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Behavioral marker-based predictive modeling of functional status for older adults with subjective cognitive decline and mild cognitive impairment: Study protocol

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Abstract

Objective: This study describes a research protocol for a behavioral marker-based predictive model that examines the functional status of older adults with subjective cognitive decline and mild cognitive impairment.

Methods: A total of 130 older adults aged ≥65 years with subjective cognitive decline or mild cognitive impairment will be recruited from the Dementia Relief Centers or the Community Service Centers. Data on behavioral and psychosocial markers (e.g. physical activity, mobility, sleep/wake patterns, social interaction, and mild behavioral impairment) will be collected using passive wearable actigraphy, in-person questionnaires, and smartphone-based ecological momentary assessments. Two follow-up assessments will be performed at 12 and 24 months after baseline. Mixed-effect machine learning models: MErf, MEgbm, MEmod, and MEctree, and standard machine learning models without random effects [random forest, gradient boosting machine] will be employed in our analyses to predict functional status over time.

Results: The results of this study will be fundamental for developing tailored digital interventions that apply deep learning techniques to behavioral data to predict, identify, and aid in the management of functional decline in older adults with subjective cognitive decline and mild cognitive impairment. These older adults are considered the optimal target population for preventive interventions and will benefit from such tailored strategies.

Conclusions: Our study will contribute to the development of self-care interventions that utilize behavioral data and machine learning techniques to provide automated analyses of the functional decline of older adults who are at risk for dementia.

Keywords

Aged, longitudinal study, mild cognitive impairment, mild behavioral impairment, ecological momentary assessment, actigraphy, machine learning

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Introduction

As one of the leading causes of disability and mortality in the aging population, dementia is a major public health concern. An estimated 50 million individuals globally had been diagnosed with dementia in 2019, and this number is expected to increase to 152 million by 2050.[1] However, clinical examinations for major precursors of dementia, such as subjective cognitive decline (SCD) and mild cognitive impairment (MCI), have low follow-up rates and are often expensive,[2] highlighting the need for resource-efficient and timely measures for these high-risk groups.[3] Since up to 40% of dementia cases may be prevented or delayed through prompt identification and elimination of modifiable risk factors, deep learning models that analyze behavioral data among SCD and/or MCI populations may help decrease the incidence and prevalence of dementia.[4]

Dementia is a growing health problem that poses significant health and economic burdens on affected individuals, their families, and society at large, creating substantial challenges for health and long-term care systems.[5] As an irreversible neurodegenerative brain disease characterized by progressive loss of memory and functional ability,[6] dementia is one of the leading causes of disability and dependency in older adults.[7] In 2019, the direct medical and social costs associated with dementia were estimated to exceed US $1313.4 billion, with low-income and middle-income countries facing greater challenges in development and access to long-term care infrastructure (e.g. residential or nursing homes) and services (e.g. home care, food supply, and transport) than high-income countries.[8]

In South Korea, the prevalence of dementia in adults aged ≥65 years is estimated to be 0.88 million (10.3%), and this number is predicted to increase to approximately 3 million (15.91%) by 2050.[9] In addition, the percentage of older Korean adults with dementia is predicted to increase annually by 27%, which vastly exceeds the global average of 17%/.[10] The prevalence of dementia is estimated to have a socioeconomic cost of 11.7 trillion KRW [∼1% of South Korea's Gross Domestic Product (GDP)], and this number is predicted to increase to 43.2 trillion KRW (∼1.5% of GDP) by 2050.[11] Thus, a preventive approach is urgently required to reduce the socioeconomic costs of dementia and protect older adults from cognitive vulnerability.[12]

SCD and MCI are the preclinical and prodromal stages of dementia, respectively.[13] SCD refers to an individual's subjective perception of cognitive decline without there being objective cognitive impairment;[14] it is among the earliest predictors of future cognitive decline.[15] MCI is characterized by objective cognitive impairment despite preserved functional ability.[16] Typically, the progression starts with normal cognition, transitions to SCD, evolves into MCI, and eventually increases the risk for dementia.[14,17] Despite the underlying pathological progression of Alzheimer's disease, neuropsychological tests often fail to differentiate SCD or MCI from normal cognitive function, leading individuals with SCD or MCI to experience worsened cognitive decline without experiencing any interventions.[18] However, scholars believe that cognitive and behavioral functions in these populations can be restored.[19] Thus, the SCD and MCI stages are considered focal points of preventive treatment via early intervention.[12]

Therefore, there is heightened emphasis on the need for reliable and advanced predictive methodologies for early intervention to maintain and improve cognitive and functional status by addressing modifiable risk factors in these at-risk groups. However, most existing literature is limited in its approach. Most data collection studies on this topic have incorporated only sleep and physical activity information via self-report questionnaires from participants or caregivers, thereby limiting the studies' reliability and validity, which could be overcome with the incorporation of passive actigraphy data.[20] Similarly, while few studies have incorporated deep learning algorithms to optimize dementia prediction, such approaches can add value by imputing missing values and analyzing real-time data from wearable devices and mobile platforms, which offer noninvasive, continuous monitoring without potential recall biases, allowing for a longitudinal and resource-efficient (i.e. large-scale and low-cost) design.[21]

By accurately forecasting the trajectory of cognitive and functional decline in individuals in the preclinical (i.e. SCD) and prodromal stages (i.e. MCI) of dementia using machine learning algorithms, previous studies have found that healthcare professionals and caregivers can proactively intervene with personalized interventions and support strategies, to prevent progression to or delay the onset of dementia.[22] For example, early identification of individuals at higher risk for cognitive impairment could facilitate timely implementation of targeted cognitive and behavioral interventions, lifestyle modifications, and caregiver support programs, resulting in a substantially slower conversion rate to dementia, and predictive models (e.g. random forest, support vector machine, etc.) that have high accuracy rates relative to more traditional (e.g. logistic regression) may aid in care planning, resource allocation, and decision making for both healthcare providers and caregivers.[22,23] Previous studies have also acknowledged that by identifying individuals in the preclinical and early stages of dementia early, various factors including lifestyle modifications, cognitive training, and risk factor management, may have the potential to proactively delay or halt the progression of cognitive and functional decline.[24]

Identifying and analyzing modifiable risk factors that may predict cognitive and functional decline in patients with SCD and MCI is crucial for developing preventive strategies to preserve functional ability in these at-risk populations.[25] A 2020 Lancet Commission Report highlighted specific modifiable risk factors for dementia and demonstrated that nearly 40% of cases could be prevented or delayed through multidomain approaches that address modifiable risk factors among at-risk individuals.[4] The following are some modifiable risk factors that predict cognitive and functional decline in individuals living with SCD or MCI. These factors were incorporated into our predictive models.

Modifiable risk factors

Physical activity. Physical activity, including participation in physical exercise, sports, activities, and active daily living, is positively associated with cognitive function, especially among older adults with MCI.[15] Recent studies have suggested that regular physical activity can help individuals with MCI reverse or slow the trajectory of cognitive decline.[26] Given the positive association between physical activity and cognitive functioning, exploring physical activity as a potential marker for reducing the risk of dementia in at-risk individuals is crucial.[26]

Sleep/wake statistics. Sleep is another modifiable risk factor that plays a critical role in maintaining cognitive functioning. Sleep is a vital physiological activity that helps the brain recover function and removes brain metabolites.[27] Several sleep-related factors, including poor quality sleep, insufficient sleep, and excessive daytime napping, have been reported to worsen with age[28] and are linked to decreased cognitive and physical functioning.[29] Considering that the 2020 Lancet Commission Report identified sleep as a putative risk factor for dementia, it is necessary to explore sleep patterns as potential modifiable risk factors for dementia prevention.[30]

Social interaction. Social interaction is another key aspect of daily life that can affect cognitive and physical function.[31] In previous studies, social networks, integration, and engagement have been associated with preserved or enhanced cognitive function as they increase mental stimulation and strategic thinking among community-dwelling older adults.[32] Moreover, social interactions can prevent cognitive decline and dementia by increasing the number of new neurons created and through enhancing hippocampal synaptic plasticity.[33] However, as older adults age, they may become less socially active because of natural age-related transitions.[34] Consequently, a decrease in daily social interactions could be a marker for early cognitive and physical function decline.[35]

Loneliness. Loneliness is closely related to social interaction, which is the distressing perception that one's social relationships, regarding quantity or quality, are below one's expectations.[36] Loneliness has been associated with older adults' lower cognitive function in numerous domains, including global cognitive function, intelligence quotient, processing speed, immediate recall, and delayed recall.[37] Owing to the changes in personal and social lifestyle associated with aging, older adults are particularly susceptible to chronic psychological stress and loneliness.[38] Loneliness has also been identified as a predictor of mortality and low quality of life among older adults.[38] Furthermore, loneliness and a decline in executive function, such as self-regulation and behavioral control, are linked to various physical and behavioral symptoms and diminished overall cognition.[39] Given that loneliness is associated with adverse outcomes, early identification of at-risk older adults is essential to prevent it.[40]

Affective symptoms. Affective symptoms such as depression and anxiety are common in individuals with MCI[41] and have been linked to cognitive and functional decline in daily activities.[42] When depression and anxiety co-occur with MCI, they are associated with accelerated cognitive decline.[43] These affective symptoms may also be positively associated with SCD. Depression in individuals with SCD has been associated with a more rapid progression to MCI and dementia than in individuals without depression.[44] The anxiety associated with SCD also increases the risk of cognitive impairment.[45] Thus, cognitive function needs to be closely monitored in individuals with affective disorders. This is because those with depression or anxiety may be at risk of greater significant functional decline.[46]

Mild behavioral impairment. Mild behavioral impairment (MBI) has been proposed as an early marker of dementia that manifests as cognitive impairment advances. MBI may be characterized by behavioral or personality changes that manifest after the age of 50 and consists of five domains: decreased motivation and drive, affective/emotional dysregulation, impulse control, social inappropriateness, and abnormal perception or thought content.[47] Increasing evidence indicates that MBI in older adults is associated with a higher risk of cognitive decline and dementia.[48] Additionally, the presence of MBI in older adults with MCI has been associated with a greater risk of progression to dementia and a lower rate of reversion to normal cognition.[49]

Methods

Aims

This study aims to establish behavioral marker-based predictive models for assessing the functional status of older adults with SCD or MCI through a detailed examination of modifiable risk factors. Our protocol outlines the framework for a 3-year prospective longitudinal study using deep learning techniques to predict changes in functional status over time. As seen in previous studies,[50,51] a study protocol serves as an outline of the design, methodology, and objectives of a planned study and delineates the methodologies and procedures for data collection/analysis with the objective of ensuring methodological transparency and rigor in research conduct.[52]

The specific objectives were to (a) investigate behavioral and psychosocial markers indicative of cognitive and physical functional status via actigraphy, in-person questionnaires, and a smartphone-based ecological measurement assessment (EMA) and (b) develop optimal deep learning models incorporating RNN and XGBoost to predict functional vulnerability over time.

Design

The study will be conducted as a 3-year prospective longitudinal study for the development of functional prediction models based on behavioral and psychosocial indicators for older adults with SCD or MCI. Behavioral and psychosocial marker data (physical activity, mobility, sleep/wake patterns, social interaction, and MBI) will be collected using passive wearable actigraphy, in-person questionnaires, and EMA. Over the course of 3 years, data collection will be conducted every 12 months (wave 1 = baseline, wave 2 = 12 months, wave 3 = 24 months). Prior to each data collection period, a face-to-face assessment of cognitive functioning will be conducted using a simple questionnaire and the Korean Mini-Mental State Examination, second edition (K-MMSE-2), to screen for SCD and MCI, respectively. Data collection via the actigraphy device and EMA will take place over the first two consecutive weeks of each wave. Moreover, by employing EMA, immediate data collection after an experience enhances the validity of actual experiences and the analysis of the influence of contextual situations on behavior.[53]

Participants

The participants in this study will be 130 older adults aged ≥65 years with SCD or MCI living in Seoul, South Korea. Participants will be recruited from the Dementia Relief Centers or the Community Service Centers. While the estimated required sample size using R (generalized linear mixed model, effect size = 0.30, k = 2, power = 0.8, α = 0.05, df = 30) is $n = 106$, a total of 127 participants will be recruited, considering a dropout rate of approximately 20%.[54–56] After rounding, the final recruitment target sample size is 130 participants.

Inclusion criteria will be as follows: (1) SCD: (a) older adults aged ≥65 years, (b) complaints regarding SCD (responds "yes" to the question "Do you consider your memory to be poorer than it was in the past?"), (c) obtaining more than 24 points on the K-MMSE-2 or assessed as normal in a cognitive examination by a health professional, and (d) being a smartphone user (for questionnaire admission) and (2) MCI: (a) older adults aged ≥ 65 years, (b) diagnosis of MCI by a health professional, (c) positive testing of ≥18 on the K-MMSE-2, and (d) being a smartphone user (for questionnaire admission).

Exclusion criteria will be as follows: (a) illiterate individuals; (b) incapability to self-report on daily responses via smartphone or inability to complete the questionnaire; (c) presence of a major neurological disease (e.g. epilepsy, stroke, Parkinson's disease, and brain damage); (d) history of major mental illness (e.g. schizophrenia, bipolar disorder, and recurrent major depressive disorder); (e) severe or deteriorated physical condition (e.g. ongoing cancer treatment and cardiovascular disease); (f) history of a substance use disorder within the past 3 years (e.g. use of narcotics and severe alcohol abuse); and (g) anyone with dementia of any type. Individuals who meet the criteria for both SCD and MCI will be categorized into the MCI group.

Potential predictors

Participants' general characteristics. Participants will be surveyed face-to-face regarding a range of demographic characteristics, including sex, age, educational level, marital status, living arrangement, and self-rated economic status. Information on their economic activity history, including the type of industry in which they worked and duration of their employment, will also be gathered. Furthermore, participants will be asked about their health conditions, which encompass visual or hearing disabilities, chronic illness status, and medication history, including the name and total number of medications taken. Finally, health-related behavioral characteristics such as smoking and drinking history will also be collected.

Mild behavioral impairment. The Mild Behavioral Impairment Checklist (MBI-C) scale[47] will be used to evaluate behavioral or personality changes in older adults, which could potentially indicate individuals at risk of developing dementia. The MBI-C consists of five subcategories (apathy, affect, impulse control, social appropriateness, and abnormal thoughts and perceptions) with 34 questions. Responses are rated on a three-point Likert scale. MBI-C scores range from 0 to 102, with higher scores indicating higher levels of behavioral impairment.

In a pilot validation study of the Korean version of the MBI-C, significant correlations with the neuropsychiatric inventory in individuals with amnestic MCI (r = 0.25) and non-amnestic MCI (r = 0.36) demonstrated its utility in assessing MBI in clinical settings.[57]

Depression. Participants' depression will be measured using the Korean-translated version of the Short Form Geriatric Depression Scale (SGDS).[58] The SGDS-K[59] will be used in this study. It consists of 15 questions, each rated "Yes" or

"No," with higher scores indicating severe depression. In a validation study of 88 older Korean adults,[60] Cronbach's α was .84 and concurrent validity was proved using other depression scales (i.e. Center for Epidemiologic Studies Depression, Hamilton Rating Scale for Depression). By showing higher scores in participants with major depression than in the nonmajor depression group, content and discriminant validity were also demonstrated. Finally, the SGDS-K had a high correlation with the GDS-K ($r = 0.9594$), proving it to be a suitable instrument for evaluating depression in older adults.

Anxiety. The Korean version of the Geriatric Anxiety Inventory (K-GAI)[61] will be used to measure participants' anxiety. The K-GAI is a form of the Geriatric Anxiety Inventory (GAI)[62] adapted for the Korean population. It comprises 20 questions, each rated on a Likert scale. K-GAI total score ranges from 0 to 20, with higher scores indicating higher anxiety levels. In a validation study involving 236 older Korean adults, the scale was found to have a high level of internal consistency (0.88).[61] Test–retest reliability also showed a significant correlation, further verifying to scale's reliability. With regard to concurrent validity, a significant correlation with Goldberg's Short Screening Scale[63] was obtained, thus verifying the scale's validity.

Sleep. Participants' sleep/wake cycle will be measured using actigraphy, a technique that utilizes the "Actiwatch Spectrum PRO of Philips Respironics" wearable wrist device (Philips Respironics, n.d.). Most data collection studies on this topic have incorporated sleep data via self-report questionnaires from participants or caregivers, thereby limiting the studies' reliability and validity, which could be overcome with the incorporation of passive actigraphy data.[19] Relative to other methods of data collection, actigraphy data was used as our choice of collection for sleep data as it allows for objective and repeated data collection on sleep duration and continuity in real-time, thereby reducing recall bias and instrument-related variability.[20] Previous studies have also found that actigraphy collection of sleep data via the wrist or hip is an appropriate measure for 24 h activity monitoring.[64] Sleep patterns will be assessed using specific indicators, including sleep time, sleep efficiency, length of arousal during sleep, total number of sleep bouts, snoozing time, wake after sleep onset, wake time, and wake bouts.

Physical activity. Meanwhile, physical activity will be gauged by total counts of valid physical activity, average count of valid physical activity per epoch, and average count of valid physical activity per epoch length in minutes. Passive wearable actigraphy will also be used for data collection of this index, as actigraphy provides objective data on overall physical activity levels, and worn actigraphs have been validated by previous studies as an appropriate measure for 24 h activity monitoring of sedentary, as well as moderate-to-vigorous physical activity.[64] Participants will be instructed to wear an actigraphy-collecting device for two consecutive weeks, including during sleep. At the end of data collection, the investigator will extract and analyze the collected data using "Actiware Software version 6.1.2" (Philips Respironics, n.d.).

Social interactions and loneliness. Using an EMA approach, a smartphone-based application with two questions will be used to capture real-time measurements of participants' frequency of social interactions and level of loneliness. EMA offers a real-time glimpse into the daily experiences of older adults with cognitive decline, providing nuanced insights into their social interactions and loneliness levels.[53] By overcoming recall bias and time restrictions, EMA will be able to capture dynamic and immediate data about intrapersonal interactions, and subjects' responses to them (e.g. mood, pain, tiredness, etc.), making it ideal for assessing momentary effects on loneliness in specific social contexts, settings, and time periods.[65]

In the aforementioned application, the app will sound an alarm and display a pop-up message at a fixed time to prompt participants to respond to the questions. Participants will then click on the message to respond to the questions. The tests will be conducted at participants' 3 mealtimes and bedtime, 4 times daily, for 2 weeks. To measure the frequency of social interactions (e.g. "After your last mealtime, how many times have you had a social encounter?"), the participant will be instructed to record the number of face-to-face meetings with another individual as well as phone and video calls lasting more than 5 min. The question used to measure loneliness ("How lonely do you feel at present?") is rated on a five-point Likert scale ranging from "Not lonely at all" (1) to "Very lonely" (5).

Predicted outcomes

Cognitive functioning. The K-MMSE-2 will be used to assess participants' cognitive function. The tool comprises seven categories: time orientation, spatial orientation, memory registration, memory recall, attention and calculation, language, and space-time configuration.[66] Performance on each question was measured on a binary scale, with a total score of 30 or higher indicating a higher level of cognitive function.[67] In a validation study on older Korean adults in an urban area, a high level of reliability was obtained based on an inter-rater reliability of .96 and a test–retest reliability of .86.[68] The participants' predicted cognitive functioning will be divided into three groups based on K-MMSE-2 scores: (1) normal (24–30), (2) MCI (18–23), and (3) severe cognitive impairment (0–17).[69]

Activities of daily living. The Korean Activities of Daily Living (K-ADL)[70] will be used to evaluate participants' physical function. It is a Korean version of the Activities of Daily Living (ADL)[71] that assesses individuals' level of dependency and physical function based on ADL performance. Each of the seven questions is rated on a three-point Likert scale. Total scores range from 7 to 21, with higher scores indicating higher physical function. In a validation study on older Korean adults divided between a healthy function group and a patient group, the K-ADL showed outstanding internal consistency (Cronbach's α=.94) and inter-rater reliability (K = 0.86∼1.0), while the correlation for test–retest reliability was ≥0.7. In addition, a significant correlation coefficient was found between K-ADL and brain-disability grade, confirming the high reliability and validity of the K-ADL in the functional assessment of older adults.[72] In another study on older Korean adults with MCI, the reported internal consistency (Cronbach's α = .75) was acceptable.[73] Participants' K-ADL outcomes will be categorized according to a cutoff score of 7; participants who score 7 will be classified as healthy, whereas those who score 8 or more will be categorized as showing dependency in ADL.[72]

Instrumental ADL. The Korean Instrumental Activities of Daily Living (K-IADL)[70] will be used to assess participants' independent performance of higher functions than those measured by the K-ADL. The K-IADL is the Korean version of the Instrumental Activities of Daily Living (IADL).[74] The scale has 10 questions, 3 rated on a 3-point Likert scale and seven rated on a 4-point Likert scale. Total score ranges from 10 to 37, with higher scores indicating higher levels of performance. In a validation study on older Korean adults divided between a healthy function group and a patient group, the K-IADL had outstanding internal consistency (Cronbach's α = .94) and inter-rater reliability (K = 0.808–0.947), while the correlation for test–retest reliability was ≥0.7, except for one question (meal preparation). In addition, a significant correlation coefficient was found between the K-IADL and the brain-disability grade, confirming the scale's high reliability and validity in the functional assessment of older adults.[75] In another study on older Korean adults with MCI or mild dementia, internal consistency was high (Cronbach's α = .90).[76] Participants' K-IADL results will be categorized according to a cutoff point score of 10; participants who score up to 10 will be considered as exhibiting healthy function, whereas those who score 11 or higher will be categorized as showing dependency in IADL.[75]

Frailty. The Frailty Phenotype Questionnaire (FPQ), a Korean version designed specifically for screening community-dwelling older adults in Korea,[77] will be used to measure the participants' frailty. The FPQ was developed based on the Fried Frailty Phenotype.[78] Considering the limitations of other frailty scales in the development process, the FPQ is more appropriate and easier to apply to community-dwelling participants. It comprises five questions that evaluate fatigue, resistance, ambulation, inactivity, and weight loss. With a total score of 5, scores of 3, 1–2, and 0 indicate frailty, prefrailty, and robustness, respectively. Kim et al. analyzed 2917 older adults using data from the Korean Frailty and Aging Cohort Survey (2016–2017) and found that the FPQ was highly correlated with the Fried Frailty Phenotype ($r = 0.643$; $p < .001$). They also found that the FPQ has high sensitivity (81.7%), specificity (82.5%), reliability (kappa = 0.361), and validity (area under the curve = 0.89). Thus, the FPQ has been validated for measuring frailty in older adults.[77] Participants' FPQ outcomes will be divided into three classifications: (1) robust (scoring 0), (2) prefrail (scoring 1–2), and (3) frail (scoring 3–5).[77]

Self-care. The Appraisal of the Self-Care Agency Scale-Revised (ASAS-R)[79] will be used to measure participants' self-care capacity. It is a modified version of the ASAS,[80] and a Korean-translated version[81] will be used in this study. The tool comprises three subcategories: self-care capacity acquisition, development, and absence. The scale has 15 questions rated on a 5-point Likert scale. Total score ranges from 15 to 75, with higher scores indicating higher levels of self-care capacity. In a validation study of 96 Korean lung cancer patients, Cronbach's α was .87, indicating high internal consistency.[81] Self-care capacity outcomes will be segmented based on a threshold score of 45; participants scoring between 15 and 45 will be deemed self-care sufficient, whereas those scoring 46 or higher will be deemed as having perceived difficulties in self-care.[79]

Table 1 provides a summary of the measurement of the potential predictors and predicted outcomes that will be investigated, as well as the comfort measures that will be used for each variable. For devices being used 24 h/day, variations in comfort levels and usage preferences among participants during nighttime and daytime hours will be accounted for using a number of comfort measures including: (1) "flexible scheduling" for EMA, whereby participants have the option to adjust the timing of EMA prompts to fit their daily routines for enhanced comfort and compliance; (2) "device breaks" for actigraphy devices, where participants are able to schedule the removal of their Actiwatch for short periods when necessary, so that the device does not interfere with daily activities; and (3) "instruction and support" for all devices, to ensure that participants are comfortable and familiar with using their devices.

Strategies for ensuring consistent data quality and addressing missingness

Handling the different frequencies of data collected from various measurement methods will be a critical aspect of

Table 1. Measurement for potential predictors and predicted outcomes.

Category	Variable	Instrument/device	Duration	Timepoint/frequency	Comfort measures		
					1[a]	2[b]	3[c]
Potential predictors	General characteristics	Face-to-face survey	One-time assessment	Initial assessment	-		
	Mild behavioral impairment	MBI-C Scale (in-person)	One-time assessment	Initial assessment	-		
	Depression	SGDS-K (in-person)	One-time assessment	Initial assessment	-		
	Anxiety	K-GAI (in-person)	One-time assessment	Initial assessment	-		
	Sleep	Actiwatch Spectrum PRO	24 h/day	Continuous measure for 2 weeks	X	X	O
	Physical activity	Actiwatch Spectrum PRO	24 h/day	Continuous measure for 2 weeks	X	O	O
	Social interactions & loneliness	EMA (smartphone app)	Four times daily	Fixed times: 3 mealtimes and bedtime for 2 weeks	O	X	O
Predicted outcomes	Cognitive functioning	K-MMSE-2 (in-person)	One-time assessment	Post assessment			
	Activities of daily living	K-ADL (in-person)	One-time assessment	Post assessment			
	Instrumental activities of daily living	K-IADL (in-person)	One-time assessment	Post assessment			
	Frailty	FPQ (in-person)	One-time assessment	Post assessment			
	Self-care	ASAS-R (in-person)	One-time assessment	Post assessment			

[a]Flexible scheduling.
[b]Device breaks.
[c]Instruction and support.
ASAS-R: Appraisal of the Self-Care Agency Scale-Revised; EMA: Ecological Momentary Assessment; FPQ: Frailty Phenotype Questionnaire; K-ADL: Korean Activities of Daily Living; K-GAI: Korean version of the Geriatric Anxiety Inventory; K-IADL: Korean Instrumental Activities of Daily Living; K-MMSE-2: Korean Mini-Mental State Examination, second edition; MBI-C: Mild Behavioral Impairment Checklist; SGDS-K: Short Form Geriatric Depression Scale.

the analysis plan. To address this issue, we will employ suitable data processing techniques that account for the temporal resolution of each measurement method. For instance, with actigraphy providing continuously monitored data and EMA assessing participants' experiences multiple times per day, we will harmonize the data by aggregating or aligning them temporally for our data analyses. Specifically, we will aggregate EMA data to match the temporal resolution of actigraphy data, ensuring compatibility for subsequent analysis. As seen in similar studies incorporating multiple measurement methods,[82,83] this process may involve segmenting the actigraphy data into epochs corresponding to the intervals of EMA assessments, allowing for direct comparisons between the two data streams.

Ensuring data quality and addressing missingness will be crucial for our investigation. To mitigate potential quality issues, we will implement several strategies. Firstly, we will provide thorough training to participants on the proper use of wearable devices and smartphone-based EMA applications, emphasizing the importance of consistent adherence to data collection protocols. Additionally, we will employ regular check-ins and reminders to encourage compliance with data collection procedures. Recognizing that participant engagement may vary, particularly regarding actigraphy wear during sleep and EMA prompt responsiveness, we will implement tailored strategies. For instance, participants will have the flexibility to remove wearable devices during periods of discomfort, ensuring comfort and compliance.[84] Moreover, we will collect detailed information on participants' daily schedules and activities to identify potential patterns of missingness and tailor reminders or prompts accordingly and address any gaps or discrepancies in the data arising from the differences in measurement frequency, which have been used for deep learning approaches with varying datasets.[21]

Predictive modeling

All analyses will be performed using R, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria) and Python (version 3.7.2; Python Software Foundation, Wilmington, DE). As seen in previous studies of longitudinal datasets incorporated into machine learning models, mixed-effect machine learning (MEml) models (i.e., MErf, MEgbm, MEmod, and MEctree) and standard machine learning models without random effects (i.e. random forest, gradient boosting machine (GBM)) will be employed in our analyses, as well as more traditional, non-machine learning approaches for analyzing longitudinal data such as generalized linear mixed-effects modeling (GLMM) for comparative purposes. Such methods are believed to be comparable to traditional methods in that they allow the incorporation of random-effects into more accurate and interpretable machine learning models. For example, contrast to conventional parametric models, that is, models for which an investigator specifies the statistical relationships between the dependent and independent variables by defining a functional form (e.g. linearity), machine learning algorithms (e.g. boosting models) can more flexibly test complex interactions between variables as they only require investigators to specify a set of covariates that may serve as effect modifiers. If issues of overfitting are avoided through techniques such as sample splitting, machine learning algorithms may have comparable accuracy and robustness of inferences to that of parametric models, while making fewer assumptions about outcome distribution.[85] As individual covariates in mental health research often only have small effects as treatment effect modifiers,[86] such advantages may allow for machine learning algorithms to provide new insights about predictors of outcomes.[85] To validate the predictive performance of these two methods, each model will be bootstrapped 1000 times for the entire sample ($n = 130$) and subsequently validated. The importance of each modifiable risk factor associated with cognitive functioning will be measured using Shapley values based on the highest-performing model to interpret how each feature contributes to the prediction of cognitive and functional decline.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board of Yonsei University Hospital (approval no.4-2022-0637). To ensure ethical integrity, all participants will be asked to provide written informed consent prior to their inclusion in the study. Individuals with severe cognitive impairment, who will be assessed as incapable of making an informed decision regarding participation, will be excluded from the study.

Discussion

In older adults with SCD and MCI, a preclinical and prodromal stage of dementia respectively, the focus should be on behavioral interventions that assist individuals with active self-care by preventing the onset of various cognitive, behavioral, physical, and psychosocial symptoms that may be experienced throughout the dementia spectrum.[87] Nevertheless, there is a lack of studies on the behavioral indicators of older adults with SCD or MCI as high-risk groups for dementia, especially with the collection of actigraphy data and the use of deep learning techniques for optimized prediction.[88] Another area in which research is notably sparse regards the implications of MBI as a potential risk factor for dementia progression. Although it is possible for older adults with SCD or MCI to reverse their declined cognitive and functional abilities, the influence of MBI on predicting the onset of dementia remains under-investigated. It is imperative to understand the mechanisms by which MBI may affect dementia trajectories. While studies are beginning to explore the relationship between certain modifiable risk factors, such as sleep disturbance and cognitive decline, using machine learning techniques,[89] novel methodologies that are easily applicable, cost-efficient, and incorporate models with high accuracy rates may be invaluable for facilitating the monitoring of Alzheimer's disease progression without requiring excessive healthcare resources.[90]

Furthermore, the influence of behavioral patterns, from sleep to physical activity, on social interactions, cognitive decline, and physical dysfunction have been aptly investigated in retrospective studies. However, this study is significant in that it is longitudinal in nature and attempts to develop a predictive model for the physical and cognitive functions of older adults with SCD or MCI based on behavioral indicators identified through repeated collection and analysis of highly reliable and valid data using machine learning. While studies establishing the feasibility of longitudinal actigraphy are limited, they have consistently demonstrated that actigraphy data, especially for resting-activity patterns and light exposure, may be invaluable in randomized controlled trials targeting older adults.[89]

For all data collection methods, our study incorporates EMA rather than conventional methods. The use of EMA is advantageous in that it is free from the influence of recall bias, as measurements are taken immediately after an experience.[53] The EMA is highly valid in ecological terms, as it allows repeated measurements of actual experiences and analyses of the influence of contextual situations on behavior[91] and provides time-dependent data. For vulnerable groups in health management, such as older adults with cognitive difficulties, EMA may improve accessibility to care, be more economically feasible, and provide greater utility compared to conventional methods.[92] Thus, employing smartphone-based EMA is a strength of this study that will allow repeated measurements of the behavioral and psychosocial states of participants in their daily activities and contribute to the design of ecological interventions for our target population.

Finally, high-risk dementia groups should be provided with behavioral interventions that are tailored to them and which reflect their personal needs and preferences to assist these groups with active self-care.[87] Machine learning-based digital health programs have recently been effectively used in health-related studies for a population-level approach to health through personalized behavioral interventions without temporal, spatial, or personnel-related restrictions based on data intellectualization through artificial intelligence.[93] Thus, the results of this study will provide basic data for developing tailored digital behavioral intervention programs based on machine learning algorithms to optimize self-care and prevent functional decline in older adults with SCD or MCI.

However, this study will have some limitations. First, as this study targets community-dwelling older Korean adults with SCD or MCI, the generalizability of the results may be limited to the targeted group. Second, because of the characteristics of this study, only participants capable of using smartphones were recruited using convenience sampling. Thus, there may be limitations in generalizing the results to the entire older adult population, particularly those who do not use smartphones. Third, participants may drop out of this prospective longitudinal study. To overcome these limitations, a small reward will be provided to each participant each time they complete the questionnaire. Finally, considering MBI, data collection will rely on questionnaires rather than EMA despite variations in accordance with the psychosocial characteristics of the participants. This implies a potential limitation in incorporating the participants' actual MBI characteristics.

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