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Monitoring reaction time to digital device in the very-old to detect early cognitive decline

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Early detection of cognitive decline is essential for timely intervention and effective management of age-related impairments. We monitored repetitive reaction times to a simple task on senior-friendly tablet computers among 72 functionally independent older adults, with a mean age of 82, ranging up to 100 years, within natural settings over two years. Functional principal component analyses revealed a consistent decrease in reaction time in line with their task experience among those without subjective cognitive decline. Conversely, individuals reporting subjective cognitive decline showed no consistent trend and exhibited wide variability over time. These distinctive reaction time trajectories in very old adults suggest the potential for monitoring as a non-invasive, convenient method for early detection of cognitive impairment.

Early detection of dementia and cognitive decline is crucial for timely intervention and effective management[1]. Traditional methods for assessing cognitive status in older individuals often involve the use of established scales or questionnaires, which can be resource-intensive, time-consuming, and stigmatizing[2]. These assessments may imply a deficit or impairment, which can negatively impact an individual's self-perception and willingness to engage in the assessment process[3]. This is especially concerning given the sensitivity of cognitive function in older age. Consequently, there is a clear need for alternative measures that offer a non-invasive and cost-effective approach to cognitive decline assessment.

In experimental settings, reaction time (RT) to digital devices has emerged as a promising measure to characterize potential cognitive decline[4,5]. Studies indicate that individuals with cognitive decline exhibit both slower RT and greater variability of RTs over time[6,7]. Particularly, the latter, wide variability over time within an individual has been indicated to be sensitive to even subtle cognitive decline[8–12]. Additionally, cognitive health is also known to affect "repetition priming", a phenomenon where improvements occur as a result of repeated practice. Several studies have indicated the size of priming in repeated tasks was significantly smaller in both the mild cognitive impairment and Alzheimer's dementia patients, compared to cognitively healthy older adults[13–17]. These studies suggest that trajectories of repetitive RT in the daily lives of older individuals may be particularly indicative of the presence of cognitive decline.

As the advance of digital technologies and the widespread use of mobile devices with touch screens among seniors has opened up a continuous effortless timely data collection of RT, detecting early cognitive decline using the RT trajectories has a potential to address the limitations of current assessment methods for cognitive decline in this demographic. However, there is a notable lack in research specific to very old populations, especially in their everyday environment. The very old population, aged over 80 years, is underrepresented in research[18,19], with even fewer studies focusing on their usage of digital technology. Hence, uncertainties persisted regarding feasibility to detect early cognitive decline of the most targeted population within their everyday lives.

This study seeks to address this gap by examining residents in a senior community equipped with a senior-friendly Internet of Things (IoT) infrastructure. We aim to compare the trajectories of repetitive RT to digital devices in the natural settings of very old adults, distinguishing between those with subjective cognitive decline and those without and to explore the potential of this measure as a screening tool for cognitive decline in the very old population.

Results

Overviews of the dataset

Over three years (from November 1, 2020, to November 30, 2023), 87 participants generated 43,121 RTs to the game and 91% (39,271) of them were obtained from 72 individuals with available cognitive

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information. Of those, 86% (33,698) were accurate responses (Supplementary Fig. 1).

The mean age of the participants was 82 years, and 75% were female based on the registration of CCRC administrative record. Among the participants, one-fourth reported subjective cognitive decline (Table 1). While the initiation and termination of using tablet computer were highly varied among individuals, half of the participants started in two months after the installation of tablet computers and continued using it more than two years (Supplementary Fig. 2).

Dense data included 1400 RTs of 28 individuals, while 1188 RTs of 72 individuals were included in Sparse data. Figure 1 shows the time-series original observations for each subject and the fitted line (a bold solid curve). A high variability across individuals and an overall gradual decrease as one experiences were observed in both datasets.

Table. 1 | Basic characteristics of participants

	All (n = 72)	CD[a] (n = 17)	ND[b] (n = 55)
Demographic characteristics			
Age (y), mean (SD, min: max)	81.9 (5.6, 69.1: 95.3)	83.9 (4.6, 77.3: 95.3)	81.3 (5.8, 69.1:94.3)
Female, n (%)	54 (75.0)	13(76.5)	41(74.5)
Reaction time related			
Number of observations, n	33,698	16,832	16,866
Date of initiation, median date	Jan-26, 2021	Dec-15,2020	Feb-19,2021
Date of termination, median date	Jan-02, 2023	Jan-26, 2022	Mar-09, 2023

[a]CD: Participants with subjective cognitive decline.
[b]ND: Participants without subjective cognitive decline.

FPCA results

FPCAs were conducted separately for those with a subjective cognitive decline (CD) and those without subjective cognitive decline (ND). Figure 2 shows four plots (design plot, mean function, scree plot, and the first few eigenfunctions) derived from each FPCA using Dense and Sparse data. The results for ND were similar regardless of datasets (a: Dense and b:Sparse in Fig. 2), in terms of the extension how much the first principal component explained the fraction of variance and the consistent trend in decrease of mean function with instances. The results for CD showed that the extent of explanations of the first component varied between datasets (Scree plot shows 40% in the Dense while 80% in the Sparse), but other features were similar between the datasets; the mean function fluctuated overtime in both datasets (c: Dense and d:Sparse in Fig. 2).

Figure 3 shows the modes of variation about the mean for the first two eigenfunctions of each FPCA. The mean function was indicated by the red line. The dark gray shows the variation of the first eigenfunction, and the light gray shows the variation of the second. In both datasets, the plot of ND indicated that RT became shorter, and a variability across individuals had a trend to convert as they experienced (a: Dense and b: Sparse in Fig. 3). In contrast, the mode of variation for CD exhibited oscillatory behavior, characterized by recurrent fluctuations in both ascending and descending directions (c: Dense and b: Sparse in Fig. 3). The numbers of functional principal components for a given FPCA output based on different criteria with threshold fraction were shown in the Supplemental table.

Sensitivity analyses

Sensitivity analyses were conducted with differently organized datasets. Results with 100 times or 100 days instead of 50 times or 50 days were consistent with the main results: constant decrease in mean function and conversion of variations for ND and fluctuation of mean function and repeated conversion and diversion overtime for CD. The results with 10 times or 10 days also showed a similar trend as the main results with a lesser clarity. The results of analyses including inaccurate responses did not differ from the main analyses (Supplemental Fig. 3).

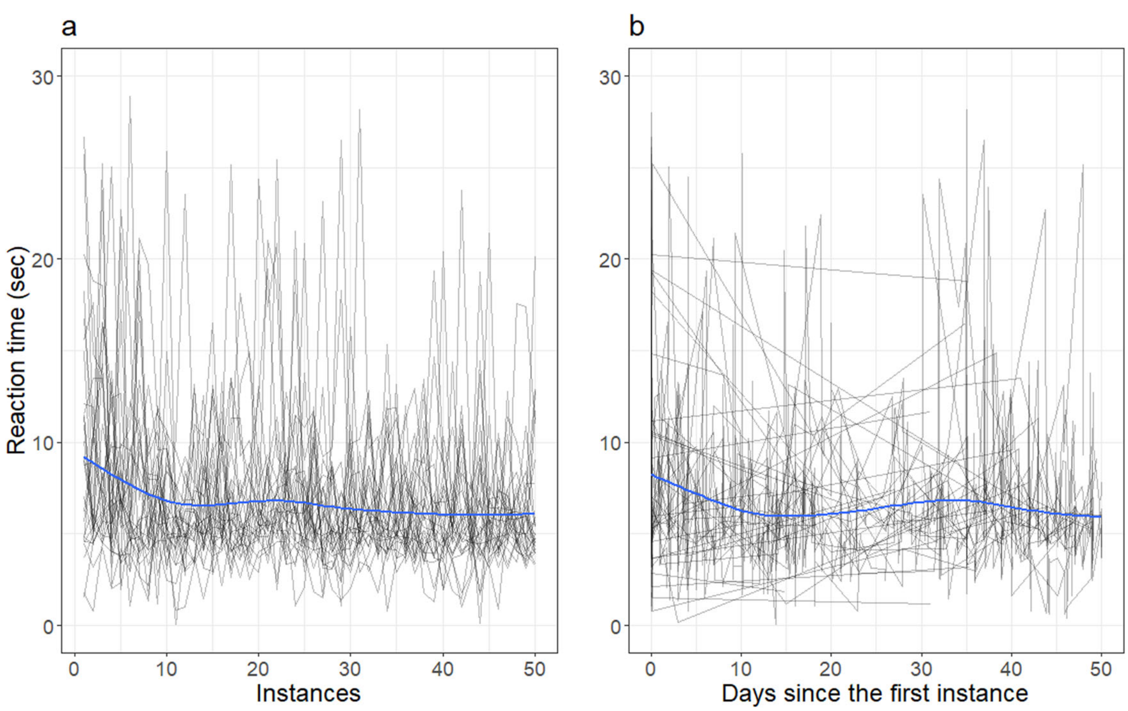

Fig. 1 | A high variability across individuals and an overall gradual decrease as one experiences of repetitive reaction times of very-old adults in natural settings. Time series plots of original observations of reaction time in the Dense dataset with 50 instances (**a**) and the Sparse dataset within 50 days (**b**). The original observations for each subject and the fitted line (a bold solid curve) are presented. A high variability across individuals and an overall gradual decrease as one experiences are observed in both datasets.

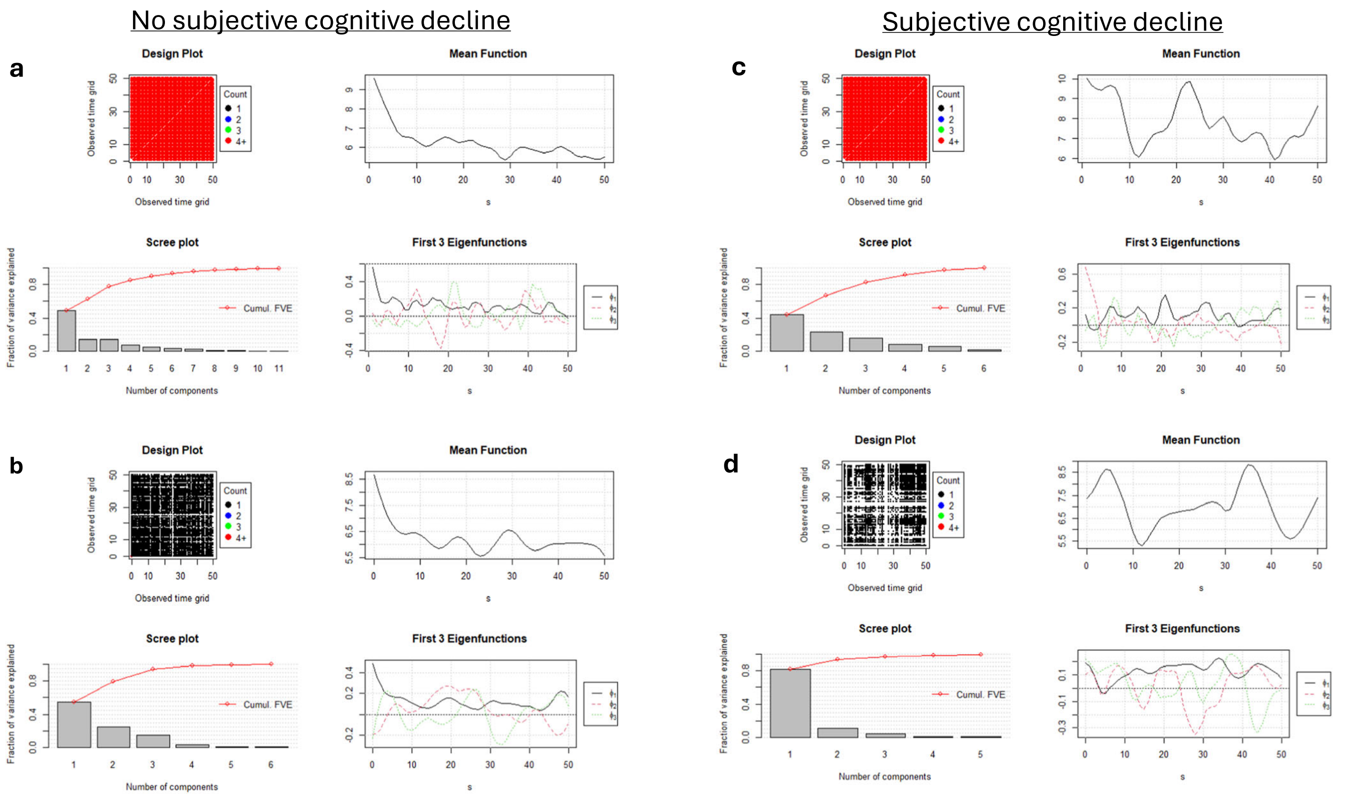

Fig. 2 | Trajectories of repetitive reaction times of very-old adults in natural settings are sensitive to subtle subjective cognitive decline. Design plot (left above), mean function(right above), scree plot(left below), and the first few eigenfunctions (right below) derived from each functional principal component analysis (FPCA). **a** FPCA results with no cognitive decline population (ND) using Dense data with 50 instances ($n = 20$) and (**b**) FPCA results with ND using Sparse data within 50 days ($n = 55$) are similar regarding the extension of explanation of the first component and the trend in the mean function, regardless of the dataset organization. **c** FPCA results with cognitive decline population (CD) using Dense data with 50 instances ($n = 8$) and (**d**) FPCA results with CD using Sparse data within 50 days ($n = 16$) show that although the extent of explanations of the first component were largely different between datasets with about 40% in the Dense dataset and 80% in the Sparse dataset, the mean functions of both dataset did not have a consistent trend, but rather fluctuate over the course.

Discussion

This study examined the repetitive RT to touch screen trajectories of functionally independent older adults in natural settings, distinguishing between individuals with and without subjective cognitive decline. Our study demonstrated that individuals with subjective cognitive decline exhibited distinct RT trajectories compared to those without, suggesting the potential of monitoring RT as a non-invasive method for early detection of cognitive impairment.

Participants without subjective cognitive decline showed consistent decrease in RT in line with their experience with the task. It was consistent with previous findings suggesting the effectiveness of repetition priming in normal aging[15–17]. Since the average age targeted in these prior studies were in their 60 s, we added a piece of evidence that it is also applicable to over 80 years population, which would be an encouraging message for the aging society. Conversely, individuals reporting subjective cognitive decline exhibited wide variability in RTs over time, which was also consistent with prior researches linking it to emerging cognitive decline[10,12].

These observed results remained consistent regardless of how the datasets were organized. This consistency suggests that the detection of cognitive decline through RT trajectories is possible through both natural observation and individually sequenced observations. Sensitivity analyses with longer durations and more observations strengthened the study's findings. Shorter durations and fewer observations, however, indicated that a certain number of instances and duration of usage are necessary to effectively detect differences in reaction times.

Several limitations should be considered in the interpretation of our study findings. Firstly, the operational definition of subjective cognitive decline, derived from responses to three questions in the CCRC institutional annual survey, may not entirely capture the complexity of cognitive decline as recognized in broader clinical and research settings. While the definition we utilized has demonstrated an association with future long-term care needs in a previous research[20], it does not fully differentiate cognitive decline from the normal aging process. Future research should include individuals diagnosed with MCI or known early cognitive deficits and explore the feasibility of utilizing reaction time trajectories as a technological approach for predicting clinical cognitive outcome.

Secondly, inaccurate responses were excluded as noise. Although the results of sensitivity analyses including inaccurate responses did not differ from the main analyses, inaccuracy may reflect decreasing cognitive function and the exclusion of inaccurate responses may have led to a bias toward null hypothesis.

Thirdly, the number of participants between the groups was imbalanced in the study and there were wider confidence intervals among CD, compared to ND. To examine the impact of this imbalance on the results, we first ensured no extreme divergence of confidence intervals (i.e., beyond the range of the graph axes) observed as shown in Fig. 3 and supplemental Fig. 3. We additionally confirmed this point focusing on the averages and confidence intervals for each observation time point with an adjustment of the confidence intervals using the bootstrap method. The additional analyses also did not show an extreme divergence and still showed clear differences in the trends between the two groups (Supplemental Fig. 4). Based on these examinations, we believe that the imbalance in the number of participants across groups is not a problem that would significantly distort the interpretation of the results. However, to assert more robust results based on statistical evidence, an adequate and evenly distributed sample size was desired.

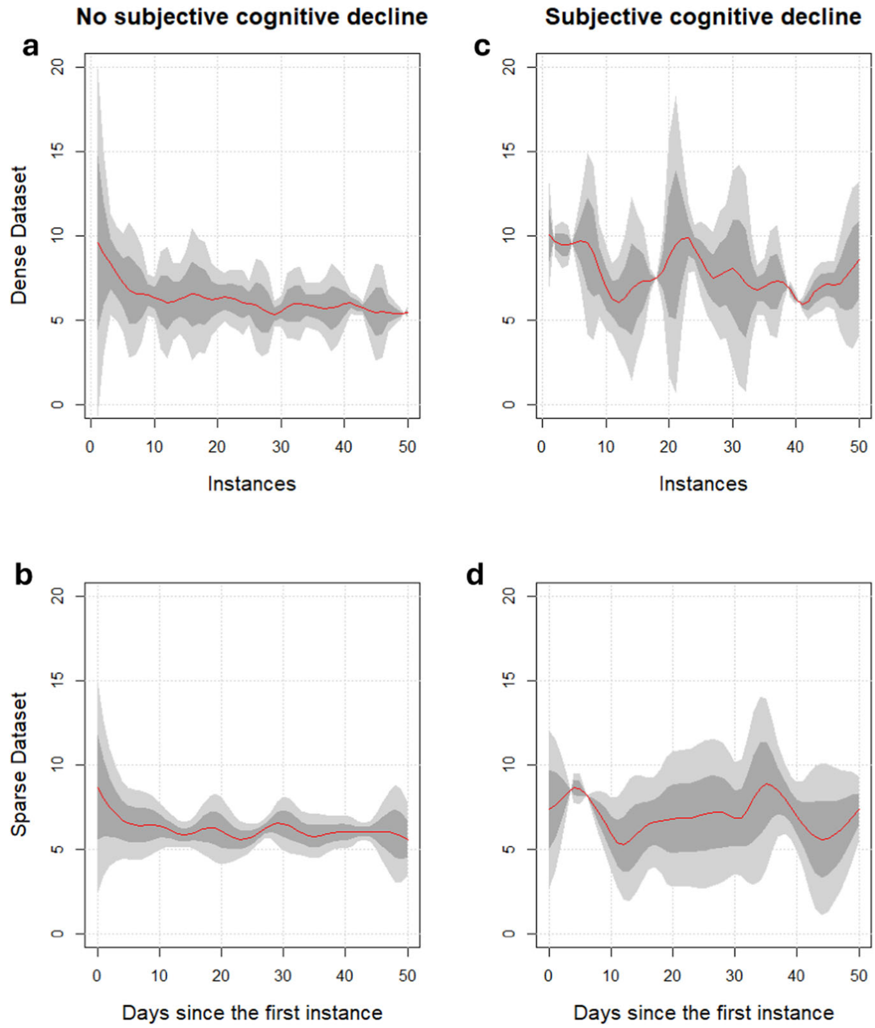

Fig. 3 | A wide intraindividual variability over time and fluctuation of the mean function of reaction time characterizes older individual with subjective cognitive decline. Modes of variation plots about the mean for the first two eigenfunctions. The mean function was indicated by the red line. The dark gray shows the variation of the first eigenfunction, and the light gray shows the variation of the second. **a** Results using the Dense dataset with the first 50 instances of those without subjective cognitive decline (ND, $n = 20$), and (**c**) results of those with subjective cognitive decline (CD, $n = 8$). **b** Results using the Sparse data within 50 days of those without subjective cognitive decline (ND, $n = 55$), and (**d**) results of those with subjective cognitive decline (CD, $n = 17$). In both datasets, the plots of ND indicated that RT became shorter as they experienced. The modes of variation for CD in both datasets exhibited oscillatory behavior, characterized by recurrent fluctuations in both ascending and descending directions.

Fourthly, our study participants were residents of a CCRC, and their socio-economic status, along with potentially higher education levels, is presumed to be above the average for their age group. While socioeconomic status can influence cognitive functioning, it is unlikely to directly impact the association between cognitive decline and the trajectory of reaction times. Thus, the generalizability of our results may not be significantly affected by participants' socioeconomic status.

Lastly, our data was collected in uncontrolled, non-experimental conditions. While intentional, this approach presented statistical challenges due to the wide variation in the number of instances and intervals among individuals. Nevertheless, the application of FPCA allowed us to successfully manage sparse data with varying observation numbers among individuals. We limited the observations to the first 50 instances or 50 days to enhance interpretability and mitigate the influence of extreme values, which led to a good interpretability of the principal components with a clear and large difference between the groups.

The final limitation point also underscores a strength of our study, specifically addressing a methodological challenge in the inclusion of very old individuals in digital-related studies in natural settings. They are known to be systematically excluded from research[21]. Further, this demographic faces difficulties in technology adoption, including lack of comfort and familiarity with technology, educational limitations, and unfavorable attitudes toward technology[22,23]. Recognizing the challenges associated with recruiting and retaining them into the study, our team adapted an approach to enhance their perception of ease of use and usefulness of digital devices that are known important factors in determining the acceptance of technology[24,25], resulting in the successful continuous engagement of very old people in our study. Additionally, the study aligned with Ecological Momentary Assessment (EMA) to collect data on individuals' thoughts and behaviors in their natural environments, marking a strength in the methodology. While EMA is a rapidly evolving field[26], it is crucial to note that not all older adults who own and use digital devices[21,23] and it is indeed a challenge to apply EMA to older adults. While some of the efforts to construct the IoT environment we made in this study may not be necessary for future generations, it remains crucial to give thoughtful consideration to the biological changes in the older generation when incorporating technology for repeated sampling of subjects' behaviors and experiences in real-time within their natural environments.

Methods

Study design

This study was conducted as part of a research project in a Continuing Care Retirement Community (CCRC) in Kyoto, Japan. The research project, initiated in 2019, aims to enhance the health of older adults through a senior-friendly Internet of Things (IoT) system (Fig. 4). A detailed description of the project can be found elsewhere[27,28]. In summary, one hundred participants carried a low-energy Bluetooth beacon card and went about their daily lives within the CCRC premises, which are equipped with beacon receivers. In November 2020, three tablet computers were additionally installed in the public area and operated until the end of December 2023. User identification on a tablet was made using a near field communication tag attached to their beacon card. A typical talk flow that runs on a tablet starts with a greeting message, followed by individual walking distance and encouraging message, a staff rock-paper-scissors game and a few quizzes about health literacy. The

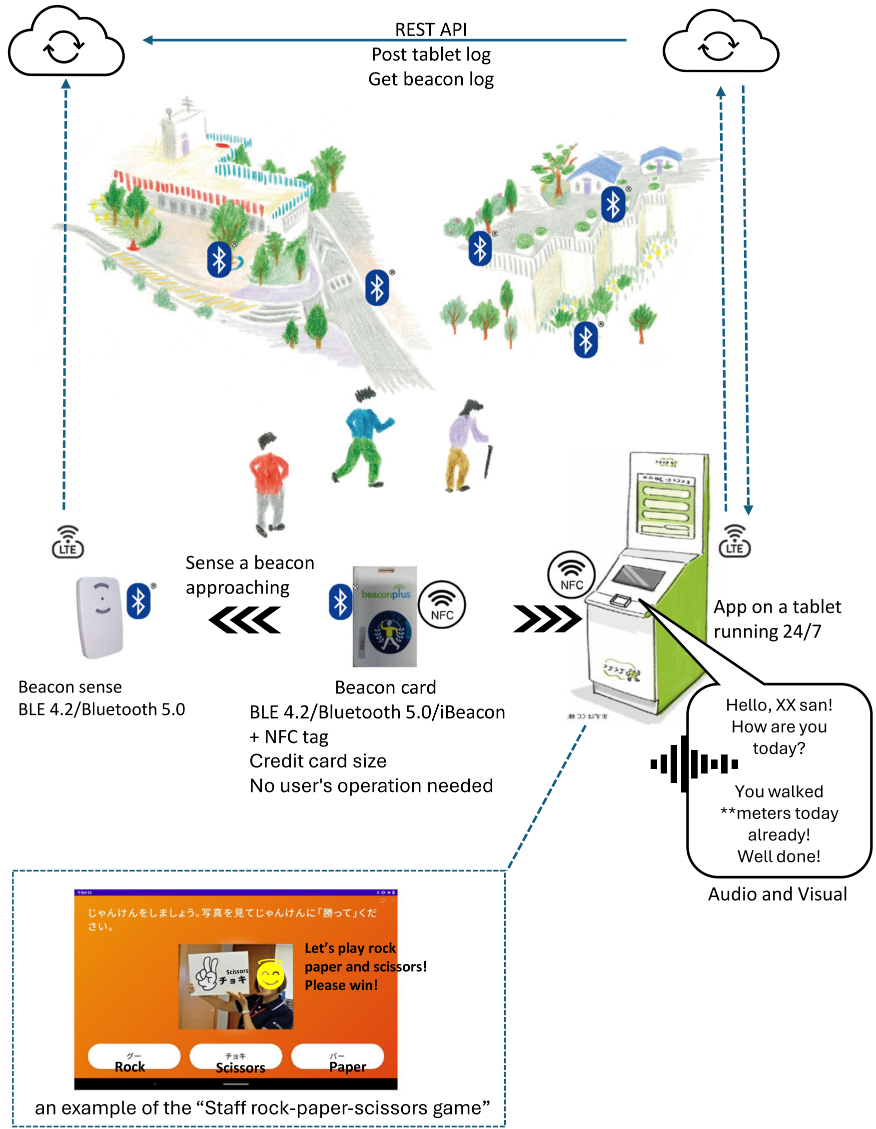

Fig. 4 | Overview of the senior-friendly IoT environment with an example of the "Staff rock-paper-scissors game".

tablet application runs 24/7 and it was the participants' choice and decision to use the tablet computer at any time as often as they like in their daily lives. A touchscreen stylus was provided for easy use.

Study population

The study population comprised participants who met two criteria. Firstly, they started using one of tablet computers by the end of 2022 at the latest, ensuring the availability of repetitive RT information. Secondly, information on the perception of cognitive decline was available from an annual CCRC survey taken in February 2022.

Measurements

Reaction time (RT). Among the several contents included in a talk flow displayed on tablet computer, RT to "Staff rock-paper-scissors game" was analyzed. In the game, one of cards showing a rock, paper, or scissors is presented by one of CCRC staff photo with a written and audio message "please win/lose!", and the three options were provided underneath. This is one of games that Japanese have been familiar with from childhood. RT was measured as the time in seconds elapsed between showing the card and touching one of the three buttons (Fig. 4). We excluded RTs associated with incorrect responses from our analyses. This decision was made based on two key findings. Firstly, our data showed consistently high overall accuracy, irrespective of subjective cognitive decline. Secondly, extremely quick responses (i.e., less than 2 s) were disproportionately more common among inaccurate responses. These findings led us to reason that the accuracy of the game might not accurately reflect cognitive health, but other factors, such as external obstacles or a user's intention to leave the tablet, could have influenced game accuracy. We included inaccurate responses in one of sensitivity analyses.

Subjective cognitive decline. Subjective cognitive decline was defined based on the participant's response to the three question items in the CCRC institutional annual survey (Textbox). At least one answer of 1 was defined as subjective cognitive decline in this study. The items and the criteria are the same as the KIHON checklists which are widely used for governmental frail screening in Japan. It was shown that the three questions were able to identify people in future long-term care needs due to cognitive decline[20].

Textbox. Question items to define participants subjective cognitive decline.

1. Do people around you say that you forget things such as asking the same questions repeatedly? (0 No 1 Yes)
2. Do you look up phone numbers yourself and make phone calls? (0 Yes 1 No)
3. Do you ever have moments when you don't know what month or day it is today? (0 No1 Yes)

Statistical analyses

As the RTs in this study were continuously collected between November 2019 and December 2023 in natural settings, resulted in different numbers of repeated time points and observations per individual, we employed Functional data analysis (FDA) in this study. FDA is a branch of statistics that analyzes data in the form of functions, rather than individual data points, providing information about curves, surfaces or anything varying over continuum such as time[29]. Among the techniques used in FDA, Functional Principal Component Analysis (FPCA) was used in our analyses to capture the main patterns or modes of variation in functional data, the way of which is similar to how principal component analysis (PCA) works for traditional data. We applied FPCAs separately to RT data derived from those with subjective cognitive decline and those without subjective cognitive decline using the R package “fdapace” in R 4.3.1[30].

We constructed two types of functional datasets. One is a dense dataset with RTs in sequential order, irrespective of intervals (Dense data). To present data points continuously across the entire range of the function, the participants were limited to those who had more than a certain number of instances. The other is a sparse dataset where data points are irregularly present across the participants (Sparse data). Because our focus is on the trajectory, we aligned the first instance across the individuals and the intervals from the first instance in seconds were used as a function in the Sparse data.

FPCA can be sensitive to noise and outliers in the functional data[31,32]. Given the characteristics of the observations that the frequency of instances per person varied greatly among individuals (min 1 to max 6082 instances during the study period) with a highly positively skewed distribution (median=14.5 instances, mean = 468 instances, IQR = 399.8, skewness = 3.38), we limited the number of instances in the Dense data and the number of days in the Sparse data to remove the effect of extreme values. The main analyses included the first 50 instances of those who have more than 50 instances in the Dense data and the first 50 days of all individuals in the Sparse data. In sensitivity analyses, other limitations such as 10 instances and 100 instances for Dense data and 10 days and 100 days for Sparse data were applied. Sensitivity analyses also applied to RTs including inaccurate responses.

The design plot, mean function, scree plot, and the first few eigenfunctions were visualized for each analysis, and the differences in predominant modes of variation between those with subjective cognitive decline and those without were interpreted and discussed.

This study was performed in accordance with the Declaration of Helsinki. The Institutional Review Board (IRB) of Kyoto University approved the study (R1669). Informed consent to participate in the project was obtained from each participant.

Data availability

The data and R codes that support the findings of this study are available from the first author upon reasonable request.

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Author contributions
Y.Y. and T.O. designed the study and was supervised by S.F. T.U., T.I., and Y.Y. collected the data. Statistical analyses were performed by Y.Y. and supervised by T.O. Interpretation and discussion of the results were led by Y.Y. in consultation with T.O. and S.F. Y.Y. wrote the manuscript, and all the authors critically reviewed the entire manuscript. All the authors approved the final manuscript.

Competing interests
The authors declare no competing interests.

Additional information
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