the IES-R (Weiss and Marmar, 1997), a 22-item self-report questionnaire measuring the 3 core PTSD symptom clusters, namely intrusion, avoidance, and hyperarousal. Each item is scored on a 5-point Likert scale of symptom intensity, with higher scores indicating greater symptoms. There were 2 subjects (patients) who did not complete this questionnaire, and valid IES-R data were obtained from 40 subjects.

The BDI-II is a 21-item self-report questionnaire widely used to measure depression severity (Beck et al., 1996). Each item is scored on a 4-point scale, with higher scores indicating more severe depressive symptoms. In this study the validated Japanese version of BDI-II (Kojima et al., 2002) was administered to all participants (both patients and controls).

The SDISS is a discretized visual analog rating scale of functional disability in 3 domains, namely work/school, social, and family life (Sheehan et al., 1996). Each domain is rated from 0 (unimpaired) to 10 (extremely impaired), which are summed to yield a global disability score ranging from 0 to 30. In this study the validated Japanese version of SDISS (Yoshida et al., 2004) was administered to all participants.

### 2.3. Cognitive assessment

Cognitive functions of participants were measured by the Japanese version (Matsui et al., 2010) of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph et al., 1998). The RBANS is a neuropsychological test battery that assesses 5 main cognitive domains derived from 12 subtests, including immediate memory (consisting of list learning and story memory), visuospatial construction (figure copy and line orientation), language (picture naming and semantic fluency), attention (digit span and coding), and delayed memory (list recall, list recognition, story recall, and figure recall). Index scores of the 5 domains can be combined to generate a total score of RBANS, which provides a global measure of neuropsychological performance. These age-corrected scaled scores are standardized such that the population mean is 100 and the standard deviation (SD) is 15. The RBANS has demonstrated sound psychometric properties in both clinical and nonclinical populations (Duff et al., 2005; Matsui et al., 2010; McKay et al., 2007; Weber, 2003). It was administered in a quiet room on a one-on-one basis, with an average completion time of around 30 min. Scoring was performed in accordance with the manual guidelines (Matsui et al., 2010; Randolph et al., 1998).

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