The Relationship Between Spatio-temporal Gait Parameters and Cognitive Function: Protocol for a Cross-sectional Study

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Study Protocol

Keywords: Mild cognitive impairment, motoric-cognitive risk syndrome, locomotor functions

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The relationship between spatio-temporal gait parameters and cognitive function: Protocol for a cross-sectional study

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ABSTRACT

Background: Motor dysfunctions, such as slower walking speed, precede the occurrence of dementia and mild cognitive impairment, suggesting that walking parameters may be effective biomarkers for detecting early sub-clinical cognitive risk. In fact, while our preliminary study had a small sample, we found several walking parameters obtained by three-dimensional motion capture system, to be correlated with computer-based assessments of various cognitive function modalities. The Cognitive-Gait (CoGait) Database Project, described in the current protocol, aims to establish a database of multi-dimensional walking and cognitive performance data, collected from a large sample of healthy...
participants, crucial for detecting early sub-clinical cognitive risk.

**Methods:** The study will recruit healthy volunteers, 20 years or older, without any neurological or musculoskeletal disorders. The estimated sample size is 450 participants, including a 10% attrition rate. Using computer-based cognitive assessments, all participants will perform six tasks: (i) the simple reaction time task, (ii) Go/No-Go task, (iii) Stroop Color–Word Test, (iv) N-back test, (v) Trail making test, and (vi) Digit Span test. Gait will be measured through joint kinematics and global positioning in participants’ lower legs, using pants with an inertial measurement unit-based three-dimensional motion capture system, while walking at a comfortable and faster pace. Finally, we will establish a prediction model for various cognitive performance modalities, based on walking performance.

**Discussion:** This will be the first study to reveal the relationship between walking and cognitive performance using multi-dimensional data collected from a large sample of healthy adults, from the general population. Although there are several methodological limitations, such as accuracy of measurements, the CoGait database is expected to be the standard value for both walking and cognitive functions, supporting the evaluation of psychomotor function in early sub-clinical cognitive risk, including motoric-cognitive risk syndrome.

**Trial registration:** None.

**Keywords**

Mild cognitive impairment, motoric-cognitive risk syndrome, locomotor functions

**BACKGROUND**

Motoric-cognitive risk (MCR) syndrome, characterized by self-reported cognitive complaints and slower walking speed, is associated with an increased risk for dementia and mild cognitive impairment (MCI) [1–4]. Detection of MCR syndrome can facilitate early intervention, such as pharmacological treatment and training for sustained cognitive and physical functions, and prevention of MCI and dementia [5–9]. In addition, patient education for lifestyle modification, addressing issues such as diet, physical, and social activities, reduces the risk of these cognitive
disorders [10–15]. In a recent survey, the incidence rate for MCR in people in their 60s was 54.9 per
1,000 persons, which strongly suggests that preventive activities for these cognitive disorders should
be started at working age, before the initial presentation of early cognitive decline [16].

There are many risk factors for dementia, such as genetic factors, lifestyle habits, sleep
quality, education, and physical and social activities, even in the absence of detectable cognitive risk
[6,7,10,11,17–19]. Thus, we argue that cognitive risk screening in healthy participants requires
additional multimodal parameters. Establishing a database of multimodal parameters that includes
these risk factors is necessary to distinguish individuals with higher cognitive risks from the general
population.

Specifically, walking performance is the most notable marker of cognitive risk [20,21]. In
fact, our preliminary observation, using a three-dimensional motion capture system and computer-
based cognitive assessments in a small sample, showed a significant relationship between some
cognitive and walking performance modalities in healthy volunteers. This suggests the feasibility of a
motion capture system to predict and screen for a decline in cognitive function (see Supplementary
Figure S1, Additional File 1). Our study will collect the detailed walking parameters and cognitive
assessment scores of a sample of healthy volunteers, aged 20 years or older, to establish more accurate
predictive models for cognitive function.

METHODS

Study design

The current study, called the Cognitive-Gait Database (CoGait) project, will follow a cross-
sectional design, aimed at elucidating the relationship between walking and cognitive performance in
healthy adults. The sample size was estimated to be 410 persons, calculated using the effect size ($f =
0.074$) of a similar study [20] under the following conditions: multiple linear model; $df = 24$, $\alpha = 0.01,$
$1-\beta = 0.8$. The upwardly corrected sample size of 450 people, accounts for an attrition rate of 10%.
The sample size calculation was performed using G*power [22,23].

Study setting and recruitment

Healthy volunteers, older than 20 years and without any neurological or musculoskeletal
disorders, will be recruited for the study. The research team consists of a research scientist at Xenoma Inc. (TF), as well as faculty members at the Tokyo University of Technology (YW, TK, and AA), and Dokkyo Medical University (SI). Recruitment will be handled by the research team members.

Study participants

Inclusion criteria

Men or women older than 20 years, without any neurological or musculoskeletal disorders potentially affecting walking and cognitive functions, will be eligible for participation. Informed consent will be sought from all participants before they declare their medical histories. In the absence of exclusion criteria (see Exclusion criteria), participants’ walking and cognitive performance will be measured (see Measures).

Exclusion criteria

Participants will be excluded from the study if their medical histories include the disorders or conditions listed in Table 1. Participants with visible abnormalities in walking function (i.e., a mobility function score of <7 on the Functional Independent Measure), as assessed by a skilled physician, physiotherapist, nurse, or research scientist, will also be excluded [24]. Only native Japanese speakers will be recruited.

Table 1. Exclusion criteria

| Exclusion criteria |
|--------------------|
| People who cannot walk independently. |
| People with any amputations. |
| People with disabilities in vision, hearing, and/or equilibrium. |
| People who cannot use a tablet owing to disabilities in their upper limbs. |
| People at high risk of falling. |
| People who cannot understand the experimental instructions in Japanese. |

Measures

General procedure

First, we will obtain written informed consent from all participants. Second, we will obtain
their personal information and medical histories (Tables 1 and 2). Unique personal identities (IDs) will be generated for participants who do not meet the exclusion criteria, and printed as QR codes, required during registration, for the walking and cognitive assessments. Upon receiving their IDs, participants’ walking will be measured (see Gait measurement). After a 10-minute break, they will participate in the cognitive assessment (see Cognitive assessment). The walking and cognitive function datasets will be securely stored in online cloud storage. An overview of the study procedures and measurements is presented in Figure 1.

Table 2. Items for collecting participants’ personal information

| Personal information | Body information | Medical information |
|----------------------|------------------|--------------------|
| Name                 | Body height      | History of neurological disorders |
| Gender               | Body weight      | History of orthopedic disorders |
| Birthday             | Sex              | History of psychiatric disorders |
| Contact              | Other disorders  |                                  |
| Education            | Medications      |                                  |
| Mother tongue        |                  |                                  |

Gait measurement

We will measure walking parameters using pants, fitted with seven inertial measurement unit (IMU) sensors (e-skin MEVA; Xenoma Inc., Tokyo, Japan), located in the e-textile segments, as shown in Figures 2A–C. The IMU sensors contain triaxial accelerometers and triaxial gyroscopes, enabling the estimation of three-dimensional joint kinematics and global positioning, according to a known algorithm [25]. Prior to the development of the current study protocol, we conducted a validity check, comparing joint angles across the e-skin MEVA and conventional optical motion capture system (VICON Nexus ver. 2.1.1, VICON, Oxford, UK). Overall, the systems were comparable (root mean square error: 3.57±1.50 °; \( r = 0.96±0.03 \), on both sides of the hip, knee, and ankle joints; see Supplementary Figure S2, Additional File 1).
To calibrate the three-dimensional model calculation prior to gait measurement, each participant will be asked to adopt two postures: leaning forward with their hands pressed against a wall (Figure 2D), and standing upright (Figure 2E). Next, participants will be asked to walk in a straight line on a 16 m walkway, including 3 m inlet zones, at the start and end points. The measurements will be conducted under two conditions: fast (maximum speed) and comfortable (self-selected speed). Participants will practice the walking task under each condition, several times before the measurements, to ensure they understand the requirements of the experimental tasks. In the fast condition, we will instruct participants to walk at their maximum speed, without running or falling. In the comfortable condition, we will instruct them to walk at their regular, comfortable speed.

The measurement datasets will comprise raw IMU sensor signals (acceleration and angular velocity), global positioning of each sensor and anatomical landmark, and joint angles in the pelvis, hip, knee, and ankle (347 parameters in total). The datasets will be automatically uploaded to cloud storage (Figure 1). The data processing methods are described below (see Data Analysis).

Cognitive assessment

Cognitive assessments will be conducted using a custom-developed web-based software application. Computer-based cognitive assessment covers a wide range of cognitive functions and minimizes floor and ceiling effects [26]. Moreover, such assessments can collect data not only in terms of the accuracy of each task, but also in temporal, spatial, and spatio-temporal domains, differentiating it from conventional paper-pencil-based cognitive assessments [27,28].

The software was coded using JavaScript® and runs on a web browser (Safari, Apple, Cupertino, CA). To ensure visual conformity, all tests will be conducted using tablets with the same model number (iPad (8th), Apple, Cupertino, CA). The measure consists of six subtests: (i) Simple reaction time (SRT) task, (ii) Go/No-Go task, (iii) Stroop Color–Word Test, (iv) N-back test, (v) Trail Making Test (TMT), and (vi) Digit span (DS) test. During the tests, the tablets will be positioned in a landscape orientation and tilted at 20 °. Participants’ right index fingers will be placed 2.0 cm behind the tablet. Before any tests, all participants will practice the tasks at least twice, with verbal instructions.
from the expert staff, using a tablet.

(i) Simple reaction time task

The flow of the SRT task is illustrated in Figure 3A. Participants will be asked to fix their
gaze on the center of the white cross (fixation point), after the warning signal (1000 Hz, 50 ms). The
target signal (red circle), will appear on a black background at random timing (1–3 seconds after the
warning signal). Participants will be asked to press the “はい (Yes)” button with their right index
finger when the signal appears [29]. The SRT task comprises 10 trials.

(ii) Go/No-Go task

The flow of the Go/No-Go task is shown in Figure 3B. The procedure of this task is similar
to the SRT task, but the target signal is either a red circle, red triangle, or red cross, on a black
background with a 2 s presentation time. Participants will be asked to respond only when the red circle
appears on the display. The task consists of 10 trials each, for the “Go” and “No-Go” paradigms [30].
The Go/No-Go ratio was determined such that the reaction time will be prolonged compared to SRT
in healthy volunteers (n = 4; M = 38.5 years, SD = 12.2; Supplementary Figure S3A, Additional File
1).

(iii) Stroop Color–Word Test

The Stroop Color–Word Test was translated from a previous study [31] and converted into
a digitized test, using a tablet. The color words are displayed as target signals after the warning signal.
The target signal is the Chinese words [RED], [BLUE], and [GREEN], with the font color set to one
of these colors, on a black background, with a 2 s presentation time (Figure 3C). Participants will be
asked to respond only when any word in a red font appears (Go trial). The Go trial consists of
congruent (color and word match) and incongruent (color and word mismatch) conditions [32]. The
ratio between congruent and incongruent groups is 1:1 [32], and the task consists of 10 trials each, for
the Go and No-Go paradigms. In addition to the Go/No-Go task, the reaction time was prolonged
compared to SRT in healthy volunteers (n = 4; M = 38.5 years, SD = 12.2; Supplementary Figure S3A,
Additional File 1).

(iv) N-back task
The N-back task is a major approach used for assessing working memory capacity [33,34]. Single digit numbers will be displayed on the tablet as target signals (Figure 4A), with a presentation time of 2 s for each target signal.

In the one-back condition, participants will be asked to respond only when the target signal is the same as the last digit number (congruent condition). In the two- and three-back conditions, they should respond only when the target signals are the same as the second- and third-digit numbers, respectively. The frequency of the congruent condition will be set to 44% of the target signals, and the number of target signals is 15 trials. In this condition, reaction times in healthy volunteers (n = 5; M = 34.4 years, SD = 4.98) were prolonged in the N = 1 and 2, compared to N = 1 (Supplementary Figures S3B and C, Additional File 1).

(v) Trail Making Test

We adapted the Japanese version of the paper-based TMT, so that the data could be uploaded to our cloud storage [35]. The TMT consists of the TMT-A and TMT-B. The TMT-A contains 25 circled numbers, ranging from 1 to 25; participants will be asked to tap the circled numbers in order, from 1 to 25 (Figure 4B). The TMT-B contains 13 circled numbers, ranging from 1 to 13, and 12 circled Japanese kana letters; participants will be asked to tap the numbers and letters following the rule 1-[あ]-2-[い]-3-[う]…[し]-13, corresponding to the original alphabet version of TMT-B (Figure 4B) [35,36]. In our adapted TMT, participants do not need to draw a line on the screen to prevent misrecognition of tapping on non-target symbols. From preliminary experiments, the process time for the TMT-B in healthy volunteers (n = 4; M = 30.3 years, SD = 4.03) was markedly prolonged compared to that for the TMT-A, which was similar to previous results (Supplementary Figure S3D, Additional File 1) [37].

(vi) Digit Span Test

The DS test is a well-established measure of working memory capacity [38,39]. The digit indicator and numeric keypad used in the DS, are shown in Figure 4C. Numerical digits are presented individually and sequentially, and participants will be asked to remember the sequence of the presentation. Next, participants will be asked to recall the sequence, using the numeric keypad. The
DS test will be conducted under forward and backward conditions. Participants will be required to recall the sequences in forward or backward direction, depending on the task condition; sequence length ranges, from two to nine numerical digits, in both tasks. Participants will be required to perform the test under both conditions, and the trials will be repeated three times for each sequence length. When participants record three mistakes in the same sequence, the DS test will be completed. In our preliminary experiment with healthy volunteers (n = 4; 29.8±2.68 yrs), the matching rate for the backward condition was relatively low, with larger sizes of target digit numbers (Supplementary Figure S3E, Additional File 1).

**Data analysis**

**Gait analysis**

From the gait measurement datasets, we will calculate the general walking parameters, such as stride length and minimum toe clearance, using the built-in software (e-skin LETS WALK, Xenoma Inc., Tokyo, Japan). The general parameters are presented in Table 3. The sweeps of raw signals, such as IMU data, joint angle, and global positioning of each sensor or anatomical landmark, will be averaged with the time normalized by the percentage of the stride cycle. When the stride cycles cannot be defined because of poor data quality, the dataset will be excluded.

**Psychological analysis**

Cognitive performance is evaluated by reaction time, process time, and task accuracy. The
reaction time will be calculated for the SRT, Go/No-Go task, Stroop Color–Words Test, and N-back test. The reaction time is defined as the interval between the onset of the target signal and the participant’s response. The process time is defined as the interval between the task onset and completion in the TMT and DS test.

Statistical analysis

In this study, we established statistical models for predicting cognitive functions based on walking characteristics. Thus, the dependent variables are reaction time, process time, and task accuracy, and the independent variables are walking parameters and averaged signal traces, in both the fast and comfortable conditions. Prior to the substitution of the independent variables in the statistical model, we will sift the variables, to prevent problems related to multi-covariance [40].

The walking parameters will be reduced to less than 25 dimensions, by principal component analysis (PCA), as needed. The statistical model will be used for multiple linear regression, with and without the random sample consensus (RANSAC) algorithm. The accuracy of the statistical model will be evaluated using Akaike’s information criterion (AIC) [41]. All statistical analyses will be performed using the Python script, with the scikit-learn library.

DISCUSSION

To the best of our knowledge, this will be the first study to reveal the relationship between walking and cognitive functions using a three-dimensional motion capture system for the general population. From a methodological perspective, the accuracy of the algorithm of three-dimensional bone modeling in e-skin MEVA was already confirmed in a previous study, and was also supported by the findings of our preliminary experiment, to compare it with conventional motion capture systems (see Supplementary Figure S2, Additional File 1) [25]. In fact, e-skin MEVA and LETS WALK, have already been applied in clinical fields, to detect abnormal walking patterns owing to spinal cord injury (Higashibaba and Irie, in submission). Thus, we believe that the accuracy of three-dimensional motion capture, using e-skin MEVA, is adequate for this study.

Conventional paper-based testing methods, such as the mini-mental state examination (MMSE), and Montreal Cognitive Assessment (MoCA), are not suitable for this study because of their
ceiling effects in healthy participants [42–45]. Moreover, web-based cognitive assessment has recently gained attention because it is feasible for detecting earlier stages of cognitive decline compared to paper-based testing [46]. In particular, our custom-made application could better correct the higher dimensional cognitive performances, including the temporal, spatial, and spatio-temporal domains, than conventional applications, which is more suitable for these feasibility studies.

The associations between walking and cognitive functions have been well described in studies on cognitive interference in walking. Killeen et al., 2017, reported that minimum toe clearance decreased in the condition during the Stroop Color–Word Test [47]. In addition, there have been several reports about these interferences, which is well-known as a dual task paradigm [48–50], considered to be compensatory mechanisms and/or overlapping functional localization [51,52]. These common neural mechanisms in walking and cognition, are related to changes in walking characteristics that precede cognitive decline. However, the relationship between these interferences in dual task paradigms and natural walking parameters without any cognitive loading, is unclear. Further studies are required to elucidate this relationship.

This study has several limitations. First, although we checked the reliability of e-skin MEVA compared to the conventional motion capture system, there are several errors in the three-dimensional model calculation because the MEVA algorithm calculates a three-dimensional model based on gender and body height, not including the length of each segment [25]. Moreover, the accuracy of the IMU-based motion capture system, relies on the pitch (cadence) of walking [53]. Second, our cognitive assessment tools have not been compared to conventional tools, such as the MMSE and MoCA, which might decrease the reliability of the overall experiment from a methodological perspective.

For gait measurement, we considered that this study focuses on revealing the relationship between walking and cognitive functions in healthy participants. Thus, the possibility of mass screening of both functions, is more important than the accuracy of the parameters. In fact, the more accurate three-dimensional motion capture, using the conventional optical system, required a much longer time for data collection, which is not feasible for our purposes [54]. In contrast, the gait analysis system, e-skin MEVA and LETS WALK, simply consists of IMU pants and a computer for recording
data, and has already been applied in clinical practice, such as rehabilitation for spinal cord injury patients (Higashibaba and Irie, in submission). At the same time, we are conducting several studies on the system’s reliability and its relationship to conventional assessment tools in motion capture (Sonobe and Amano, in preparation).

For the cognitive assessments, our web-based applications were created, based on a well-established psychological paradigm that is sensitive to early cognitive decline, even in healthy participants, in whom functional localizations were already detected [55–61]. In fact, our preliminary experiments obtained results similar to those of previous studies (see Supplementary Figure S3, Additional File 1) [31,37,62,63]. We also plan to conduct an additional validity examination, to compare our application with conventional paper-pencil based (e.g., MMSE and MoCA) and/or web-based testing (Irie and Abe, in preparation).

Finally, a few participants with MCI or MCR will be included in this study, owing to our inclusion criteria. However, the database developed in this study could provide standard values for both walking and cognitive functions, which would support the evaluation of psychomotor function, including the MCR syndrome. Our research team also plans to conduct a cohort study for participants in this study, to define the risks of MCR and MCI. This CoGait project database will be developed for use as a worldwide platform, for cross-sectional and longitudinal studies on cognition, walking, and frailty, as well as other studies in the field of geriatrics.

**List of abbreviations**

- **AIC**: Akaike’s information criterion
- **DS**: Digit span
- **IMU**: Inertial measurement unit
- **MCI**: Mild cognitive impairment
- **MCR**: Motoric cognitive risk
- **MMSE**: Mini-Mental State Examination
- **MoCA**: Montreal Cognitive Assessment
DECLARATIONS

Ethics approval and consent to participate

This research protocol was approved by the local ethics committee of the Tokyo University of Technology (approval no. E20HS-038) and Dokkyo Medical University (approval no. 2021-011), in accordance with the Declaration of Helsinki. Prior to conducting our study, we will obtain participants’ written informed consent and assure them of their right to withdraw their consent at any time, for any reason.

Consent for publication

At registration, we will obtain participants’ consent for publication. When a participant withdraws consent, we will exclude their data from the published data.

Availability of data and materials

After publication, the database of walking and cognitive parameters developed in this study will be published as a public repository. Access permissions will be managed by the Tokyo University of Technology and Xenoma Inc.

Competing interests

The authors have no conflicts of interest to disclose. YW received research funding from Xenoma Inc., associated with the Cooperative Research and Development Agreement. SI received research funding from Xenoma Inc., as a donation to Dokkyo Medical University.

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Authors’ contributions

TF, SI, YW, TK, and AA contributed to the study design. TF, SI, and YW were involved in the preliminary experiments of gait measurements. TF, SI, and AA were involved in preliminary cognitive assessments. All authors critically revised the report, commented on drafts of the manuscript, and approved the final report.

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Footnotes

None.

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Figure 1. Schematic diagram of the experimental procedure

The experiments consist of four phases or sessions: informed consent, registration of personal information (i.e., height, gender, and birthday), gait measurement with e-skin MEVA, and cognitive assessment, using the tablet. The datasets were automatically uploaded to online cloud storage.

Figure 2. The wearable motion capture system “e-skin MEVA”

A–C: The IMU pants, from the frontal (A), lateral (B), and posterior (C) views. The IMU sensors were placed on the lateral surfaces of the upper and lower legs, and the dorsal surfaces of the foot and sacrum. The sensor on the sacrum is equipped with a removable attachment, with Bluetooth® wireless communication. D and E: The poses for calibration. Prior to the measurement, participants must pose in two ways: leaning forward (D) and standing upright (E).

Figure 3. Cognitive assessments using the reaction time paradigms

A: Simple reaction time (SRT) task: In addition to the presence of the fixation point, the warning signal (WS) rings (1000 Hz, 50 ms). Participants should tap “はい” (Yes), as soon as possible after the WS. Feedback is presented after the responses. B: Go/No-Go task: The flow of the task was almost the same as that of the SRT. However, in this task, participants were asked not to respond to a non-target presentation (triangle and cross). C: Stroop Color–Word Test: All experimental paradigms and flows are similar to those in the Go/No-Go task. Participants responded only to the red Chinese letters.

Figure 4. Cognitive assessments using the process time paradigms

A: N-back test. The N-back test is one of the most established assessments of working memory capacity. Participants are asked to respond when the target signal is the same as the last digit number. B: Trail Making Test (TMT). The TMT consists of TMT-A (numeric numbers alone) and TMT-B (a mixture of numeric numbers and Japanese kana letters). In the TMT-A, participants are instructed to tap the numerical digits in ascending order. In the TMT-B, participants also tap the targets in ascending order, but they should tap the numerical digits and kana letters alternately. C: Digit span
This test uses a numeric keypad and numeric number indicator. Participants are asked to remember the target sequence of numerical digits individually shown in the indicator. After the presentation, they are asked to recall the sequence in the same or reversed orientation, using the keypad. After inputting the digit sequences, they tap the Enter (Etr) key. In addition, they can fix the input using the All Clear (AC) and Delete (Del) keys.

ADDITIONAL MATERIAL

File name: Additional File 1
File format: DOC
Title of data: Preliminary results
Description of data: We performed preliminary experiments before developing this study protocol. Figure S1 depicts the result of a pilot observation of the relationship between the walking and cognitive parameters in a small population. Figure S2 shows the result of comparisons of joint angles between MEVA and VICON (conventional motion capture system). Figure S3 presents the results of preliminary experiments of cognitive performance, using a custom-made web-based application. Figure S4 shows the rule for the Japanese kana letters in the TMT-B test.
Figure 1

Schematic diagram of the experimental procedure The experiments consist of four phases or sessions: informed consent, registration of personal information (i.e., height, gender, and birthday), gait measurement with e-skin MEVA, and cognitive assessment, using the tablet. The datasets were automatically uploaded to online cloud storage.
Figure 2

The wearable motion capture system “e-skin MEVA” A–C: The IMU pants, from the frontal (A), lateral (B), and posterior (C) views. The IMU sensors were placed on the lateral surfaces of the upper and lower legs, and the dorsal surfaces of the foot and sacrum. The sensor on the sacrum is equipped with a removable attachment, with Bluetooth® wireless communication. D and E: The poses for calibration. Prior to the measurement, participants must pose in two ways: leaning forward (D) and standing upright (E).
Cognitive assessments using the reaction time paradigms

A: Simple reaction time (SRT) task: In addition to the presence of the fixation point, the warning signal (WS) rings (1000 Hz, 50 ms). Participants should tap "Yes" as soon as possible after the WS. Feedback is presented after the responses.

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Figure 4

Cognitive assessments using the process time paradigms A: N-back test. The N-back test is one of the most established assessments of working memory capacity. Participants are asked to respond when the target signal is the same as the last digit number. B: Trail Making Test (TMT). The TMT consists of TMT-
A (numeric numbers alone) and TMT B (a mixture of numeric numbers and Japanese kana letters). In the TMT-A, participants are instructed to tap the numerical digits in ascending order. In the TMT-B, participants also tap the targets in ascending order, but they should tap the numerical digits and kana letters alternately. C: Digit span (DS) test. This test uses a numeric keypad and numeric number indicator. Participants are asked to remember the target sequence of numerical digits individually shown in the indicator. After the presentation, they are asked to recall the sequence in the same or reversed orientation, using the keypad. After inputting the digit sequences, they tap the Enter (Etr) key. In addition, they can fix the input using the All Clear (AC) and Delete (Del) keys.

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1.pdf](#)