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TITLE:

Traditional Trail Making Test Modified into Brand-New Assessment Tools: Digital and Walking Trail Making Test

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SUMMARY:

Here, we present a protocol to show how to perform two types of cognitive assessment tools derived from the paper-pencil version of the Trail Making Test.

ABSTRACT:

The Trail Making Test (TMT) is a well-accepted tool for evaluating executive function. The standard TMT was invented more than 60 years ago and has been modified into many versions. With the development of digital technologies, TMT is now modified to a digitized version. The present study demonstrated digital TMT (dTMT) performed on a computer, and Walking TMT (WTMT) on the floor. Both revealed more information compared with the traditional version of TMT.

INTRODUCTION:

With a rapidly aging population, dementia is considered to be a major public health concern. The number of elderly patients with dementia worldwide is about 47 million according to the World Health Organization[1]. Executive function impairment is not only a common type of cognitive dysfunction in aged individuals, but has been reported as a predictor of progression from mild cognitive impairment (MCI) to clinical Alzheimer's disease (AD)[2,3]. As the third most widely used test in neuropsychology[4], the Trail Making Test (TMT) is employed as a well-accepted tool to evaluate executive functions, especially sustained attention and set-shifting[5], even in elderly patients[6].

The standard TMT is a paper-pencil test consisting of two parts: tMT-A and TMT-B[5]. The former calls for the test-taker to draw lines connecting randomly distributed numbers (1–25) on a test paper in ascending order (1->2->3…), whereas the latter requires the test-taker to set numbers and letters (1->A->2->B…) alternatively. The performance of TMT is generally scored in the time taken to complete each part correctly[7]. TMT has been translated into different languages. The Chinese version of TMT was developed in 2006[8]. Since Chinese characters are quite distinct from English letters, the Chinese version of TMT was used in our procedure.

Apart from the standard version, TMT has been modified in different ways by researchers (e.g., oral TMT[9], driving TMT[10], walking TMT (WTMT)[11]) to assess specific populations or find details under different conditions, such as driving and walking. Of note, some studies conferring different numbers compared with the standard TMT are also reported to be of high validity and reliability. For example, THINC-Integrated Tool (THINC-it) developed by the McIntyre group used 9 numbers and letters for TMT-B[12]; WTMT reported by Schott and colleagues used 15 numbers for TMT-A[13]. In the same way, many evaluating systems of TMT have been built beyond the complete time scoring, which are reported to be helpful in finding more items besides executive dysfunction, or to be accessible for participants who are not suitable to complete the standard TMT. For example, some researchers investigated the errors in TMT and found that errors in TMT-B were associated with mental tracking and working memory in patients with psychiatric disorder[14]. Another group from Greece suggested derived TMT scores [TMT-(B–A) or TMT(B/A)] as indices to detect impairment in cognitive flexibility across the adult life span[15]. Generally, alternative evaluating systems of TMT can be summarized as follows: (1) completion time analysis—TMT completion time is calculated in seconds[16]; (2) error analysis—different types of TMT errors are classified and quantified[14]; (3) intermanual differences—different abilities of completing TMT between the dominant hand and the nondominant hand are compared[17]; and (4) derived Trail Making Test indices—different characterizations between completing TMT-A and TMT-B are analyzed[15]. The alternative scoring methods provide additional information. For example, the utility of TMT error analysis could reveal cognitive deficits not traditionally captured using completion time as the sole outcome variable in patients with schizophrenia and depression[14]. The lack of any significant intermanual difference helped to discriminate the cognitive dysfunction from the influence of the motor disorder[17]. Derived TMT indices could detect impairment in cognitive flexibility across the adult life span and minimize the effect of demographics and other cognitive background variables[15].

With advances in modern technology, computer-based digital applications have been increasingly integrated into traditional cognitive interventions, most of which are designed as similar to the original test as possible, rather than created as new tools. Digital or computerized TMT (dTMT) has been proven to have the potential to capture additional information, with the structure of the existing test mainly unchanged in recent years [18,19].

This study aimed to introduce a computer-based Chinese version of dTMT-A and dTMT-B, as well as a WTMT. Both are modified TMTs and have been confirmed to have high sensitivity and specificity to screen patients with MCI, Parkinson's Disease, Alzheimer's Disease, and so forth, based on the movement of upper and lower limbs[20,21]. Detailed scoring methods were also presented because digital technologies incorporated into dTMT and WTMT might help capture more information compared to the paper-pencil version of TMT.

PROTOCOL:

The development of the dTMT and initial application was approved by The Seventh Medical Center of PLA Army General Hospital Review Board. Subjects signed approved informed consent documents prior to testing TMT.

1. General method development

1.1. Use a tablet (e.g., Microsoft Surface Pro 2) with high-quality inertial sensors embedded within the device and a compatible electronic pen (**Figure 1**).

1.2. Use the Intelligent Device for Energy Expenditure and Activity (IDEEA) monitor, composed of five sensors (each 16 x 14 x 4 mm^3, 2 g), with one attached over the sternum, two attached to the front side of each thigh, and the other two attached under each foot. Connect the sternum and thigh sensors via a solid cable to a small 32-bit microprocessor (70 x 44 x 18 mm^3, 59 g), and wire the foot sensors (**Figure 2**).

2. Design and testing of the dTMT

NOTE: As mentioned earlier, dTMT has two parts: dTMT-A and dTMT-B. These two tests should be performed sequentially (dTMT-A proceeding dTMT-B), without being reversed.

2.1. dTMT-A procedure

2.1.1. Carry out the dTMT-A in a quiet and comfortable environment.

NOTE: Participants enrolled to complete dTMT should have the educational level of more than 2 years of preliminary school; otherwise, they might have difficulty in reading and recognizing Chinese characters in dTMT-B. Meanwhile, ensure that the participants have no obvious visual and upper limb disability.

2.1.2. Ask the participants to sit in front of a desk, and adjust the computer position, background light, and the electronic pen.

2.1.3. Check the near visual acuity of participants to ensure that they can easily read the numbers on the screen.

NOTE: Some aged subjects maybe need a pair of glass in case that the circles on the screen are too small for the subjects with presbyopia.

2.1.4. Show the instructions of dTMT-A as follows: Please draw a line as rapidly as possible joining consecutive numbers (i.e., 1->2->3…9) in the circles randomly distributed on the screen. A pre-test trial (150 s maximum) is necessary because most participants need to familiarize how to draw on the surface of a computer.

2.1.5. Demonstrate the major differences between dTMT-A and standard TMT-A. First, if the circle is correctly lined, its color can be changed. Second, if the circle is not correctly lined, its color remains unchanged, and the subjects need to re-line it from the last circle.

NOTE: Connecting all the circles fluently with straight lines is encouraged.

2.1.6. Advise the participants to avoid errors and time wastage. Encourage the participants to draw the line fluently, but as accurately as possible; however, give no priority.

2.1.7. Ask the participants to select **PartA** on the screen (**Figure 1** lower panel) to complete dTMT-A without interruption. All the dTMT-A data are gathered on the computer automatically.

NOTE: If data are collected for investigating intermanual differences, one more test needs to be carried out with the other hand. The sequence of left-/right- hand test is at random.

2.2. dTMT-B procedure

2.2.1. Repeat step 2.1.

2.2.2. Show the instructions of dTMT-B as follows: Please draw a line as rapidly as possible joining the numbers and Chinese characters (i.e., 1->壹->2->贰…玖) alternatively in the circles randomly distributed on the screen.

NOTE: Make sure all the Chinese characters are recognized by subjects. A pre-test trial (150 s maximum) is also necessary because some participants need to familiarize how to draw in the numbers and Chinese characters alternatively on their own.

2.2.3. Ask the subjects to select **PartB** on the screen (**Figure 1** lower panel) to complete dTMT-B without interruption. All the dTMT-B data are gathered in computer automatically.

NOTE: If data are collected for investigating intermanual differences, one more test needs to be carried out with the other hand. The sequence of left-/right- hand test is at random.

3. Direct data collection and definitions in dTMT

3.1. Determine the total time to completion: the time taken (ms) to draw a line connecting all circles in the correct order.

3.2. Determine the number of errors: the number of times a line is drawn to a circle in the incorrect order.

3.3. Determine the time to completion for each step: the time taken in milliseconds to draw each step.

3.4. Determine the time inside each circle: the time spent in milliseconds to draw inside circles.

3.5. Determine the inside circle percentage (%): time inside each circle divided by total time to completion.

3.6. Determine the time inside each tolerance circle: the time spent in milliseconds to draw inside tolerance circles.

3.7. Determine the inside circle tolerance percentage (%): time inside each tolerance circle divided by total time to completion

3.8. Determine the line canceling times in each step: the times a line is canceled in each step. The tolerance circle has a diameter five times more than that of a real circle.

3.9. Determine the optimal pathway of each step: the nearest line in millimeters of each step.

3.10. Determine the actual pathway of each step: the actual line in millimeters of each step.

3.11. Determine the pathway deviation of each step: the actual line in millimeters minus the nearest line in millimeters of each step.

3.12. Determine the variability of pathway deviation: Coefficient of the variation of the pathway deviation of each step.

3.13. Determine the velocity of drawing of each step: the actual line in millimeters of each step divided by the time to completion for each step.

NOTE: The average value was calculated by summing up the values collected step by step. Indirect data reflecting different points between hands or parts were derived based on the direct data.

4. Design and testing of the WTMT

NOTE: Similar to dTMT, WTMT also has two parts: WTMT-A and WTMT-B. These two tests should be performed sequentially (WTMT-A proceding WTMT-B), without being reversed.

4.1. WTMT-A procedure

4.1.1. Carry out WTMT-A in a quiet and comfortable environment. Ensure that there is room light. Randomly distribute coins with numbers at each of 15 positions in a 16 m^2 area (4 x 4 m^2). Draw a 30 cm diameter around each coin (**Figure 3**).

NOTE: The participants enrolled to complete WTMT should have the educational level of more than 2 years of preliminary school; otherwise, they might have difficulty in reading and recognizing Chinese characters in WTMT-B. Meanwhile, ensure that the participants have no obvious visual and lower limb disability.

4.1.2. Connect the Intelligent Device for Energy Expenditure and Activity (IDEEA) to the PC and enter the subject's anthropometric data.

4.1.3. Attach five biaxial mini-accelerometers (16 x 14 x 4 mm^3, 2 g) with medical tape over the sternum, to the front side of each thigh and under each foot (**Figure 4**). Connect all the accelerometers through thin, flexible cables to a microprocessor/storage unit (70 x 44 x 18 mm^3, 59 g) attached with a clip to the clothes.

NOTE: The IDEEA is a multiple accelerometer-based system comprising five biaxial accelerometers located on the upper trunk, thighs and feet. The IDEEA was initially developed to estimate energy expenditure during activities of daily living[22,23], but has an additional capability to quantify many of the commonly used gait cycle parameters[24].

4.1.4. After the device is equipped, ask participants to walk up and down a walkway without any targets at a comfortable walking speed to warmup.

4.1.5. Show the instructions of WTMT-A as follows: Please walk on numbered targets in a sequential order as rapidly as possible joining consecutive numbers (i.e., 1->2->3…15) in the coins randomly distributed on the floor.

4.1.6. Encourage the participants to walk fluently, but as accurately as possible; However, no priority is given. Perform WTMT-A only once.

4.1.7. Ensure the safety of the participants, because dual-task walking in a challenging environment may increase the risk of falling[25]. For both pre- and post- tests, a 5 s step pause is needed for IDEEA to discriminate walking from standing.

NOTE: Either footstep on the coin is considered as on the target. If the participants walk in the wrong order, guide them until they walk in the right order. All the WTMT-A data are gathered in the IDEEA microprocessor/storage unit automatically.

4.2. WTMT-B procedure

4.2.1. Repeat the steps as in Section 4.1.1.

4.2.2. Show the instructions of WTMT-A as follows: Please walk on numbered targets in a sequential order as rapidly as possible joining consecutive numbers (i.e., 1->壹->2->贰…柒>8) in the coins randomly distributed on the floor. Make sure all the Chinese characters are recognized by the participants.

4.2.3. Perform WTMT-B only once.

4.2.4. Ensure the safety of the participants, because dual-task walking in a challenging environment may increase the risk of fallings[25]. For both pre- and post- tests, a 5 s step pause is needed for IDEEA to discriminate walking from standing.

NOTE: Either footstep on the coin is considered as on the target. If the subjects walked in the wrong order, guide them until they walk in the right order. All the WTMT-B data are gathered in the IDEEA microprocessor/storage unit automatically.

5. Direct data collection and meaning explanation in WTMT

NOTE: As shown in **Figure 5**, the human gait cycle has been divided into different subphases. In detail, spatial and temporal parameters are defined and calculated as follows.

5.1. Determine the steps (n): the number of steps completed during level walking, including the right and left limbs.

5.2. Determine the swing duration (%): the phase percentage starting from toe-off until initial ground or stair contact for any given foot.

5.3. Determine the stance duration (%): phase percentage between the heel strike of one foot and the heel strike of the contra-lateral foot.

5.4. Determine the speed (m/s): the average velocity over two consecutive strides.

5.5. Determine the step length (m): the difference in length between the initial heel strike of the right or left foot and the heel strike of the contralateral foot.

5.6. Determine the stride length (m): the distance between the successive points of the initial contact of the same foot, right -left-right (R-L-R) or left-right- left (L-R-L).

5.7. Determine the gait variability of step length: coefficient of the variation of step length.

NOTE: Completion time and errors are also collected and counted by the examiner, instead of IDEEA.

6. Data collection and statistics

6.1. Use one-way-ANOVA and Fisher's LSD to compare the differences between the groups. The demographic data are listed in **Table 1**. dTMT-A, dTMT-B, WTMT-A, and WTMT-B data are shown in **Tables 2-5** respectively. A $P < 0.05$ was considered to indicate a statistically significant difference.

REPRESENTATIVE RESULTS:

Seven aged patients with Mild Cognitive Impairment (Elderly with MCI), seven aged subjects with Parkinson's Disease (Elderly with PD), and seven aged healthy individuals (Healthy Elderly) were recruited, and dTMT-A, dTMT-B, WTMT-A, and WTMT-B, were performed. After the tests, data were collected and analyzed using SPSS software.

As a whole, the demographical data of participants showed that all groups were matched well in terms of age, gender, educational level, dominant hand, Clinical Dementia Rating (CDR) score, Global Deterioration Scale (GDS) score, TUG: timed Up and Go Test (TUG), and so forth ($p > 0.05$). As shown in **Table 2**, most of the data of dTMT-A between Healthy Elderly, Elderly with MCI, and Elderly with PD were similar, such as Total time to completion (18.15 ± 5.12 s vs. 19.67 ± 7.12 s vs. 19.85 ± 3.89, P = 0.812), Number of Errors (0.14 ± 0.38 vs. 0.29 ± 0.49 vs. 0.29 ± 0.49, P = 0.796), and so forth. This means all the participants had similar scores if they are assessed by traditional TMT-A. However, there existed some different variables captured by dTMT-A. As shown in **Table 2**, Elderly with PD exhibited a larger total pathway deviation of each step (P_b=0.017, P_c=0.048), a larger variability of pathway deviation (P_b=0.000, P_c=0.000), and a lower velocity of drawing of each step (P_b=0.001, P_c=0.025) compared with Elderly with MCI and Healthy Elderly, respectively.

As shown in **Table 3**, the differences in completing dTMT-B were reflected in more aspects relative to dTMT-A. Aged patients with MCI needed a longer time of completion (P=0.000) and had more errors (P=0.000), more time inside the circle (P=0.000) or tolerance circle (P=0.000), more pathway deviation (P=0.035), and lower velocity in drawing (P=0.000) compared with healthy elderly. Meanwhile, Elderly with PD needed a longer time of completion (P=0.000), and had more errors (P=0.000), more time inside the circle (0.000) but less time inside the tolerance circle (P=0.000), more pathway deviation (P=0.032), larger variability of pathway deviation (P=0.001), and obviously lower velocity of drawing of each step (P=0.000) compared with aged healthy individuals. All the results indicated that dTMT can detected amount of significant differences between aged healthy participants and aged patients.

As shown in **Table 4**, gait data in WTMT-A could detect more differences between Elderly with PD in comparison with other individuals, especially in terms of speed (P_b=0.000, P_c=0.002), step length (P_b=0.004, P_c=0.016), stride length (P_b=0.005, P_c=0.019), and so forth. All these data implied that WTMT-A could capture obvious differences between aged PD patients and aged healthy participants.

As shown in **Table 5**, gait data in WTMT-B could find more differences between groups. Aged patients with MCI and PD needed a longer time (P_a=0.001, P_b=0.000) and more steps to complete the test (P_a=0.000, P_b=0.000). Their step and stride length seemed shorter relative to aged healthy participants. In addition, aged patients with PD showed even more severe trend in comparison with MCI subjects. The marked differences are step length (0.045 m ± 0.02 vs. 0.049 m ± 0.02, P_c=0.002), stride length (0.91 m ± 0.04 vs. 0.96 m ± 0.03, Pc=0.012), and Gait variability of step length (0.112 ± 0.0030 vs. 0.120 ± 0.0034, Pc=0.000).

FIGURE AND TABLE LEGENDS:

Figure 1. Computer. Computer for dTMT-A and dTMT-B (upper panel), print screen of dTMT, subjects choose Part A to start dTMT-A, or Part B to start dTMT-B (lower panel).

Figure 2. IDEEA. Device for WTMT-A and WTMT-B.

Figure 3. Example of WTMT-A and WTMT-B. As shown in the figure, subjects need to begin from START and walk to the END.

Figure 4. IDEEA accelerometers and the location. The figure showed how to wear the IDEEA accelerometers correctly.

Figure 5. Human gait cycle divided into different subphases. Stand phase was about 60% of gait cycle, and Swing phase was about 40% of gait cycle.

Table 1. Demographic data of participants. Mean ± SD. M:F: Male: Female; R%: Right hand percentage; yrs: years; MMSE: Mini Mental State Examination.; MCI: Mild Cognitive Impairment; PD: Parkinson's Disease; CDR: Clinical Dementia Rating; GDS: Global Deterioration Scale; TUG: timed Up and Go Test; S: Seconds

Table 2. dTMT-A data of participants. Mean ± SD. MCI: Mild Cognitive Impairment; PD: Parkinson's Disease. One-way-ANOVA and post hoc analysis with LSD. a: $P < 0.05$ Elderly with MCI relative to Healthy Elderly; b: $P < 0.05$ Elderly with PD relative to Healthy Elderly; c: $P < 0.05$ Elderly with PD relative to Elderly with MCI.

Table 3. dTMT-B data of participants. Mean ± SD. MCI: Mild Cognitive Impairment; PD: Parkinson's Disease. One-way-ANOVA and post hoc analysis with LSD. a: $P < 0.05$ Elderly with MCI relative to Healthy Elderly; b: $P < 0.05$ Elderly with PD relative to Healthy Elderly; c: $P < 0.05$ Elderly with PD relative to Elderly with MCI.

Table 4. WTMT-A data of participants. Mean ± SD. MCI: Mild Cognitive Impairment; PD: Parkinson's Disease. One-way-ANOVA and post hoc analysis with LSD. a: $P < 0.05$ Elderly with MCI relative to Healthy Elderly; b: $P < 0.05$ Elderly with PD relative to Healthy Elderly; c: $P < 0.05$ Elderly with PD relative to Elderly with MCI.

Table 5. WTMT-B data of participants. Mean ± SD. MCI: Mild Cognitive Impairment; PD: Parkinson's Disease. One-way-ANOVA and post hoc analysis with LSD. a: $P < 0.05$ Elderly with MCI relative to Healthy Elderly; b: $P < 0.05$ Elderly with PD relative to Healthy Elderly; c: $P < 0.05$ Elderly with PD relative to Elderly with MCI.

DISCUSSION:

Traditional paper-pencil TMT has been well used worldwide for more than 50 years. However, digital TMT is advantageous. First, traditional TMT is considered as an executive function tool, while both dTMT and WTMT have aspects reflecting motor ability besides cognitive function. Considering that the cognitive-motor dual task has gained great attention in recent years[26], digital technologies can provide researchers with more information on this integrated task compared with the traditional TMT[27]. Second, digital TMT is a sensitive tool compared with the traditional version. Digital TMT does not need additional time relative to traditional ones, which has enough compliance of subjects.

A critical step in the protocol is to perform dTMT and WTMT with no interruption, because both tests collected time variables. Subjects need to complete the tests fluently. Any delay induced by examiners, or misunderstanding, distraction, etc., should be minimized or eliminated.

There are two modifications to be mentioned. First, for dTMT, the real-time pressure of the stylus onto the screen is a sensitive variable for drawing, which has been confirmed in a digital Clock Drawing Test[28]. With more development, software that could detect the stylus pressure onto the screen during dTMT will give physicians more information in future. Second, for WTMT, a new device that can detect and analyze trunk sway might be helpful to find more evidence in movement disorder patients[29,30], because IDEEA only provides gait data. However, as far as we know, IDEEA is the first digital accelerometry used in WTMT.

The current study introduced two types of TMTs in a digitized version. These new types of TMTs were derived, rather than being an exact copy of the traditional TMT. Robert P. Fellows found that the computerized TMT needed fewer circles compared to the traditional TMT, in case the circles were too crowded[31]. However, this difference cannot impede the wide use of the digital TMT in the future.

Since digital technology is becoming more and more popular in our daily life, digital devices should be used in early diagnosis of cognitive disorders and movement disorders[32]. dTMT and WTMT are both derived from traditional TMT but can capture more variables than the paper-based TMT. Both new modified TMTs could be used to screen patients with cognitive disorders and movement disorders. Particularly for those patients with upper limb disability, WTMT is particularly useful.

A limitation of the present study was its small sample size. Consequently, the sensitivity and specificity of digital TMT could be demonstrated. However, dTMT and WTMT could find additional information for the physicians to determine the cognitive function and motor ability of the participants. However, more studies are needed to validate the findings.

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DISCLOSURES:

The authors have nothing to disclose.

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Figure1 new

Figure2

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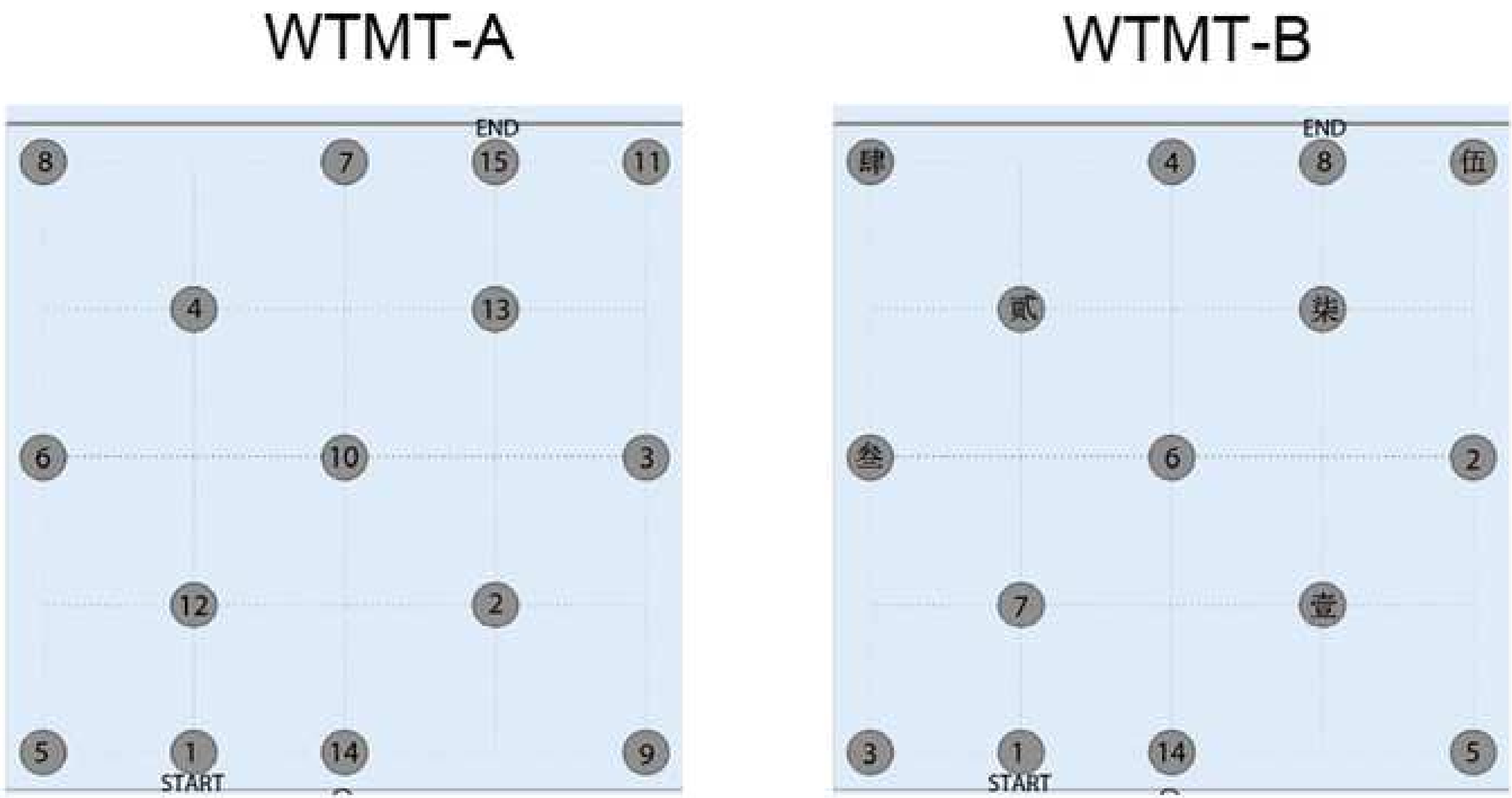
WTMT-A
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Figure5

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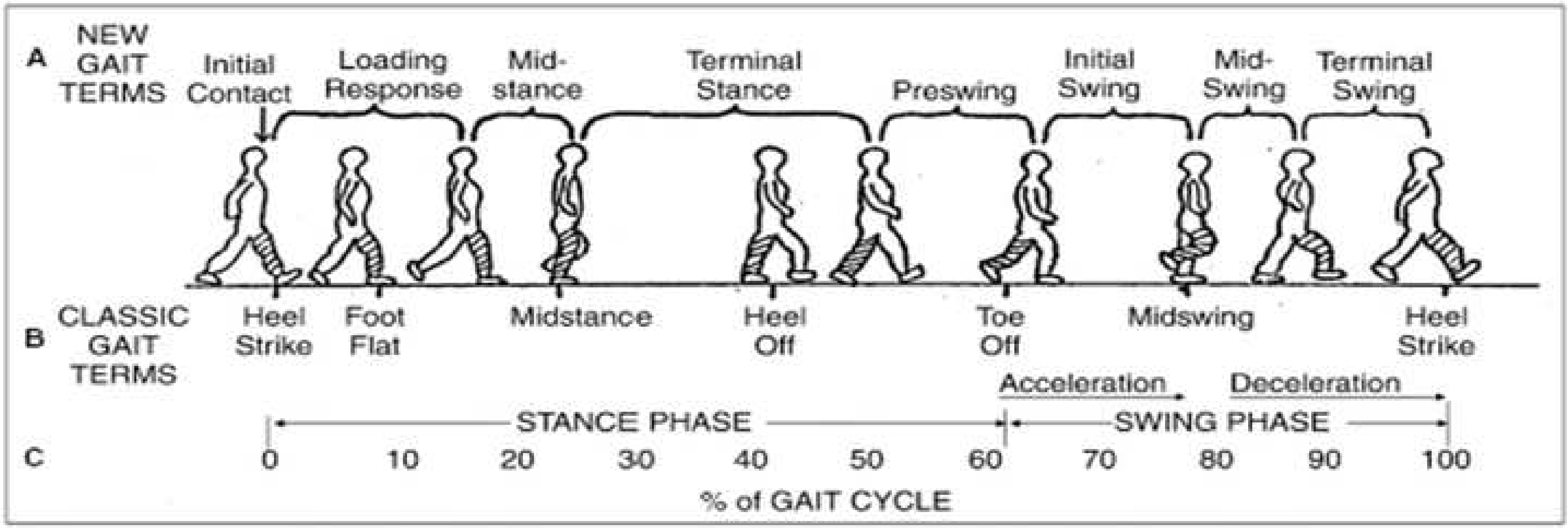

	Healthy Elderly N=7	Elderly with MCI N=7	Elderly with PD N=7	P Value
Age	67.14±4.22	65.14±3.39	66.29±3.90	0.63
Gender(M:F)	4:03	5:02	4:03	0.589
Dominant hand(R%)	100	100	100	
Education (yrs)	10.00±1.91	11.43±2.51	10.14±1.36	0.353
MMSE	29.00±1.15	27.86±1.35	28.43±1.27	0.263
CDR	0.14±0.24	0.5±0.00	0.29±0.39	0.066
GDS	2.28±0.49	2.71±0.76	2.29±0.75	0.487
TUG (S)	10.07±1.51	11.02±0.60	11.72±1.24	0.052

	Healthy Elderly N=7	Elderly with MCI N=7	Elderly with PD N=7	P Value
Total time to Completion	18.15±5.12	19.67±7.12	19.85±3.89	0.821
Number of Errors	0.14±0.38	0.29±0.49	0.29±0.49	0.796
Total time inside each circle	6.94±1.99	6.91±3.31	7.81±2.46	0.773
Inside circle percentage	39.13±7.70	35.42±10.25	40.02±11.63	0.665
Total time inside each tolerance circle	1.57±0.80	2.09±0.88	1.85±0.49	0.442
Inside tolerance circle percentage	8.74±3.02	10.80±3.07	9.61±3.55	0.498
Total Line cancelling times	0.14±0.38	0.29±0.49	0.14±0.38	0.764
Total pathway deviation of each step	38.41±2.52	39.30±3.07	42.99±3.99[b,c]	0.039
Variability of pathway deviation	1.72±0.24	2.36±0.55[a]	3.66±0.46[b,c]	0
Velocity of drawing of each step	21.38±2.59	19.00±2.40	15.70±2.55[b,c]	0.002

	Healthy Elderly N=7	Elderly with MCI N=7	Elderly with PD N=7	P Value
Total time to Completion	32.07±10.93	67.56±9.87[a]	89.95±12.12[b, c]	0
Number of Errors	0.14±0.38	2.86±1.07[a]	1.29±0.49[b, c]	0
Total time inside each circle	6.03±1.72	27.83±5.05[a]	7.81±2.46[b, c]	0
Inside circle percentage(%)	19.16±3.86	41.47±6.76[a]	22.46±3.35[c]	0
Total time inside each tolerance circle	3.51±0.91	9.73±1.46[a]	3.93±2.21[c]	0
Inside tolerance circle percentage(%)	11.26±2.20	14.47±1.62[a]	4.57±2.86[b, c]	0
Total Line cancelling times	0.29±0.38	0.86±1.07	0.43±0.53	0.35
Total pathway deviation of each step	86.02±7.36	95.36±6.76[a]	95.56±8.78[b]	0.051
Variability of pathway deviation	2.158±0.173	2.024±0125	2.659±0.332[b, c]	0
Velocity of drawing of each step	16.85±1.79	8.41±1.09[a]	4.91±0.91[b, c]	0

Table 4 Click here to access/download;Table;Tab4.xlsx

	Healthy Elderly N=7	Elderly with MCI N=7	Elderly with PD N=7	P Value
Total time to Completion	68.43±4.86	76.57±7.66	98.29±9.36[b, c]	0
Number of Errors	0.29±0.49	0.29±0.49	0.57±0.53	0.487
Steps (n)	80.86±2.34	81.29±3.30	81.71±3.90	0.886
Swing duration (%)	36.86±1.32	35.03±0.84[a]	35.48±1.25[b]	0.022
Step duration (%)	63.00±1.35	64.97±0.84 [a]	64.52±1.25[b]	0.014
Speed (m/s)	1.01±0.10	0.82±0.57[a]	0.68±0.04[b, c]	0
Step length (m)	0.51±0.02	0.50±0.01	0.49±0.02[b, c]	0.01
Stride length (m)	1.02±0.04	1.00±0.02	0.96±0.04[b, c]	0.011
Gait variability of step length	0.111±0.0011	0.112±0.0011	0.113±0.0014	0.156

Table 5 Click here to access/download;Table;Tab5.xlsx

	Healthy Elderly N=7	Elderly with MCI N=7	Elderly with PD N=7	P Value
Total time to Completion	78.57±4.86	92.29±7.72[a]	109.00±5.66[b, c]	0
Number of Errors	0.57±0.79	1.14±1.07	0.86±0.69	0.479
Steps (n)	89.71±2.63	96.71±2.29[a]	100.57±3.74[b, c]	0
Swing duration (%)	37.20±1.21	36.56±1.23	36.47±1.15	0.476
Step duration (%)	62.80±1.21	63.44±1.23	63.53±1.15	0.476
Speed (m/s)	0.98±0.06	0.83±0.08[a]	0.73±0.03[b, c]	0
Step length (m)	0.51±0.02	0.49±0.02	0.45±0.02[b, c]	0
Stride length (m)	1.01±0.04	0.96±0.03[a]	0.91±0.04[b, c]	0
Gait variability of step length	0.114±0.0033	0.120±0.0034[a]	0.112±0.0030[c]	0.001

Name of Material/ Equipment	Company	Catalog Number
Minisun	LLC	
Surface Pro 2	Microsoft	

Comments/Description

Intelligent Device for Energy Expenditure and Activity (IDEEA)

computer

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Author(s):	Wei Wei, Hóngyi Zhào, Yu Liu, Yonghua Huang

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Reply:

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Reply:

Thank you for your suggestion, we asked for the language editing help from native English speaker, and have improved the grammatic level of our manuscript.

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Reply:

Thank you for your help. I noticed this point, and have changed the usage of language. Now the original language is used.

4. Please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:

Thank you, we have added them in new-versioned manuscript.

a) Critical steps within the protocol

Reply:

Critical steps within the protocol is the procedure of performing dTMT and WTMT with no interruption, because both tests collected time variables. As a result, subjects needed to complete the tests fluently. Any delay induced by examiners, or misunderstanding, distraction, etc, should be minimized or eliminated.

b) Any modifications and troubleshooting of the technique

c) Any limitations of the technique

Reply:

There are two modifications need to be mentioned. First, for dTMT, real-time pressure of stylus onto the screen is a sensitive variable for drawing, which has been confirmed in digital Clock Drawing Test28, with development of technologies, software that could detect the pressure of stylus onto the screen during dTMT will give physicians more information in future. Second, for WTMT, new device that can detect and analyze sway of trunk might be helpful to find more evidence in movement disorder patients29,30, because IDEEA only detect gait data. However, as far as we know, IDEEA is the first digital accelerometry used in WTMT.

d) The significance with respect to existing methods

e) Any future applications of the technique

Reply:

Since digital technology is becoming more and more popular in our daily life, and digital devices should be used in early diagnosis of cognitive disorders and movement disorders32. dTMT and WTMT are both derive from traditional TMT, but are capable to capture more variables than the paper-based TMT. In our opinion, both new modified TMT could be used in screening patients with cognitive disorders and movement disorders. Besides, for those patients with upper limb disability, WTMT is particularly useful.

5. Please rephrase the Short Abstract to clearly describe the protocol and its applications in complete sentences between 10-50 words: “Here, we present a protocol to …”

Reply:

Thank you, we have rephrased the Short Abstract, please find it in new-versioned manuscript.

6. Please adjust the numbering of the Protocol to follow the JoVE Instructions for Authors. For example, 1 should be followed by 1.1 and then 1.1.1 and 1.1.2 if necessary. Please refrain from using bullets or dashes.

Reply:

Thank you, we made the adjustment of the number.

7. Please add a one-line space between each of your protocol steps.

Reply:

Thank you, we have added it.

8. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., “Do this,” “Ensure that,” etc.). Any text that cannot be written in the imperative tense may be added as a “Note.”

Reply:

Thank you for reminding us, we confirm that.

9. There is a 2.75 page limit for filmable content. Please highlight 2.75 pages or less of the Protocol steps (including headings and spacing) in yellow that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

Reply:

Yes, we have highlighted 2.75 pages of the protocol steps.

Thank you.

10. For steps that are done using software, a step-wise description of software usage must be included in the step. Please mention what button is clicked on in the software, or which menu items need to be selected to perform the step.

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Reply:
Yes, we confirm that.
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Reply:
Yes, we confirm that.

Reviewers' comments:
Reviewer #1:
The use of TMT is not new. However, the idea of this protocol is comprehensible and well described.

There are a few vulnerabilities, which should be considered.

Major Concerns:
1. Please point out what more information can dTMT you mentioned in this manuscript give than traditional TMT?
Reply:
dTMT has been proved to be capable of not only measuring the same aspects of cognition as the traditional TMT, but also monitoring other cognitive processes not captured by the

traditional TMT alone [1]. As a whole, dTMT could capture the time to completion, as well as number of errors are considered as the main additional information dTMT can give than traditional TMT. In detail, specific data that can be captured in dTMT instead of traditional TMT is of importance. For example, time inside circles and movement velocity (or velocity of drawing) mentioned in dTMT could give be more helpful than traditional TMT, which have been noticed by us and other researchers [1,2].

2. It is recommended to explain why digital TMT does not need too much additional time relative to traditional ones and why digital TMT method is quite a sensitive tool compared with traditional version.

Reply:

dTMT does not need too much additional time relative to traditional ones, because the circles are positioned in dTMT just as traditional TMT, and subjects need to complete the same task as tradional TMT. The only difference that dTMT is completed through stylus and computer screen while the traditional TMT is completed through pencil and paper. More than one group has reported in their research that dTMT is quite a sensitive tool compared with traditional version in patients with different diseases [2,3].

3. Please give more information of the degree of damage to subjects recruited in the MCI group and PD group.

Reply:

Thank you for your advice.

We added the results of the Clinical Dementia Rating (CDR) score, the Global Deterioration Scale (GDS) score, and Timed Up and Go Test (TUG) score in tab 1, so as to reflect the degree of damage to subjects recruited in the MCI group and PD group.

4. Try not to include comments on the results in the results section, such as "gait data in WTMT-A could detected more differences between Elderly with PD in comparison with other subjects". Meanwhile it is recommended to give the specific value.

Reply:

We tried not to comment the results, instead, we compared the results. Meanwhile, we give the specific value. Please find them in new-versioned manuscript.

Minor Concerns:

1. IDEEA for the first time used in the manuscript in line 80 should be given the full name.

Reply:

Thank you for your advice. The Intelligent Device for Energy Expenditure and Activity (IDEEA). This full name has been given in the manuscript.

2. dTMT needs more than 2-year education (line 91).

Reply:

Thank you for your question. Participants enrolled to complete dTMT should have the educational level of more than 2-year of preliminary school, otherwise, they might have difficulty in reading and recognizing Chinese characters in dTMT-B. This point has been changed in the manuscript.

3. WTMT needs more than 2-year education (line 154).

Reply:

Thank you for your question. Participants enrolled to complete WTMT should have the educational level of more than 2-year of preliminary school, otherwise, they might have difficulty in reading and recognizing Chinese characters in WTMT-B. This point has been changed in the manuscript.

4. The sentence should be "CAUTION: The WTMT-B was performed only once. (line 187).

Reply:

Thank you for your suggestion, it is corrected.

5. The sentence should be "NOTE: All the WTMT-B data are gathered in IDEEA microprocessor/storage unit automatically. (line 194)"

Reply:

Thank you, it is corrected.

6. "Step duration (line 202)" should be "stance duration".

Reply:

Thank you, it is corrected.

Reviewer #2:

The paper presents the dTMT and WTMT, both of which are interesting tests, however, it would be helpful to more clearly explain which processes each suggested outcome measure is thought to index, potential uses of the tests, and the relative benefits of these two tests compared to the standard TMT. Detailed comments are provided below.

At present, there are numerous grammatical and linguistic mistakes, which in some cases make the text hard to understand - the text would benefit from being sent to an English language editing service.

Reply:

Thank you for your advice, you are right. Our manuscript has been improved by an English language editing service.

Abstract

28 - Could you provide specific examples that demonstrate the additional information provided by the digital and walking TMT compared to the traditional version?

Reply:

Yes. dTMT-B score was not only found to be correlated with paper-based TMT-B. Furthermore, "*dTMT-B's additional data might be able to help monitor other cognitive process not captured by paper-based TMT alone*" (Line 14-15, Page 1) [1]. The investigators focused on the correlation between dTMT performance with other cognitive tests, such as Telephone Interview for Cognitive Status score and Frontal Assessment Battery score, both of correlations were positive, though small (r=0.10 and r=0.29, respectively).

For WTMT, additional information was provided compared to traditional version, for example, predicting the risk of falling. Alexander and colleagues reported a strong correlation between W-TMT results and P-TMT B, in the discussion section, the author suggested that "*Future studies should test whether W-TMT (especially W-TMT B) performance ultimately predicts falls better than does P-TMT B, particularly in falls with an environmental hazard etiology.*"(Line 57-60. Page1561) [5]. In 2010, Yamada et al found that WTMT, rather than traditional TMT, was significant related to falling (*odds ratio 1.160,* *95% confidence interval 1.107~1.214; p <0.001*) [6].

These examples might be not suitable to add in Abstract section, I wonder if they are recommended to be presented in other section of manuscript?

Introduction

47 - what is meant by 'find more details in other perspectives'?

Reply:

What we wanted to say was that "find details under different conditions, such as driving and walking."

We have changed it in new-versioned manuscript.

Thank you.

47-49 - this sentence is difficult to understand

Reply:

I am sorry the meaning of this sentence is hard to understand. Most TMT are design as 25 numbers (1-25) for TMT-A (shown in Fig S1), and 13 numbers (1-13) plus 12 letters/characters (A-L) for TMT-B (Shown in Fig S2). However, there still exist many TMT that are designed with fewer numbers or letters/characters [7,8]. These TMTs are confirmed to have high validity and reliability. They are designed with fewer numbers and characters because the protocols are different.

"Of note, some investigations conferring different less numbers than the standard TMT are also reported to be of high validity and reliability." is changed as "Of note, some investigations conferring different fewer numbers than the standard TMT are also reported to be of high validity and reliability."

52 - can you provide examples of what other properties (besides executive functioning) the TMT is thought to index?

Reply:

Many TMT evaluating system have been invented to index cognitive dysfunction properties besides executive dysfunction. For example, some researchers investigate the errors in TMT, and they found that errors in TMT-B was associated with mental tracking and working memory in psychiatric disorder patients [9]. Another group from Greece suggested derived TMT scores (TMT-(B−A) or TMT(B/A)) as indices to detect impairment in cognitive flexibility across the adult life span [10].

Thank you for your question, we have added these examples into the manuscript.

53-58 - do these alternative scoring methods provide additional information or some other benefit compared to the standard scoring method (time taken to complete the task)? Are there any particular problems associated with using the alternative methods?

Reply:

Yes, these alternative scoring methods provide additional information. For example, ①the utility of TMT error analysis could reveal cognitive deficits not traditionally captured using completion time as the sole outcome variable in schizophrenia and depression patients [9];

②the lack of any significant intermanual difference was helpful to discriminate the cognitive dysfunction from the influence by the motor disorder [11]; ③derived Trail Making Test indices were able to detect impairment in cognitive flexibility across the adult life span, and minimize the effect of demographics and other cognitive background variables [10].

We have added these points in the manuscript.

In my opinion, the problem for using alternative scoring methods is rare, except for the lack of well-accepted procedure and fitted cutoff score. Considering the advantages of alternative scoring methods, more future studies are need to investigate the validity and reliability of alternative scoring system in different types of patients.

61-63 - what kind of additional information? Can you be specific about how the dTMT/WTMT is more useful than the traditional paper and pen version?

Reply:

The examples are introduced previously.

dTMT is found to be helpful to monitor other cognitive process not captured by paper-based TMT alone. For example, dTMT performance, instead of paper-based TMT, correlated with other cognitive tests, such as Telephone Interview for Cognitive Status score and Frontal Assessment Battery score [1].

For WTMT, Yamada et al found that WTMT, rather than traditional TMT, was able to predict the risk of falling [6].

Protocol

76-83 - could alternative equipment be used?

Reply:

Yes, other equipment could be used.

For dTMT, Microsoft Surface Pro 3, 4 and 5 and other windows system computer with digital pen are also compatible for the software. We have added it into the manuscript.

For WTMT, maybe GAITRite or other gait analyzer could be helpful, but no other gait monitor was introduced by other researchers as far as we know. As a result, we did not add other equipment into the manuscript.

Thank you for your recommendation.

89 - 2.1.1 not 2.1.2. Would it always be necessary for researchers to collect all of this information? It is not necessary for scoring the test, so surely it would depend on what their specific research questions are?

Reply:

Thank you for your suggestion, we have deleted repeated collection of information.

94 - young people may also need glasses. Should there be a step in the protocol to check that participants can easily read the numbers on the screen?

Reply:

Actually, we only collected aged subjects in current study. But you are right, we decided to add a step in the protocol to check if the participants can easily read the numbers on the screen, because even young people may also need glasses.

Thank you very much for your suggestion, and we have changed it in manuscript.

98-104 - this makes it sound like the participant completes a practice version of the test before the researcher explains it to them. Is this correct? How are participants told to balance speed and errors in their completion of the test?

Reply:

Yes, dTMT is quite a simple test, and most participant could understand what they need to do in our clinical practice. Participants are encouraged to draw the line fluently, but as accurately as possible, but no priority is given as paradigm, since dTMT is a kind of dual task, and priority or trade-off is not investigated in our study. Actually, in some other studies about dual task, a definite priority could be chosen by researchers in their paradigm [12].

106 - what happens when a participant makes an error? In general, there is very little information about what the dTMT program actually does - more information is necessary.

Reply:

Just as Line 111 mentioned, if the circle is not correctly lined, its color would be unchanged, and the subjects need to re-line it from the last circle. Thank you.

109 - what are participants told about the dTMT - B and how it differs from the dTMT-A?

Reply:

They are told to complete another TMT with numbers and Chinese characters. Different points from dTMT-A are shown in section 2.2.2

121-144 - why are all these results needed? What information do they provide?

Reply:

As shown in introduction (Paragraph 3), these results are based on the different TMT evaluating system.

132 - unclear what is meant here.

Reply:

Tolerance area was reported and designed by Dahmen's study [1] at first time, so as to replicate the paper-based TMT as much as possible, since the tip of stylus was thicker than a pen in their study. And this digital design was proved to be quite good for healthy aged individuals. However, in our study, those subjects with MCI who showed cognitive dysfunction were recruited. We found the MCI patients sometimes pause in tolerance area quite obviously relative to the subjects with normal cognitive function. As a result, we conserve this design, and checked, calculated and compared the time inside the tolerance circle. Our preliminary results showed that this is sensitive index, especially in dTMT-B.

Actually, for digital version of Clock Drawing Test, the similar design existed too. Analysis of paucity during drawing (so called Post-clock face circle latency, Pre-1st hand latency, Pre-2nd hand latency, etc) was also found to be a sensitive method for the discovery of cognitive decline [13].

144 - which confounding factors? How would replaying the TMT help to control for them?

Reply:

Sorry, this sentence should be deleted.

147 - WTMT, not dTMT

Reply:

You're right. It's a mistake

152-153 - same comment as for 89.

Reply:

Thank you once again for your suggestion, we have deleted repeated collection of information.

154 - why is a 2 year education needed? What is considered a sufficient visual disability to exclude someone from the task (e.g. using glasses?)

Reply:

Thank you for your question. Participants enrolled to complete WTMT should have the educational level of more than 2-year of preliminary school, otherwise, they might have difficulty in reading and recognizing Chinese characters in WTMT-B. This point has been changed in the manuscript.

For the similar reason, basic visual ability is needed, since the WTMT needs area of 4 meters ×4 meters. Researchers need to ensure that participants can easily read the numbers on the floor.

167 - are there any practice tests for the WTMT. If not, why not?

Reply:

Thank you for your advice.

As far as we know, practice tests for the WTMT in some researches are rare (or, only a straight walk before WTMT was designed) [5,6], for other researches, there existed a small practice test (not a whole WTMT) for the participants to familiarize the condition [14,15]. We did not design practice test for WTMT, because we have asked the participants to walk straight for a few steps (about 5-15 steps) to confirm the comfortability after IDEEA device was worn.

173 - how can a researcher 'confirm the safety of the subject'?

Reply:

Clinically, physicians would find the risk of falling of patients with MCI and PD through examination and interview [16,17]. Some questionnaires and rating scales are also helpful for researchers to find out the possibility of subjects' risk of falling (eg. Downton Fall Risk Index, Fall Risk Index) [18,19]. The reason for confirming the safety of the subject is that dual task walking is regarded as a "brain stress test" [20]. As we know, stress could cause gait disorder and increase the risk of falling for elderly [21].

175 - how is this pause accounted for in terms of the results of the WTMT? How valid/reliable are the data from the IDEEA?

Reply:

We ask the participants to make a 5-second step pause, so as to be helpful for us to analyze the data collected by IDEEA easily. Actually, IDEEA has its own time system, which could be a authorized method for us to discriminate which data were from the WTMT. We make a step pause just for the researchers could easily get the data. It's not a step indispensable. Just for the convenience.

187 & 194 - WTMT-B, not WTMT-A

Reply:

Thank you, it's my mistake, and I have corrected it.

198-209 - why are all these results needed? What information do they provide?

Reply:

These results are collected variables that IDEEA provided. Basically, they are all about length and duration. They can give us information in detail, which have more accuracy compared with other researchers using “simple time measurement” (Line 51-54, Page390) [6].

211-218 - would be better placed under 'representative results'. Have these data been published elsewhere?

Reply:

Thank you, we have placed it under representative results section. These data have not been published yet.

Representative results

What do the results actually tell us? This is not currently explained anywhere in the manuscript.

Reply:

Thank you for your question.

We wanted to show the results of three groups of participants when they complete dTMT and WTMT.

We tried to compared the variables of participants of each group, and find obvious differences by using modified TMT.

As a whole, dTMT and WTMT could captured more information that cannot be discovered by traditional TMT.

We just re-built the Representative results, please find them in new-versioned manuscript

Discussion

255-260 the benefits of the dTMT/WTMT compared to the traditional TMT should be more clearly outlined e.g. that the dTMT doesn't take much longer than the traditional TMT is not a benefit, instead it suggests that there is not a substantial deficit (in terms of time) with the dTMT.

Reply:

You are right, thank you for your explanation. We have rearrange the paragraph in the new-versioned manuscript.

263-264 - what does this mean for the validity/reliability of the test?

Reply:

The validity/reliability of the test has been analyzed by group colleagues of Fellows [22].

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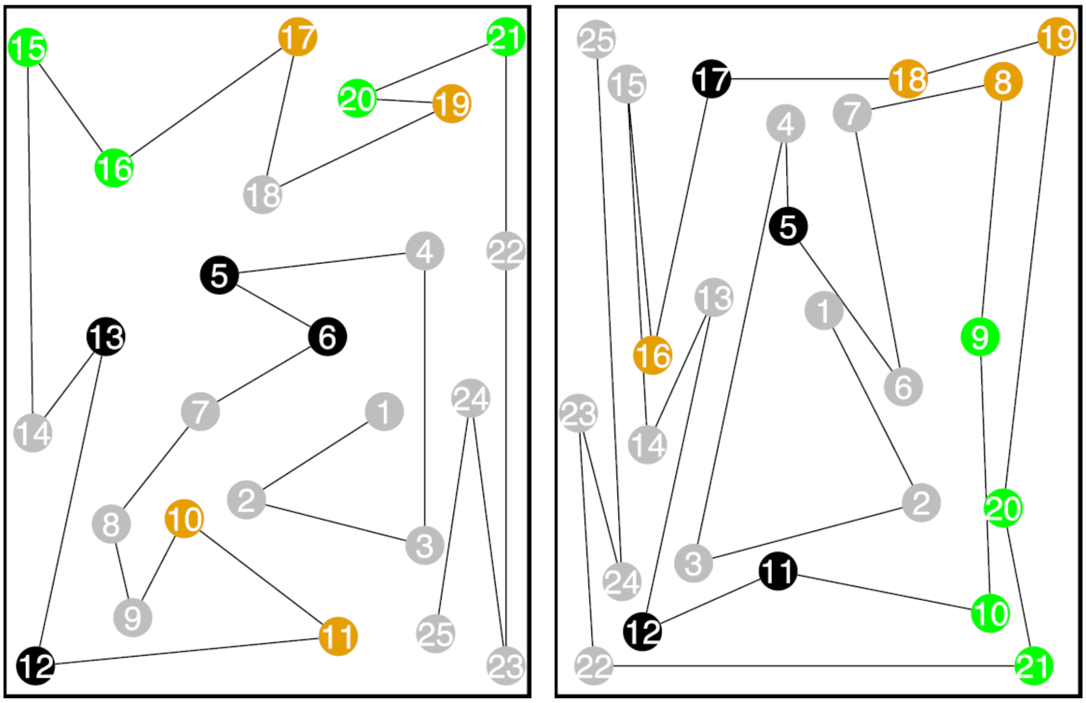

Fig S1

Figure is cited from “Klaming, L., et al. Non-dominant hand use increases completion time on part B of the Trail Making Test but not on part A. Behavior Research Methods, 50(3), 1074-1087 (2017).

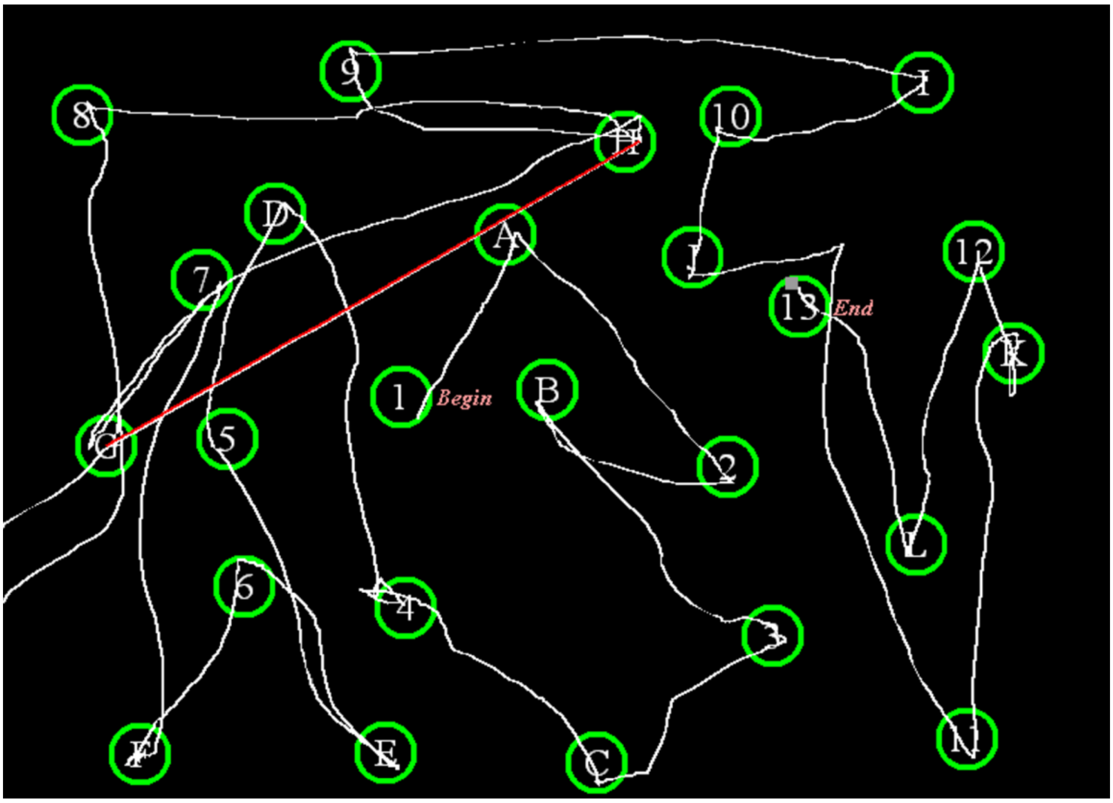

Fig S2

Figure is cited from “Woods, DL., et al. The Effects of Aging, Malingering, and Traumatic Brain Injury on Computerized Trail-Making Test Performance. PLOS ONE, 10(6), e0124345 (2015).”