Biomedical Engineering Letters (2024) 14:13–21
https://doi.org/10.1007/s13534-023-00306-7

ORIGINAL ARTICLE

A comprehensive research setup for monitoring Alzheimer's disease using EEG, fNIRS, and Gait analysis

Minhee Kim[1] · Sehyeon Jang[2] · Donjung Lee[3] · Seungchan Lee[4] · Jeonghwan Gwak[5] · Sung Chan Jun[2] · Jae Gwan Kim[1]

Received: 3 April 2023 / Revised: 10 June 2023 / Accepted: 12 July 2023 / Published online: 9 August 2023

Abstract
Alzheimer's disease (AD) has a detrimental impact on brain function, affecting various aspects such as cognition, memory, language, and motor skills. Previous research has dominantly used electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) to individually measure brain signals or combine the two methods to target specific brain functions. However, comprehending Alzheimer's disease requires monitoring various brain functions rather than focusing on a single function. This paper presents a comprehensive research setup for a monitoring platform for AD. The platform incorporates a 32-channel dry electrode EEG, a custom-built four-channel fNIRS, and gait monitoring using a depth camera and pressure sensor. Various tasks are employed to target multiple brain functions. The paper introduced the detailed instrumentation of the fNIRS system, which measures the prefrontal cortex, outlines the experimental design targeting various brain functioning programmed in BCI2000 for visualizing EEG signals synchronized with experimental stimulation, and describes the gait monitoring hardware and software and protocol design. The ultimate goal of this platform is to develop an easy-to-perform brain and gait monitoring method for elderly individuals and patients with Alzheimer's disease.

Keywords Brain monitoring system · Electroencephalogram · Functional near-infrared spectroscopy · Gait monitoring · Alzheimer's disease

1 Introduction

Statistics Korea reported in 2022 that there are approximately 9.01 million individuals aged 65 or older, accounting for 17.5% of the total population. This indicates that Korea is currently facing the challenges of an aging society and is transitioning into a super-aged society as the numbers keep increasing. Among the population of elder, around 10% of the elderly population in Korea suffer from dementia, leading to hospitalizations or visiting clinic. Currently, there is no cure available for dementia, and thus, efforts focus on prevention and delaying the progression of symptoms.

✉ Jae Gwan Kim
jaekim@gist.ac.kr

Minhee Kim
minhee@gm.gist.ac.kr

Sehyeon Jang
shjang@gist.ac.kr

Donjung Lee
naka1006@gmail.com

Seungchan Lee
chans@kimm.re.kr

Jeonghwan Gwak
james.han.gwak@gmail.com

Sung Chan Jun
scjun@gist.ac.kr

[1] Department of Biomedical Science and Engineering, Gwangju Institute of Science and Technology, Gwangju 61005, Republic of Korea

[2] School of Electrical Engineering and Computer Science, Gwangju Institute of Science and Technology, Gwangju 61005, Republic of Korea

[3] Korea Photonics Technology Institute, Gwangju 61007, Republic of Korea

[4] Department of Medical Device, Korea Institute of Machinery & Materials, Daegu 42994, Republic of Korea

[5] Department of Software, Korea National University of Transportation, Chungju 27469, Republic of Korea

Alzheimer's disease (AD) is the most common cause of dementia, characterized by the formation of amyloid plaques and neurofibrillary tangles, which result in neuronal cell death and affect various aspects of brain. Early detection of Alzheimer's disease is crucial in order to delay symptom deterioration. The primary screening methods used in Korea include the Mini–Mental State Examination (MMSE), a questionnaire assessing general cognitive function, and the Seoul Neuropsychological Screening Battery (SNSB), which evaluates brain functions across different domains [1, 2]. However, these screening methods have limitations, as MMSE is not effective in identifying early-stage dementia such as mild cognitive impairment (MCI) [3]. Also, both tests are influenced by socio-educational factors and are unsuitable for illiterate individuals [4, 5].

To address these shortcomings, there is a need for a quantitative, objective, and easy-to-handle screening tool. Current screening techniques employ noninvasive methods such as electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) due to their portability compared to bulkier modalities like MRI and PET. EEG measures neural electrical activity, while fNIRS detects hemodynamic activity related to blood circulation. Moreover, fNIRS can be customized at lower costs compared to other modalities.

In order to comprehensively examine Alzheimer's disease, it is essential to measure various functions affected by brain abnormalities, including cognitive function, memory function, language function, and motor function. To address this, we have designed a platform to measure brain and gait function to screen early AD. This platform enables the continuous measurement of brain function and gait, and we have prepared a technical report outlining the necessary steps for developing the AD screening platform. The platform consists of a brain function measurement system based on EEG and fNIRS, and a gait measurement system based on a depth camera and pressure sensors, as described in Fig. 1.

Previous studies in the literature have primarily focused on the experimental results, lacking sufficient details regarding the device development and systemic parameter settings for EEG, fNIRS, and gait monitoring. This lack of information hampers the understanding and reproducibility of the research procedures for other researchers referencing these studies. Therefore, the purpose of this paper is to provide detailed information on our research setup, including the hardware and software configurations. This study presents an experimental setup comprising a commercial EEG system, a custom fNIRS system, and a commercial gait monitoring system for an Alzheimer's disease study. We also describe the design of the experimental setup employed to conduct the experiment.

2 Materials and methods

2.1 Hardware

The brain monitoring system for AD, as shown in Fig. 2, comprised two main components: a 32-channel dry electrode EEG system (g.Nautilus, g.tec, Austria) covering the entire brain, and a custom-built four-channel fNIRS system used to measure the prefrontal cortex. Both the EEG and fNIRS devices had sampling rates of 500 Hz and 8 Hz, respectively. The fNIRS system consisted of two dual-wavelength LEDs (OE-MV7385-P, OptoENG, Republic of Korea) and five photodiodes (OPT101, Texas Instruments, USA), with wavelengths of 730 nm and 850 nm being used. The signal captured by the photodiodes was amplified using quad-operational amplifiers. The LEDs emitted light of each wavelength alternately for a brief duration, controlled by digital pins in the microcontroller. The LEDs were supplied with a constant current through a transistor-based current circuit. The circuit design details are provided in S1 of the supplementary material. The system components were fabricated using a flexible material called TPU and created using a 3D printer based on the design developed in a 3D CAD program.

Additionally, the gait monitoring system (Tango+ STEP, OPTONICS, Republic of Korea) included a depth camera to measure body balance during walking and a pressure sensor-equipped mat to analyze the gait pattern. The specific characteristics of the brain and gait monitoring system are listed in Table 1.

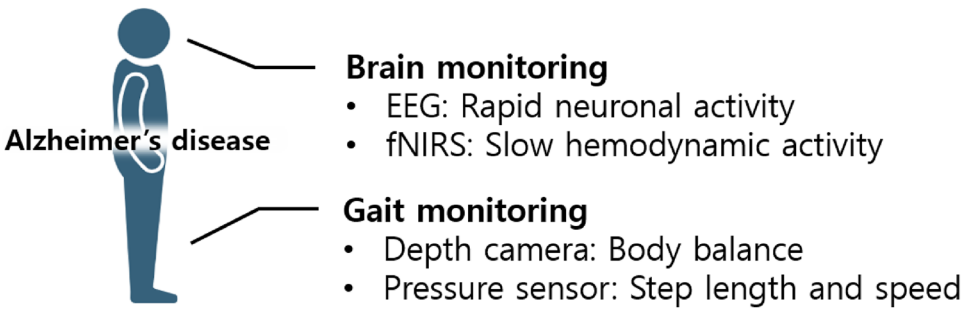

Fig. 1 A schematic concept of the measurement system for Alzheimer's disease

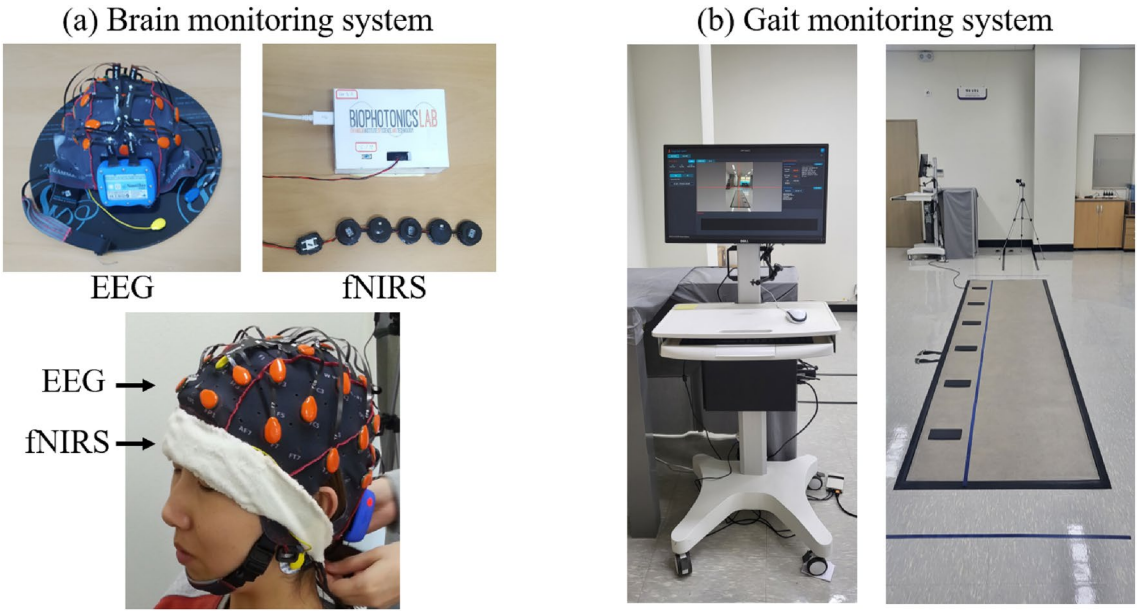

Fig. 2 The system configuration. **a** The brain monitoring system and **b** The gait monitoring system

Table 1 Characteristics of the acquisition systems

Characteristics	Acquisition system		
	EEG	fNIRS	Gait
Manufacturer/Name	g.tec/g.Nautilus	Lab built	OPTONICS / Tango+ STEP
Number of channels	32	4 (Long), 2 (Short)	Image acquisition
sensor	Dry electrode (g.SAHARA)	5 optodes (5 photodiodes, 2 LEDs)	Pressure sensor, depth camera
Signal transmission method	Wireless	USB	USB
Operating software	BCI2000	The standalone executable program generated using MATLAB	The standalone executable program

2.2 Software

2.2.1 EEG software

We utilized BCI2000 software to develop the EEG operating system, which allows for the customization and visualization of appropriate stimuli for subjects. This software enables real-time recording and plotting of EEG signals while synchronizing the experimental protocol with the EEG data. To run the EEG system in BCI2000, two files, namely "parameter" and "batch" files, were required.

The parameter configuration in BCI2000 was divided into several sections, including Visualize, System, Source, Storage, Application, Connector, and Filtering. A detailed description of the BCI2000 environment can be found in S2 of the supplementary material. The Visualize tab was used to set up real-time signal visualization. Briefly, we specified the IP address of the EEG device as 127.0.0.1 to establish the connection between BCI2000 and the EEG device. The Storage tab determined the data directory, subject number, session, and file format, which we saved as.dat files. The Application tab allowed us to set the window size of the experimental paradigm and parameters for sequencing, such as stimulation duration, interstimulus duration, number of stimulations, and sequence type. The Application tab also facilitated the customization of basic BCI2000 parameters for our study. For instance, we used oddball, 1-back, and verbal fluency tasks, involving simple drawings and text, so we modified the stimuli to customized icons and text. Each set of parameters was saved as.prm files, resulting in separate. prm files for each task.

The batch files contained the sequence of commands to initialize the experimental paradigm and visualize the EEG signals. When the batch file was executed, it initiated the g.Nautilus server and established the connection with the software and loaded the previously saved.prm files. The UI of the batch file is shown in Fig. 3. Clicking on the "Config" button displays a parameter configuration window where

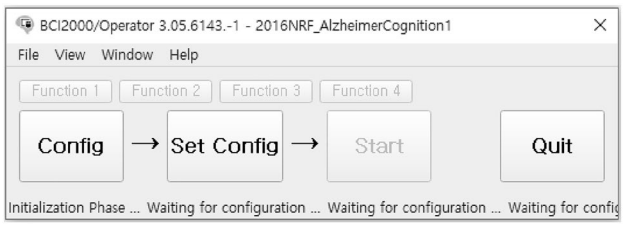

Fig. 3 BCI2000 user interface for EEG recording

the number of channels, sampling rate, and previously set stimulation parameters could be verified. Once the parameter check was completed, the technician pressed enter key, and the configuration window closed. Additionally, by clicking "Set Config," the configuration was compiled to the device, and the EEG signal appeared on the monitor. The technician then assesses the signal quality of the subject before beginning the measurement. If any abnormal spikes were observed prior to the experiment, the technician would adjust the placement of EEG electrodes on the subject's head accordingly. After verifying all signals and ensuring the system was ready, the technician pressed "Start" to initiate the experiment.

2.2.2 fNIRS software

We programmed the operational functions of the fNIRS system using Arduino. This involved implementing code on Arduino to switch the LED wavelength and read values from the photodiodes. The photodiode values were then displayed as a line on the Serial Monitor. The specific Arduino code can be found in S3 of the supplementary material.

Next, we designed a graphical user interface (GUI) using MATLAB to visualize the real-time values. The GUI templates are depicted in Fig. 4. The configuration of the GUI was accomplished using MATLAB's GUIDE function. The first step was to retrieve the signal from the microcontroller via the Serial Monitor using "get" function in MATLAB. The voltage signal was read into MATLAB variables using the "fscanf" function. The fNIRS channels CH1 and CH2 were positioned on the right prefrontal cortex, while CH3 and CH4 were located on the left side. The channel labeled as "Near" represented the channel with a short source-detector separation.

To establish a connection with the fNIRS device, the technician verified the comport of the device, entered the corresponding number (e.g., "COM4"), and clicked on the "CONNECT" button. The text on the button changed to "DISCONNECT" once the software detected the fNIRS device on the computer. Upon clicking the "START" button, the fNIRS device began running, and the changes in hemoglobin concentration were displayed. The conversion of these changes into real-time data was achieved using the modified Beer-Lambert law [6]. All channel signals were plotted on six graphs. The top left corner of each graph displayed the intensity of light for the two wavelengths, enabling the technician to check the signal intensity.

While the program was running, the "START" button changed to "STOP." Upon completion of the experiment, the

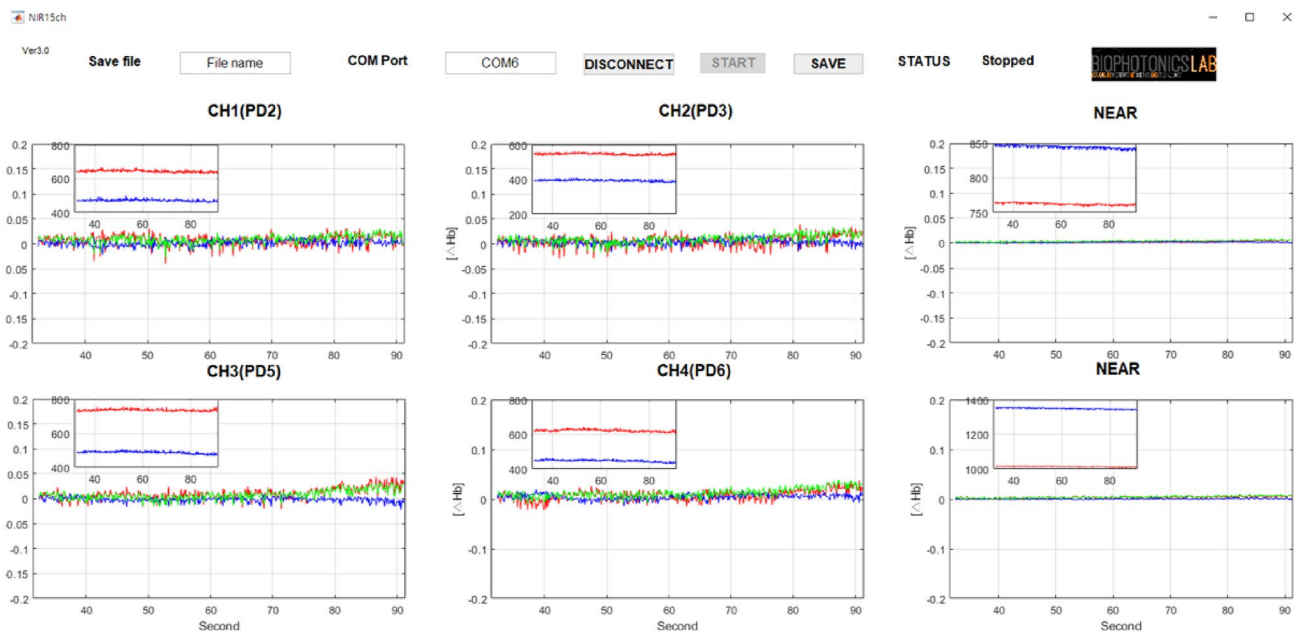

Fig. 4 GUI design for fNIRS device

technician clicked the "STOP" button to cease data display. Clicking "SAVE" enabled the fNIRS data to be saved in the folder where the fNIRS program was located. The MATLAB code for the GUI implementation can be found in S4 of the supplementary material.

To monitor EEG and fNIRS programs on one monitor, we used Xsplit, a broadcast program that combines real-time recordings for comfortable observation of multi-device data projected on a screen. As shown in Fig. 8, on the top left of the screen, the video camera is recorded in real-time along with the fNIRS and EEG signal to ensure that the technician can observe a sudden signal change according to movement. Figure 5 shows the visualization template, including a video camera, button trigger, and task video attached, according to the divided section. After the brain measurement, the gait measurement is performed separately.

2.2.3 Gait software

The Tango+ STEP, gait monitoring system, consists of a depth camera installed to measure the balance of the body when walking and a specially fabricated mat equipped with a force-sensitive resistor to assess the gait pattern. For gait monitoring, the skeleton and step events were recorded via the software provided by company. The UI of software is shown in Fig. 6. Using depth image information, real-time 3D joint coordinates are created and measured to store information such as gait parameters and major joint angles. Gait parameters include gait length and width of the right and left feet and velocity of walking. Angle parameters analyzed from image information include hip-knee angle, knee, shoulder, elbow, arm, body, and head inclination. After the measurement, a document summarizing this information can be saved and printed in the software.

2.3 Experimental protocols

For brain monitoring, we employed the measurement during visual oddball, 1-back, and verbal fluency tasks as part of the experimental paradigm to assess basic cognition, working memory, and language function, respectively. Prior to each task, a cross mark appeared on the monitor, and the subject was instructed to stare at the center point. Before beginning the task, the resting state signal was recorded for one minute. In the oddball task, consecutive circles appeared in random order on the monitor, and the subject was instructed to press a button when the color of the circle changed. The circles were displayed for 0.5 s and disappeared with an interstimulus interval (ISI) of 1–1.5 s.

In the 1-back task, the subject was shown one of three figures in random order and instructed to remember the previous figure. They were then required to press a button when the current figure matched the previous one. Each figure was displayed for 1 s, and the ISI was the same as that of the oddball task. The verbal fluency task consisted of six stimuli, three phonemic tasks, and three semantic verbal tasks. The subject was given a phonemic or semantic word and asked to continuously produce related words for 30 s. Afterward, they were instructed to discontinue word generation and stare at

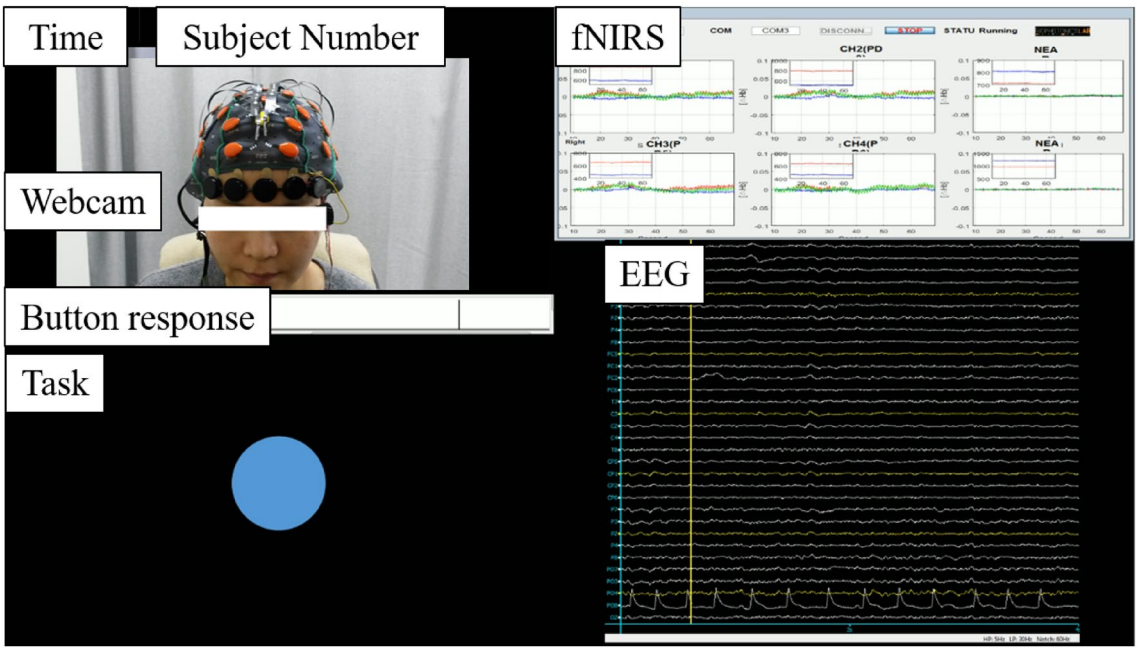

Fig. 5 Interface for real-time brain monitoring

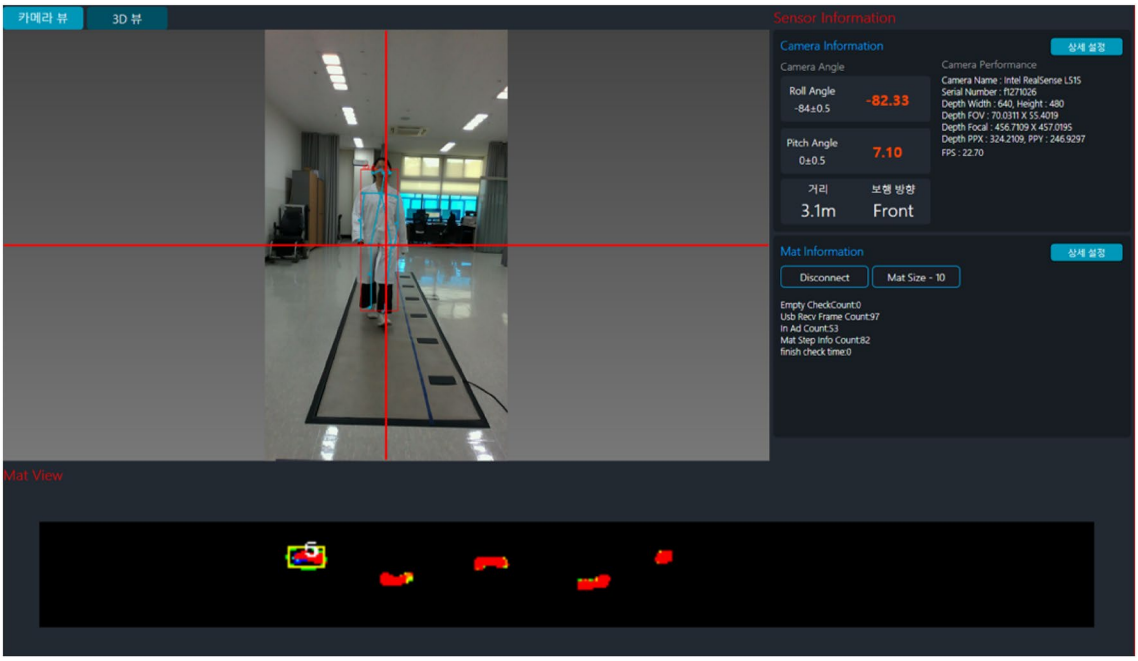

Fig. 6 The gait monitoring software

the cross mark on the monitor for another 30 s. This cycle was repeated.

After completing the brain signal measurement, the gait monitoring protocol was introduced and performed. The subject first walked straight and then returned. They were then instructed to walk while simultaneously counting numbers upward and downward. The specific sequence is described in Fig. 7.

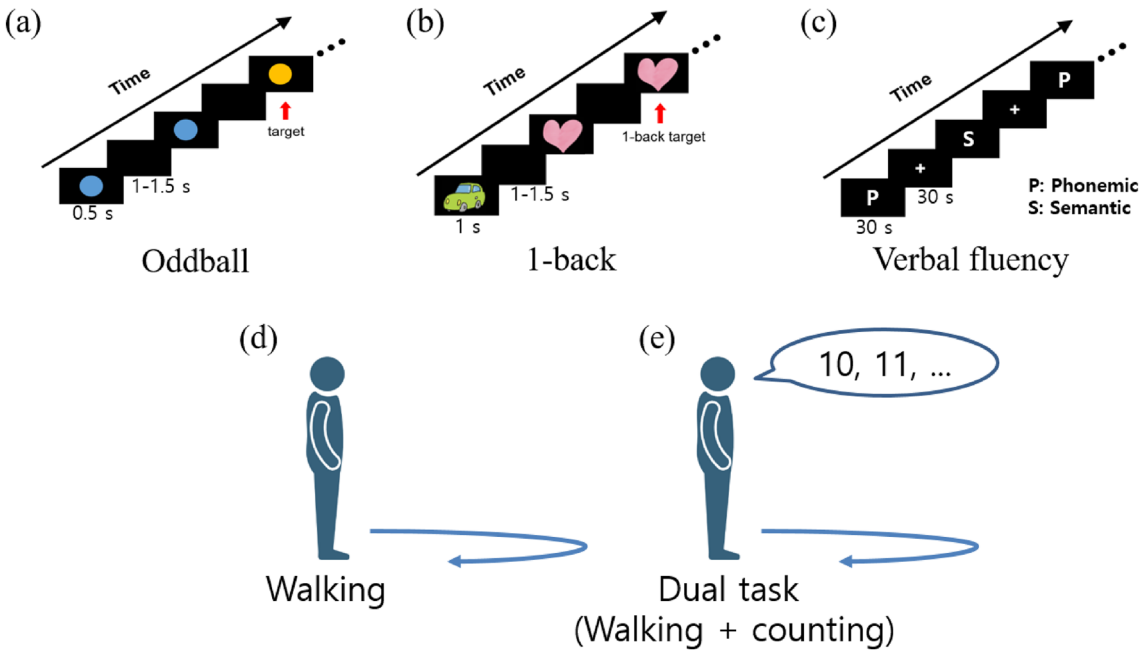

Fig. 7 The experimental paradigm: **a** Oddball task, **b** 1-back task, **c** Verbal fluency task, **d** Walking, **e** Dual task (Walking and number counting)

2.4 Experimental procedure

The experiment was conducted in a specially designed room at the Gwangju Senior Technology Center. The data measurement procedure is summarized in Fig. 8. The subject recruitment was carried out at the Gwangju Dementia Prevention and Management Center. When a subject visited the center, the research staff explained the experiment and obtained their consent to participate. A schedule for the measurement was then set. When the subject visited the AD monitoring center, the research staff provided a detailed explanation of the entire experimental procedure to them and obtained their signed consent form. The subject was seated comfortably in a chair, which was positioned in front of a monitor, and the chair's location was fixed to align with the monitor's middle line.

The room was divided into sections for brain monitoring and gait monitoring. Initially, the subject performed the tasks in an isolated area within the brain monitoring space. The technician sat in the operator's room and used a webcam placed beside the subject to observe the signal quality. Simultaneously, the technician monitored the ongoing task on a monitor that replicated the one in the subject's side. After the brain measurement was completed, they moved to the gait monitoring space and continued the measurement. All the procedure took approximately one hour to complete.

After completing the experiments, the data files were copied and saved on a backup drive. The technician then transferred the files to a physical memory drive and took them to the research institute. Subsequently, the data was uploaded to a data server accessible by researchers within the same network. To access the server, users needed specific credentials, including a designated ID and password. The data files were organized by subject number for easy retrieval.

3 Results

We presented preliminary data on fNIRS as part of our AD monitoring platform. Firstly, we compared healthy control individuals with those diagnosed with MCI (mild cognitive impairment) during the Verbal Fluency Task (VFT) [7]. We observed a greater change in oxyhemoglobin concentration in MCI patients, with a rapid increase at the beginning of the task. Secondly, we computed functional connectivity from resting-state, oddball, 1-back, and VFT paradigms [8]. The MCI group exhibited higher connectivity within the right and inter-prefrontal area during the resting state while showing significantly lower connectivity within the left and inter-prefrontal area during VFT compared to the healthy control group. Additionally, we validated a deep learning model for multi-class AD classification using fNIRS raw data from 140 patients, achieving an accuracy of 0.9 [9]. Furthermore, a deep learning approach has been explored to diagnose the prodromal stage of AD using resting-state EEG data [10]. Similarly, the machine learning-based classification models with wearable sensors have been applied to a multilevel gait study [11]. The analysis based on camera and pressure sensors is currently being investigated as an ongoing study. After single module analysis is complete, the multi-domain study is required to improve the screening accuracy of AD.

4 Discussion

During the brain function measurement, we employed an EEG system to capture the neural activity across the entire brain area, while the fNIRS system specifically focused on the hemodynamics of the prefrontal cortex. The oddball, 1-back, and verbal fluency tasks were carefully designed to assess relevant brain functions such as attention, memory,

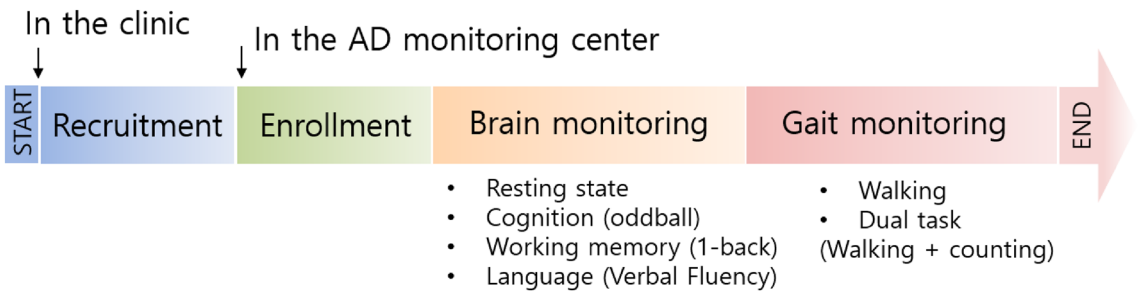

Fig. 8 The procedure of monitoring AD

and language. Although these tasks primarily activate the occipital, temporal, and parietal lobes, the frontal and prefrontal regions are also closely associated with their functioning. Previous research by McCarthy et al. demonstrated distinct frontal activation patterns in response to rapidly repeated stimulation within a group of subjects undergoing the oddball task [12]. This suggests that the frontal cortex exhibits rapid responsiveness to repetitive stimuli. Furthermore, both EEG-NIRS techniques have identified fast optical signal and event-related potential response in the prefrontal cortex due to the oddball stimulus [13].

The n-back task, commonly used in EEG and fNIRS studies, is designed to assess working memory. Fraga et al. conducted a clinical study comparing event-related desynchronization among healthy older adults and individuals with MCI and AD [14]. They found significant differences between the control and the AD group, indicating altered working memory levels in AD. Similar investigations have quantified changes in blood oxygenation in the prefrontal cortex during the n-back task in healthy adults and MCI patients, highlighting its utility in assessing cognitive workload [15, 16].

The verbal fluency task is widely employed in fNIRS studies, as it elicits high levels of brain activation in the prefrontal cortex when individuals generate words related to specific phonemic or semantic categories [17]. Yeung et al. have revealed altered patterns of lateralization during the semantic verbal fluency task in MCI patients [18]. Moreover, comparisons between healthy older adults and individuals with MCI and AD have demonstrated variations in mental workload across different stages of AD [19–21]. In EEG studies, the verbal fluency task has shown an association between theta power and naming performance [22].

Video recording during the experiment is crucial for identifying artifacts in EEG and fNIRS signals. Technicians utilize real-time webcam recordings to observe the subject's condition, and these videos are saved alongside the data for subsequent analysis. The presence of artifacts, such as eye blinking or slight head movements, can be marked and documented with timestamps, supporting the preprocessing in terms of the identification and elimination of unwanted signal. The video recordings include EEG, fNIRS, and synchronized button response data. The button response task requires the subject to pay attention and provides insights to the technician to sense their understanding of the rule of the task. In general, individuals with MCI and AD may encounter difficulties in understanding the procedures, resulting in erroneous button presses. Thus, button response accuracy and reaction time can serve as indicators of AD progression.

Gait is a fundamental daily activity and also it is considered one of the symptoms of the dementia stage. The monitoring of walking and body balance is impacted by abnormal brain function and therefore those factors can be key characteristics of AD screening in an early stage. Research has demonstrated that individuals with mild cognitive impairment caused by Alzheimer's disease exhibit noticeably slower walking speeds compared to the normal population [23]. Recognizing the importance of assessing these physical aspects can contribute to early detection and intervention in AD cases.

While previous studies on Alzheimer's disease (AD) monitoring using EEG and fNIRS have predominantly focused on brain function during rest or working memory tasks, our proposed method encompasses a broader range of tasks. Our approach includes assessments during resting state, working memory, cognitive tasks, and verbal fluency tasks.

In the literature search, we found four relevant papers that focused on AD studies utilizing EEG and fNIRS. Li et al. investigated alterations in brain networks in AD and utilized EEG–fNIRS to identify weaker and suppressed cortical connectivity during a working memory task [24]. Cicalese et al. employed a machine learning algorithm to classify different stages of AD using EEG and fNIRS features [25]. They achieved promising results with an Area Under Curve of up to 0.88. Perpetuini et al. targeted the detection of early AD through working memory failure and achieved notable outcomes [26]. Lastly, Chiarelli et al. quantified the relationship between theta and alpha brainwave bands with changes in hemoglobin concentration [27].

In contrast, our AD monitoring platform integrates both brain function measurements and gait analysis. This comprehensive approach allows for the evaluation of not only brain functioning but also step function and body balance. By capturing multiple features for analysis, our method offers an efficient monitoring approach for AD.

5 Conclusion

In this study, we have described the development of a real-time monitoring platform for Alzheimer's disease (AD) using EEG, fNIRS, and gait monitoring sensors. The platform aims to effectively detect various domains affected by AD, including cognition, working memory, language, and motor function. The preliminary data from a single module suggests that this platform has the potential to be utilized as a screening tool for AD. We hope that the detailed technical description provided for setting up the system and software will be valuable for researchers planning to design AD-related studies.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13534-023-00306-7.

Acknowledgements This work was supported by Brain Research Program, National Research Foundation of Korea (NRF-2016M3C7A1905475) and Healthcare AI Convergence Research & Development Program through the National IT Industry Promotion Agency of Korea (NIPA) funded by the Ministry of Science and ICT (No. S1601-20-1016)

Author Contributions Conceptualization: JGK, SCJ, JG; Methodology: MK, SJ, DL, SL; Formal analysis and investigation: MK, SJ; Writing–original draft preparation: MK; Writing—review and editing: MK, JGK; Funding acquisition: JGK, SCJ, JG; Supervision: JGK, SCJ.

Declarations

Conflict of interest The authors declare that there's no conflict of interest related to this study.

Ethical approval This study was approved by the Institutional Review Board at the Gwangju Institute of Science and Technology.

References

1. Mf F. "Mini–mental state'' A practical method for grading the cognitive state of patients for the clinician. J Psychiatr res. 1975;12(3):189.
2. Kang Y, Na D, Hahn S. Seoul neuropsychological screening battery. Incheon: Human brain research & consulting co. 2003.
3. Devenney E, Hodges JR. The mini–mental state examination: pitfalls and limitations. Pract Neurol. 2017;17(1):79–80.
4. Carnero-Pardo C. Should the mini–mental state examination be retired? Neurol (Engl Ed). 2014;29(8):473–81.
5. Han C, Jo SA, Jo I, Kim E, Park MH, Kang Y. An adaptation of the Korean mini–mental state examination (K-MMSE) in elderly Koreans: demographic influence and population-based norms (the AGE study). Arch Gerontol Geriatr. 2008;47(3):302–10.
6. Delpy DT, Cope M, van der Zee P, Arridge S, Wray S, Wyatt J. Estimation of optical pathlength through tissue from direct time of flight measurement. Phys Med Biol. 1988;33(12):1433.
7. Kim M, Nguyen T, Gwak J, Lee JJ, Choi KY, Lee KH, et al. Investigation of cerebral hemodynamic changes in mild cognitive impairment due to Alzheimer's disease during a verbal fluency task. In: 7th international conference on the development of biomedical engineering in Vietnam (BME7) translational health science and technology for developing countries 7. Springer; 2020. pp. 379–382.
8. Nguyen T, Kim M, Gwak J, Lee JJ, Choi KY, Lee KH, et al. Investigation of brain functional connectivity in patients with mild cognitive impairment: a functional near-infrared spectroscopy (fNIRS) study. J Biophoton. 2019;12(9): e201800298.
9. Ho TKK, Kim M, Jeon Y, Kim BC, Kim JG, Lee KH, et al. Deep learning-based multilevel classification of Alzheimer's disease using non-invasive functional near-infrared spectroscopy. Front Aging Neurosci. 2022;14:810125.
10. Park J, Jang S, Gwak J, Kim BC, Lee JJ, Choi KY, et al. Individualized diagnosis of preclinical Alzheimer's disease using deep neural networks. Exp Syst Appl. 2022;210: 118511.
11. Jeon Y, Kang J, Kim BC, Lee KH, Song JI, Gwak J. Early Alzheimer's disease diagnosis using wearable sensors and multilevel gait assessment: a machine learning ensemble approach. IEEE Sens J. 2023;23(9):10041–53.
12. Mccarthy G, Luby M, Gore J, Goldman-Rakic P. Infrequent events transiently activate human prefrontal and parietal cortex as measured by functional MRI. J Neurophysiol. 1997;77(3):1630–4.
13. Proulx N, Samadani AA, Chau T. Quantifying fast optical signal and event-related potential relationships during a visual oddball task. Neuroimage. 2018;178:119–28.
14. Fraga FJ, Mamani GQ, Johns E, Tavares G, Falk TH, Phillips NA. Early diagnosis of mild cognitive impairment and Alzheimer's with event-related potentials and event-related desynchronization in N-back working memory tasks. Comput Meth Progr Biomed. 2018;164:1–13.
15. Herff C, Heger D, Fortmann O, Hennrich J, Putze F, Schultz T. Mental workload during n-back task-quantified in the prefrontal cortex using fNIRS. Front Human Neurosci. 2014;7:935.
16. Yang D, Hong KS, Yoo SH, Kim CS. Evaluation of neural degeneration biomarkers in the prefrontal cortex for early identification of patients with mild cognitive impairment: an fNIRS study. Front Human Neurosci. 2019;13:317.
17. Heinzel S, Metzger FG, Ehlis AC, Korell R, Alboji A, Haeussinger FB, et al. Aging-related cortical reorganization of verbal fluency processing: a functional near-infrared spectroscopy study. Neurobiol Aging. 2013;34(2):439–50.
18. Yeung MK, Sze SL, Woo J, Kwok T, Shum DH, Yu R, et al. Altered frontal lateralization underlies the category fluency deficits in older adults with mild cognitive impairment: a near-infrared spectroscopy study. Front Aging Neurosci. 2016;8:59.
19. Arai H, Takano M, Miyakawa K, Ota T, Takahashi T, Asaka H, et al. A quantitative near-infrared spectroscopy study: a decrease in cerebral hemoglobin oxygenation in Alzheimer's disease and mild cognitive impairment. Brain and cognition. 2006;61(2):189–94.
20. Tang TB, Chan YL, Functional connectivity analysis on mild Alzheimer's disease, mild cognitive impairment and normal aging using fNIRS. In: 40th annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE. 2018;2018, pp. 17–20
21. Yap KH, Ung WC, Ebenezer EG, Nordin N, Chin PS, Sugathan S, et al. Visualizing hyperactivation in neurodegeneration based on prefrontal oxygenation: a comparative study of mild Alzheimer's disease, mild cognitive impairment, and healthy controls. Front Aging Neurosci. 2017;9:287.
22. Brickman AM, Paul RH, Cohen RA, Williams LM, MacGregor KL, Jefferson AL, et al. Category and letter verbal fluency across the adult lifespan: relationship to EEG theta power. Arch Clin Neuropsychol. 2005;20(5):561–73.
23. Gras LZ, Kanaan SF, McDowd JM, Colgrove YM, Burns J, Pohl PS. Balance and gait of adults with very mild Alzheimer's disease. J Geriat Phys Ther (2001). 2015;38(1):1.
24. Li R, Nguyen T, Potter T, Zhang Y. Dynamic cortical connectivity alterations associated with Alzheimer's disease: an EEG and fNIRS integration study. NeuroImage: Clin. 2019;21:101622.
25. Cicalese PA, Li R, Ahmadi MB, Wang C, Francis JT, Selvaraj S, et al. An EEG–fNIRS hybridization technique in the four-class classification of Alzheimer's disease. J Neurosci Meth. 2020;336:108618.
26. Perpetuini D, Chiarelli AM, Filippini C, Cardone D, Croce P, Rotunno L, et al. Working memory decline in Alzheimer's disease is detected by complexity analysis of multimodal EEG–fNIRS. Entropy. 2020;22(12):1380.
27. Chiarelli AM, Perpetuini D, Croce P, Filippini C, Cardone D, Rotunno L, et al. Evidence of neurovascular un-coupling in mild Alzheimer's disease through multimodal EEG–fNIRS and multivariate analysis of resting-state data. Biomedicines. 2021;9(4):337.