



Original Article

Gender-specific factors associated with the Japanese version of the trail making test among Japanese workers

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Abstract. [Purpose] The Trail Making Test is a valuable tool for predicting the transition from mild cognitive impairment to dementia. This cross-sectional study aimed to investigate gender-specific factors associated with the Trail Making Test using body composition and motor function among Japanese workers. [Participants and Methods] Demographic data, body composition, motor function, and cognitive and attentional functions (Trail Making Test, Part B) were analyzed among 627 workers who underwent health assessments during the 2019 fiscal year. After conducting univariate analysis, multiple regression analysis was performed. [Results] The presence of metabolic syndrome risk factors was found to significantly prolonged the performance time of the Trail Making Test-B in male workers. In addition, low fat-free mass and the 30-second chair stand test also significantly prolonged the performance time of the Trail Making Test-B in male workers. Among female workers, the presence of metabolic syndrome risk factors affected the performance time of the Trail Making Test-B. Therefore, MetS risk factors affect the performance times of the Trail Making Test-B in both male and female workers. [Conclusion] As male and female workers exhibit different body composition and motor function items in the Trail Making Test-B, gender differences should be considered when formulating measures to prevent cognitive and attentional decline.

Key words: Body composition, Motor function, Trail Making Test

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INTRODUCTION

As the older adult population increases, the number of older adults with dementia also increases, becoming a large problem¹⁾. Therefore, in addition to early detection of cognitive decline, it is necessary to take measures against cognitive decline in younger generations such as the working generation.

Executive function (a cognitive function), consists of inhibition, working memory, and cognitive flexibility²⁾. The Trail Making Test (TMT), a test battery of attentional functions, has been shown to assess executive functions centered on cognitive flexibility, such as information processing speed and mental flexibility³⁾. In addition, the TMT is useful in predicting the transition from mild cognitive impairment to dementia⁴⁾, and is listed as one of the evaluation scales for assessing cognitive impairment in the 2017 Clinical Practice Guidelines for Dementia Diseases⁵⁾. The Japanese version of the TMT⁶⁾ shows the required time for each age group based on measurement data of healthy individuals, in order to be widely used for early

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detection of dementia. Early detection and early preventive measures are important for preventing the onset of dementia. There is a gender difference in cognitive decline⁷⁾, and a study examining 234 people diagnosed with mild cognitive impairment reported that females progress to dementia at a higher rate⁸⁾. Clarifying gender differences in factors related to cognitive and attentional function decline using the TMT in the working generation, including among the younger age group, can lead to early detection of cognitive and attentional function decline. Additionally, it is important to formulate strategies for the prevention of dementia in the future.

Regarding the factors that affect TMT, previous studies reported that age, years of education, grip strength, and a circle task that shows hand movements were related to TMT, but the related factors differed between men and women⁹⁾. In another report, motor functions such as grip strength and walking ability were associated with TMT, but no gender difference was observed¹⁰⁾. However, both studies were conducted among older adults, and there is no consensus on whether there is a gender difference. Furthermore, there are large gender differences in body composition and motor function. Another previous study investigating the relationship between body composition and motor function and TMT reported that the body mass index (BMI)¹¹⁾ and the 30-second chair stand test (CS-30)¹²⁾ is associated with TMT, but no gender-specific studies have been conducted. Similarly, studies among older adults have reported that visceral fat accumulation, one of the diagnostic criteria for metabolic syndrome (MetS), is associated with cognitive decline and structural changes in the brain, but the gender difference is unknown¹³⁾. Therefore, the purpose of this study was to extract the gender-specific factors related to the TMT in the working generation, including the younger generation. Hence, we conducted a cross-sectional examination according to gender, using body composition and motor function.

PARTICIPANTS AND METHODS

In the 2019 fiscal year, the Kyushu Rosai Hospital Research Center for the Promotion of Health and Employment Support conducted health measurements at 14 offices of six companies in the suburbs of Kitakyushu, Fukuoka Prefecture, Japan. The participants consisted of 655 workers who underwent health measurements. The types and sizes of participating companies were as follows: 7,814 in the construction industry (two companies, four offices), 155 in the manufacturing industry (one company, one office), 2,625 in the electricity, gas, heat supply, and water industries (two companies, eight offices), 364 in the service industry (one company, one office), and the participation rate in the health measurement was 6.0%. To ensure the health of workers, specific equipment was brought to the companies to measure body composition, motor function, and hemodynamics. In addition to explaining the measurement results, individual guidance was provided to improve lifestyle habits. This study was conducted in response to the provision of data obtained by completely anonymizing the health measurements provided. Of the 655 participants, a total of 627 were included in the analysis; six participants with a history of cerebrovascular disease, three participants who provided insufficient information in the questionnaire, and 19 participants who were unable to measure their motor function were excluded (Table 1).

This study was approved by the Ethics Committee of Kyushu Nutrition Welfare University, Higashi Chikushi Junior College (approval no. 2003).

Age, gender, height, educational background, and diseases being treated were recorded using a self-administered questionnaire. Additionally, the presence or absence of MetS factors (hypertension, dyslipidemia, diabetes, and obesity) was considered. Participants with one or more symptoms of hypertension, dyslipidemia, diabetes, or obesity were considered to have MetS risk factors.

Body weight, BMI, body fat percentage, and fat-free mass were measured using a body composition analyzer (InBody770, InBody, Seoul, South Korea) and bioelectrical impedance analysis. Measurements were performed in a standing position for approximately 90 seconds.

Motor function was assessed using the CS-30 and grip strength. Both the measurements were conducted during health measurements. The CS-30 evaluates the functional strength of the lower extremities. The participants' starting position was a sitting posture on a 40 cm stepping stool, with lower limbs spread shoulder-width apart and upper limbs crossed in front of the chest. Participants were instructed to stand up and sit down as many times as possible with their arms folded, and the number of times they stood up during a 30-second interval was recorded. Grip strength was measured using a digital grip

Table 1. Information about the participants' occupations

Variables	All participants (n=627)	Male workers (n=477)	Female workers (n=150)
Employment status			
Full-time employee (n, %)	497 (79.3)	396 (83.0)	101 (67.3)
Part-time employees (n, %)	14 (2.2)	3 (0.6)	11 (7.4)
Temporary employee (n, %)	34 (5.4)	11 (2.3)	23 (15.3)
Contract employee (n, %)	73 (11.6)	58 (12.2)	15 (10.0)
Others (n, %)	9 (1.4)	9 (1.9)	0 (0.0)

The values obtained from analyses were presented as frequencies and percentages for categorical data.

strength meter (Grip-D; Takei Kiki Kogyo, Niigata, Japan). The participants were in a standing position, with upper limbs hanging down as the basic posture. Measurements were taken twice alternately on the left and right sides, and the average of the maximum values on each side was adopted.

For cognitive and attentional functions, two TMT Japanese versions⁶⁾, Part A (TMT-A) and Part B (TMT-B), are utilized. In this study, we adopted TMT-B, which has been shown to have a higher reliability coefficient than TMT-A¹⁴⁾. The original TMT was a neuropsychological assessment developed in 1944 as part of the Army Specific Testing Battery¹⁴⁾. TMT scores have been shown to be associated with other neuropsychological assessments¹⁵⁾, and studies using TMT are conducted for various disorders including cognitive function in older adults^{4, 16)}. In the Japanese versions of TMT, the data of the healthy group in each age group from 20s–80s were evaluated using a male-to-female ratio of approximately 1:1. In Japan, these versions are also used as an index of attention function and processing ability necessary for car driving¹⁷⁾. The mean and standard deviation were shown and standardized⁶⁾. While TMT-A measures the time taken to connect Numbers 1 to 25 with lines, TMT-B measures the time taken to connect Numbers 1 to 13 and hiragana letters alternately with lines. This measurement was conducted during the health measurements.

To examine the relationship between the results of the TMT-B and participant information, body composition, and motor function, Spearman's rank correlation coefficient was used for continuous variables, and the Mann–Whitney U test was used for categorical variables. These statistical analyses were performed separately for male and female participants. A multiple regression analysis was also performed using the forced injection method for all participants and for male and female participants, with these items as the independent variable, TMT-B as the dependent variable, and age and final educational attainment as adjustment variables. To avoid potential multicollinearity issues, if the correlation coefficient of the input independent variables showed a value of 0.8 or higher, we selected items that matched the significance of this study from a professional perspective. Additionally, we confirmed that the variance inflation factor of the independent variables was less than 10. All analyses were performed using SPSS Statistics 26.0 (IBM Co., Armonk, NY, USA). Two-tailed p-values less than 0.05 were considered statistically significant.

RESULTS

The values obtained from the analyses were presented as medians (interquartile ranges) for continuous variables and as frequencies and percentages for categorical data. Table 2 shows the participants' basic information, body composition, motor function, and TMT-B. A total of 627 participants (477 male workers and 150 female workers) were included in the statistical

Table 2. Demographic information, body composition, motor function, and TMT-B of participants

Variables	All participants (n=627)	Male workers (n=477)	Female workers (n=150)
Demographic information			
Age (years)	49.0 (42.0–56.0)	51.0 (42.0–57.0)	46.0 (40.8–51.0)
Height (cm)	168.0 (163.0–173.0)	170.0 (167.0–174.0)	159.0 (155.0–162.0)
MetS risk factor (n, %)	188 (30.0)	172 (36.1)	16 (10.7)
Highest educational qualification			
Junior high school students (n, %)	3 (0.5)	1 (0.2)	2 (1.3)
Senior high school students (n, %)	186 (29.7)	155 (32.5)	31 (20.7)
Specialized training colleges	28 (4.5)	14 (2.9)	14 (9.3)
Junior colleges and technical colleges (n, %)	102 (16.3)	49 (10.3)	53 (35.3)
University students (n, %)	236 (37.6)	189 (39.6)	47 (31.3)
Graduate students (n, %)	68 (10.8)	66 (13.8)	2 (1.3)
Others (n, %)	4 (0.6)	3 (0.6)	1 (0.7)
Body composition			
Body weight (kg)	66.3 (58.2–73.8)	69.6 (63.7–75.9)	52.2 (48.0–57.6)
Body mass index (kg/m ²)	23.3 (21.2–25.4)	23.9 (22.0–25.9)	20.7 (18.9–22.5)
Body fat percentage (%)	23.9 (20.0–28.4)	22.5 (19.2–26.6)	28.1 (24.0–33.2)
Fat-free mass (kg)	51.1 (43.8–56.5)	53.2 (49.9–58.2)	37.5 (34.8–40.6)
Motor function			
30-second chair stand test (times)	25.0 (21.0–30.0)	25.0 (21.5–30.0)	25.0 (21.0–31.0)
Grip strength (kg)	38.0 (30.2–43.1)	40.2 (36.6–44.5)	24.5 (21.5–26.9)
TMT-B (second)	44.4 (36.1–55.1)	44.8 (36.5–55.3)	42.1 (35.0–53.0)

The values obtained from analyses were presented as medians (interquartile ranges) for continuous variables and as frequencies and percentages for categorical data.

MetS: metabolic syndrome; TMT-B: Trail Making Test Part B.

analysis. The highest educational qualification was as follows: three junior high school students (0.5%), 186 senior high school students (29.7%), 28 specialized training colleges (4.5%), 102 junior colleges and technical colleges (16.3%), 236 university students (37.6%), 68 graduate students (10.8%), and four others (0.6%).

Table 3 shows the results of the correlation analysis with the TMT-B for all participants and male and female workers. Among all participants, a significant positive relationship was observed between TMT-B and age ($p < 0.001$), and a significant negative relationship was observed with CS-30 ($p = 0.006$). Among male workers, TMT-B was significantly positively correlated with age ($p < 0.001$) and significantly negatively correlated with height ($p = 0.006$), weight ($p = 0.029$), fat-free mass ($p = 0.003$), and CS-30 ($p = 0.005$). Among female workers, TMT-B had a significant positive relationship with age ($p < 0.001$) and a significant negative relationship with fat-free mass ($p = 0.022$).

Table 4 shows the relationship between the TMT-B and the presence or absence of MetS risk factors in all participants and male and female workers. In all participants and male and female workers, those with MetS risk factors showed a significant increase TMT-B performance time.

Table 5 shows the results of the multiple regression analysis, using the forced injection method with the TMT-B as the dependent variable for all participants and male and female workers. The correlation coefficient between height and fat-free mass, weight and BMI, and weight and fat-free mass for all participants; that between body weight and BMI, and body weight and fat-free mass for male workers; and that between body weight and BMI for female workers was 0.8 or higher. In this study, items excluding height and weight were included as independent variables. Table 5 lists items for which a significant relationship was observed. In all participants and male workers, the presence of MetS risk factors was shown to significantly prolong TMT-B performance time. Low fat-free mass and CS-30 were also shown to significantly prolong TMT-B performance time. In female workers, only the presence of MetS risk factors affected TMT-B performance time. The multiple regression model created under all conditions was significant.

DISCUSSION

Previous studies have investigated factors affecting the results of the TMT, an evaluation index of cognitive and attentional functions^{9, 10}. However, no studies have included the younger generation or considered gender differences. Our results suggest that the presence of MetS risk factors affects the decline in TMT-B in both male and female workers. Furthermore, in male workers, a decrease in body composition (e.g., fat-free mass) and motor function (e.g., CS-30), adversely affected the TMT-B. Therefore, we speculate that multiple factors affect the TMT-B. Meanwhile, in female workers, only the presence or

Table 3. Correlation with TMT-B by all participants, male, and female workers

Variables	All participants	Male workers	Female workers
	Correlation Coefficient	Correlation Coefficient	Correlation Coefficient
Age (years)	0.417**	0.418**	0.380**
Height (cm)	-0.063	-0.126**	-0.138
Body weight (kg)	-0.039	-0.100*	-0.091
Body mass index (kg/m ²)	-0.003	-0.024	-0.031
Body fat percentage (%)	0.001	0.022	0.030
Fat-free mass (kg)	-0.048	-0.137**	-0.186*
30-second chair stand test (times)	-0.110**	-0.128**	-0.071
Grip strength (kg)	0.001	-0.054	-0.159

** $p < 0.01$ and * $p < 0.05$ assessed by Spearman's rank correlation coefficient.
TMT-B: Trail Making Test Part B.

Table 4. Differences in TMT-B results depending on the presence or absence of MetS risk factors

Variables	All participants	Male workers	Female workers
	Value	Value	Value
MetS risk factor			
Yes	49.5 (39.7–62.2)**	48.3 (39.7–62.2)**	52.0 (41.4–68.3)*
No	42.1 (35.4–52.7)	42.8 (35.6–52.9)	41.2 (34.6–52.0)

** $p < 0.01$ and * $p < 0.05$ assessed by the Mann–Whitney U test.
MetS: metabolic syndrome; TMT-B: Trail Making Test Part B.

Table 5. Results of multiple regression analysis with TMT-B as the dependent variable

Variables	Unstandardized coefficients	Standardized coefficients	95% CI	VIF
All participants				
MetS risk factor	5.345	0.163**	2.767 to 7.924	1.252
Fat-free mass (kg)	-0.420	-0.244**	-0.732 to -0.109	6.604
30-second chair stand test (times)	-0.191	-0.075*	-0.378 to -0.004	1.095
Male workers				
MetS risk factor	4.785	0.149**	1.913 to 7.657	1.227
Fat-free mass (kg)	-0.429	-0.160*	-0.799 to -0.058	2.936
30-second chair stand test (times)	-0.265	-0.099*	-0.493 to -0.037	1.095
Female workers				
MetS risk factor	7.563	0.173*	0.475 to 14.650	1.242

**p<0.01 and *p<0.05 assessed by multiple regression analysis by forced injection method with age and highest educational qualification as adjustment factors.

MetS: metabolic syndrome; CI: confidence intervals; VIF: variance inflation factor; TMT-B: Trail Making Test Part B.

absence of MetS risk factors was associated with the TMT-B, and the results differed from those of male workers. Thus, it is necessary to consider gender differences when formulating measures to prevent cognitive and attentional function decline.

Meanwhile, this study shows that MetS is associated with TMT-B regardless of gender. A previous study also reported that, after adjusting for gender, the presence of MetS increases the risk of developing mild cognitive impairment by 1.46 times, and that an increase in MetS risk factors leads to the risk of mild cognitive impairment regardless of gender¹⁸). Chronic inflammation of adipose tissue and insulin resistance associated with obesity have been shown to cause neuroinflammation and may lead to cognitive decline^{19, 20}). However, no relationship between fat-free mass and TMT has been found; that is, the clarification of the relationship between fat-free mass and cognitive and attentional functions is a new finding. The World Health Organization recommends physical activity for adults with normal cognitive functions to reduce the risk of cognitive decline²¹). Physical activity has been reported to have a positive effect on brain structure²²). Furthermore, physical activity that maintains or enhances fat-free mass may be similarly effective. Thus, it is suggested that multifaceted strategies for improving fat-free mass are important, not only from the perspective of reducing mortality²³), but additionally in preventing the onset of dementia. However, fat-free mass was associated with TMT-B only in male workers and not in female workers. The median fat-free mass of female workers was lower than that of male workers, and the interquartile range was narrower. As such, the limited variation in the numerical values and the small number of participating female workers may have impacted the results of this study. Future studies should conduct an in-depth examination of how changes in fat-free mass affect changes in TMT.

Regarding the relationship between the TMT and motor function, a significant negative relationship was observed between grip strength and TMT-B in older males⁹), and grip strength is associated with Δ TMT (TMT-A-TMT-B)¹⁰). However, in this study, no relationship was observed between grip strength and TMT-B. In general, grip strength reaches a peak in the 30s, after which a slight decline is observed; however, it declines sharply from the late 50s²⁴). Therefore, it is expected that grip strength has little effect on TMT in the working generation. Additionally, Ohsugi et al.¹²) reported a significant negative relationship between the TMT-A and CS-30, especially in older male and female adults. However, in this study, CS-30 was associated with only male workers and the TMT-B. Generally, the TMT-A evaluates attentional selection and sustained functions, whereas the TMT-B evaluates attention allocation abilities. The TMT-B may be more complex and takes longer to complete²⁵). Another study that targeted older adults showed that the TMT-B is effective in recognizing early cognitive decline¹⁶). However, Ohsugi et al.¹²) did not observe the same results; the simpler test (TMT-A) may be affected by motor function in older adults, whereas the more difficult task (TMT-B) is likely more affected by motor function in both middle-aged and older adults. In addition, in this study, while no relationship between CS-30 and TMT-B was observed in female workers, a gender difference was observed. There was no gender difference in CS-30 itself (p=0.776), and even when compared with age-specific reference values, both male and female participants showed standard values²⁶). Although we were presently unable to find a sufficient answer to this question, it may be owing to the fact that the number of female workers participating was lower than that of male workers. Future research should examine why these relationships were observed in the present study. However, it is postulated that while CS-30, which assesses motor function, especially the functional strength of the lower extremities, has an impact on the TMT in the working generation, the outcomes only materialize in male workers and may vary depending on the task. Therefore, understanding these facts and implementing the appropriate measures is crucial.

This study has some limitations. First, we used the performance time of the TMT Japanese versions. This instrument provides a quick neurocognitive function evaluation. However, it does not measure all aspects of cognitive function. Second, this study was observational. Therefore, a possible causal relationship could not be established in a longitudinal study. Third, approximately 6% of all employees participate in health measurement. Participation in the health measurement was not

compulsory, and was based on the wishes of the participants, indicating potential selection bias. Fourth, risk factors that affect cognitive function (work content, exercise, smoking, etc.)^{21, 27)} were not investigated in this study. Finally, the study's target population, working adults, comprised a wide age range (21–74 years). As the TMT is strongly affected by aging³⁾, factors affecting the TMT differ depending on the age group even within the working generation. Therefore, it would be useful to clarify the factors related to the TMT by age group, to develop strategies to pretend future cognitive and attentional decline.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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