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Multimodal Biomedical Signal Acquisition Setup to Assess Chronic Pain in Older Adults With Alzheimer's Disease

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***Abstract*—Chronic pain often goes unrecognized and untreated in individuals with Alzheimer's disease and related dementias (ADRD), mainly due to limited capacity to verbalize pain. Addressing this issue requires the development of reliable objective biomarkers for pain. In the present pilot study, we explored the feasibility and acceptability of using a wearable electroencephalograph (EEG) and a screen-based eye tracker system to identify neural signatures of chronic pain in this population. First, we developed a multimodality biomedical signal acquisition setup with four parts: hardware to record biomedical signals, software to monitor and synchronize multiple inputs, an experimental paradigm with resting state and a cognitive task to assess pain, and an online database to collect subject demographics and subjective measures in a secure environment. EEG signals were recorded using an FDA-cleared 32-channel EEG device with 3-axis accelerometer while gaze and pupil dilation were captured via a head-free, video-based eye tracker. A cognitive task was designed using 32 custom-generated images representing pain/no-pain conditions in addition to 16 images with painful and neuter expressions from the Delaware Pain Database. EEGs, accelerometer, and eye tracker data were synchronized with the behavioral paradigm by sending digital triggers from paradigm module on a MATLAB/Simulink model that was designed for the study. Finally, a database was created on RedCap with 16 separate instruments from cognitive and pain assessment tools to the feasibility and acceptability surveys.**

Keywords—Alzheimer, pain, multimodal, eye-tracker, EEG

I. Introduction

Alzheimer's disease and related dementias (ADRD) impact 6.7 million Americans [1]. Pain is highly prevalent in ADRD patients, and influences their behavior, mood, and physical function, contributing to cognitive decline [2]. Due to altered pain perception and communication challenges in dementia, it's often expressed as neuropsychiatric symptoms. Patients may receive antipsychotics instead of proper pain control, leading to uncontrolled pain and adverse effects [3]. Tools developed to assess pain in this population rely on subjective measures from caregivers and healthcare providers. Accurate assessment of pain is crucial for clinicians to effectively diagnose and treat pain in this vulnerable group.

Objective tools to measure pain are of the utmost importance. For developing neural pain biomarkers, electroencephalogram (EEG) offers several advantages. It is more accessible, noninvasive, safe, and compatible with other sensory and modulatory devices, and it can be used easily in both clinical and home settings. Recent reviews indicated that more groups are investigating the EEG patterns as a potential biomarker of chronic pain. For example, studies using machine-learning showed that EEG features can successfully detect pain intensity, pain phenotypes, pain states, and outcome measures (e.g., responder *vs* non-responder) in people with chronic pain [4-5]. Although EEG has been widely used for diagnostic and prognostic purposes in adults with Alzheimer's disease (AD) and has showed changes in neural dynamics [6], its functional use in pain assessment in people with dementia remains largely unexplored, with only one feasibility study available [7].

Eye tracking is a rapidly developing technology and is being used increasingly in clinical research. Its utility as a potential tool for pain assessment has been explored in several approaches such as facial expression analysis, pupillometry, attentional bias, and peripheral physiological changes. In particular, its ability to measure gaze and attention poses a novel way of measuring neurophysiological function relating to pain. One study indicated that patients experiencing chronic pain showed faster responses in fixating on pain-provoking pictures as compared to the control group [8]. Another study showed that individuals with chronic pain had increased average gaze durations when looking at pictures that showed injuries compared to pain-free subjects [9]. While these approaches are promising, more research is needed to establish reliable and validated eye-tracking parameters for pain assessment. Nevertheless, the potential of eye-tracking in pain assessment highlights its versatility as a tool for understanding and objectively measuring subjective experiences.

In the current study, we investigated whether employing a wearable EEG in conjunction with an eye tracker is both feasible and well received. We sought to determine whether the cognitive task that we developed using this setup could serve as an objective and accurate biomarker for assessing pain

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perception in older adults with mild-to-moderate ADRD with chronic pain.

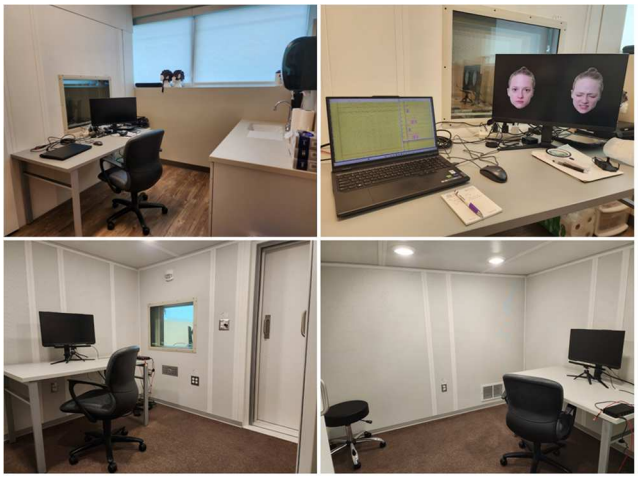

Figure 1. Clinical Research Unit. Electrophysiology suite consists of two rooms. Top panel shows the room-1 from two views, outside of the isolation chamber. Bottom panel demonstrates the room-2, an electromagnetic interference (EMI)-shielded chamber.

II. Materials and Methods

A. Clinical Research Unit

The electrophysiology suite at the Florida Atlantic University Clinical Research Unit (CRU) is designed for use by researchers exploring cortical brain potentials and cognition in a stable environment. It houses an 8x8 120a Series Double-Wall RF-shielded, sound attenuating booth with roof mounted ventilation, noise-lock doors, and double-glazed windows. The isolated testing room is built for neural measurements with high signal-to-noise ratio and high temporal precision. It consists of two rooms (Figure 1): data acquisition room (top panel) and experiment room (bottom panel). Both rooms are equipped with 24-inch, flicker free monitors that are connected to a data acquisition laptop via HDMI splitter. It duplicates the visual stimuli on the monitors at each room and allows researchers to follow each step without interrupting the subject. Because we included only subjects with a caregiver accompanying them, we placed a stool for the caregivers in the experiment room for support for the subjects.

B. Biomedical Signal Acquisition

Neural signals were collected using an FDA-cleared, 32-channel, wearable EEG headset (g.Nautilus PRO 32 flexible, gTec Inc, Graz, Austria) at 500 Hz sampling rate while the subject sat on an upright armchair with back support, at a distance of 70 cm from a computer monitor, relaxed position. EEG recordings were performed with noninvasive, wet electrodes (g.SCARABEO, gTec Inc, Graz, Austria), inducing no discomfort to the subject. Signals were high pass filtered at 0.1 Hz and referenced to earlobe with a clip electrode.

The EEG headset is integrated with a 3-axis accelerometer. In addition to neural signals, acceleration data were captured to monitor subject's movements. These will be used in the offline analysis to identify and correct motion artifacts in the EEG data and to correlate brain activity with specific movements or activities during the tasks.

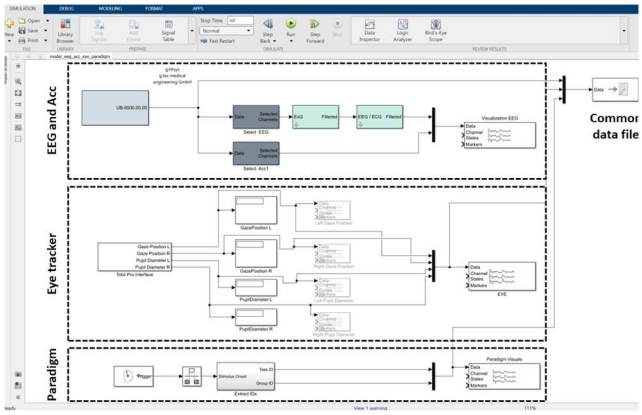

Figure 2. Simulink data acquisition and monitoring model. The model consists of 3 main components: EEG and accelerometer, eye tracker, and paradigm presenter.

Simultaneously with the EEGs, gaze and pupil dilation data were recorded using a high-resolution, video-based eye tracker (Tobii Pro Fusion, Tobii AB, Danderyd, Sweden) in a head-free setup where the subject could move freely without restrictions. The eye tracker system, mounted on a tripod over the desk, captured pictures of each eye at 120 Hz, computed gaze location (in screen pixel coordinates) and pupil diameter, and parsed the data via the Simulink block into visual events.

To synchronize biosignals coming from multiple modalities at different sampling rates, visualize the data stream in real time, and store the data to a MATLAB file, a Simulink (MathWorks, Inc. USA) model was developed using g.HIsys library (gTec Inc, Graz, Austria) and standard Simulink blocks (Figure 2). Acquisition of EEGs and acceleration data was performed via g.tec amplifier block which also allowed impedance check and selection of various settings, such as sampling rate, filters, denoising, and channel configuration. To transfer the gaze and pupil dilation data from eye tracker into the Simulink model, the Tobii Pro Simulink Interface was utilized and customized for the project. Finally, we designed an XML schema based on our visual paradigm and sent the stimulus-specific digital triggers to the data file using the Paradigm block.

C. Experimental Design

The visual paradigm was designed to assess cognitive functions and attention to pain. It included 32 custom-generated images representing pain/no-pain conditions in addition to 16 images with painful and neuter expressions from the Delaware Pain Database [10], a validated, publicly available data set. These images depict painful situations without additional emotional attributes, along with their neutral counterparts. Particularly, 16 images were created to depict pain/no-pain situations from daily life (e.g., cutting finger) including mechanical, thermal, and pressure pain while another 16-image set was created to depict chronic pain conditions (e.g., chronic back pain) and matched no-pain conditions (Figure 3).

The experiment began with resting state EEG with eyes-open state. Once the resting state was completed, visual

paradigm was initiated. The three groups of images (actions, faces, and chronic pain conditions) were shown in a randomized order by swapping positions of the pain/no-pain images. Each set was repeated 4 times. The neural responses to visual stimuli and the duration of time spent on each stimulus was measured in a completely passive way. The subject was not given any instructions, which is important, as individuals with dementia may be challenged to follow complex instructions; the subject was not asked to reflect on, respond to, or remember any items.

D. Subjective Measures

Collection of all subject-reported data and clinical characteristics was performed electronically using Research Electronic Data Capture (REDCap, Nashville, Tennessee), a secure web-based application. We designed a user-friendly project with five key features, composed of 16 instruments, to ensure that researchers were able to easily complete data collection: inclusion/exclusion criteria, participant enrollment and consent, demographic information, cognitive function (e.g., Mini-Montreal Cognitive Assessment, Number Symbol Coding Task) and pain (e.g., Brief Pain Inventory, Pain Catastrophizing Scale) assessment forms, and feasibility and acceptability surveys.

To examine the practicality and viability of the setup, we calculated recruitment, enrollment, and completion rates. To test the setup's acceptability by the subjects, a questionnaire was administered at the end of the intervention regarding the EEG and eye tracker experience on a Likert scale of 0 (*strongly disagree*) to 5 (*strongly agree*). We asked participants about the comfort of wearing the EEG cap, the use of the eye tracker, their satisfaction with the study, and their willingness to recommend the study to other people.

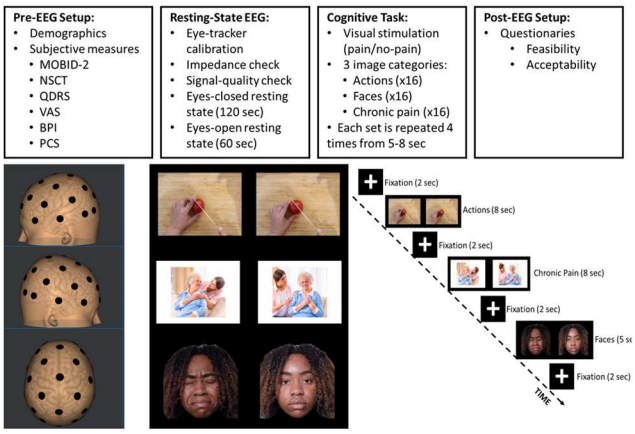

Figure 3. Experimental Paradigm. Once the eye tracker was calibrated and the EEG channels underwent an impedance check, resting state EEG were captured and the cognitive task began. Each image (target) was followed by a 2-second fixation crosses (non-target) representing null events. The entire paradigm took approximately 32 minutes.

III. Results

The study involved 4 participants (3 females), ranging in age from 76 to 93 years. The demographic distribution included one

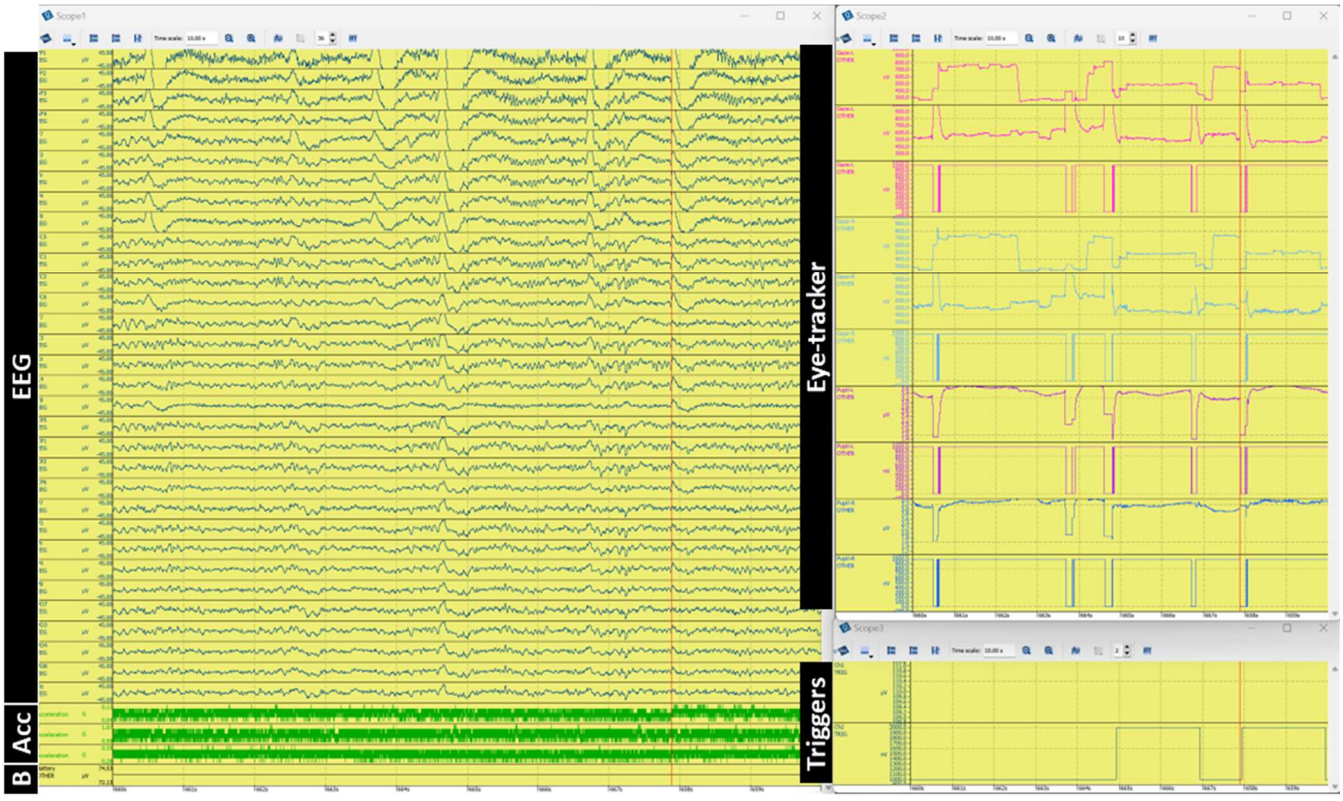

Figure 4. A screenshot of the running instance of Simulink model. Each window representing a different input. From top-left to bottom-right: EEGs, accelerometer, battery level of the EEG headset, eye tracker data including left/right gaze and pupil diameter, and digital triggers sent at each target/non-target event. All windows were set to 10 seconds and red cursors demonstrates the synchronized multimodal signals.

Hispanic/Latino participant and three non-Hispanic White participants. Diagnoses varied, with one participant having AD, two with dementia of unspecified type, and one with dementia related to Parkinson's disease. Cognitive evaluations revealed that participants exhibited various stages of dementia, with one in moderate stage and three in mild stage. The participants' pain severity, assessed with the Visual Analog Scale, indicated that three participants reported mild to moderate pain, while one reported severe pain. Notably, three participants expressed that pain significantly impacted their ability to walk, relationships with people, and enjoyment of life.

Throughout the cognitive tasks, three participants completed the tasks without major distractions; one required a break during the 30-minute session and struggled to maintain focus. Of the four participants, only one was able to calibrate the eye tracker properly, necessitating further assistance. Regardless, all participants tolerated the EEG cap well, with all channels robustly captured and cognitive task successfully completed in most (Figure 4). All participants exhibited good tolerance to the study design, showing no signs of behavioral changes. In terms of acceptability, all participants reported comfort with the EEG cap and eye tracker, expressed satisfaction with the study, and indicated a willingness to recommend it to others.

IV. Discussion

In the realm of pain assessment, measuring pain objectively is very important for the ADRD population. Previous research has hinted at the potential for increased reliability by integrating various assessment modalities. Our study was intended to contribute to this endeavor by exploring the correlation between multimodality assessment and pain in older adults with ADRD. While prior studies have linked EEG patterns with dementia, our investigation represents one of the initial attempts to establish such correlations with pain in this population.

In the study design, particular emphasis was placed on enhancing the comfort of persons with ADRD. The deliberate decision to minimize the use of wires and other potential distractions was intended to create an environment conducive to participation. The positive aspect of participant tolerance to the study design, as evidenced by their comfort with the EEG cap and eye tracker, suggests promise of feasibility in our study design.

However, our study faces limitations, particularly in cases of moderate dementia, where impaired attention posed challenges in completing cognitive tasks and calibrating the eye tracker. While our findings suggest the study's general acceptance by participants with various degrees of dementia, it may be less feasible for those with more moderate to severe cognitive impairment. Future studies could address this limitation by considering a shortened duration for cognitive tasks and use of a wearable eye tracker for improved feasibility. Also, the calibration phase of the eye tracker, despite being generally comfortable for all participants, emerged as a challenging aspect that warrants further refinement even for those with milder cognitive impairment. Despite these limitations, our study was effective and holds promise for pain assessment in this population. Minor adjustments, such as those suggested, may enhance the applicability of our methodology for persons with more moderate to severe cognitive impairment, thereby expanding its potential impact on pain assessment in this vulnerable population.

Studies have shown that gaze patterns measured by eye tracking can be used to assess the level of pain a person is experiencing and how chronic pain influences person's attentional biases and emotional processing [11]. The integration of EEG into pain measures can give insights into neural correlates of affective processing (e.g., changes in the amplitude of event-related potentials) and temporal dynamics of neural responses to pain-related stimuli [12]. This not only leads to better understanding of the neural mechanisms underlying pain perception, attentional processes, and emotional responses in chronic pain but holds the potential to inform development of targeted interventions, thereby improving patient care and improving their quality of life. Based on our data on the feasibility and acceptability of EEG in this population, future research is needed to test and confirm validity of EEG as an objective pain measure for older adults with mild ADRD.

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References

[1] 2023 Alzheimer's disease facts and figures. Alzheimer's and Dementia. 2023; 19(4). Doi: 10.1002/alz.13016

[2] van Dalen-Kok et al. "Association between pain, neuropsychiatric symptoms, and physical function in dementia: a systematic review and meta-analysis." BMC geriatrics 15.1 (2015): 1-18.

[3] Gibson et al. "An examination of pain perception and cerebral event-related potentials following carbon dioxide laser stimulation in patients with Alzheimer's disease and age-matched control volunteers." Pain Research and Management 6 (2001): 126-132.

[4] Zolezzi et al. "EEG frequency band analysis in chronic neuropathic pain: A linear and nonlinear approach to classify pain severity." Computer Methods and Programs in Biomedicine 230 (2023): 107349.

[5] Witjes et al. "Heterogeneous cortical effects of spinal cord stimulation." Neuromodulation. 26.5 (2023): 950-960.

[6] Jiao et al. "Neural biomarker diagnosis and prediction to mild cognitive impairment and Alzheimer's disease using EEG technology." Alzheimer's research & therapy 15.1 (2023): 1-14.

[7] Pu et al. "Portable EEG monitoring for older adults with dementia and chronic pain-A feasibility study." Geriatric Nursing 42.1 (2021): 124-128.

[8] Mahmoodi-Aghdam et al. "Chronic pain and selective attention to pain arousing daily activity pictures: Evidence from an eye tracking study." Basic and clinical neuroscience 8.6 (2017): 467.

[9] Fashler et al. "Keeping an eye on pain: investigating visual attention biases in individuals with chronic pain using eye-tracking methodology." Journal of pain research (2016): 551-561.

[10] Mende-Siedlecki et al. "The Delaware Pain Database: a set of painful expressions and corresponding norming data." Pain reports 5.6 (2020).

[11] Chan et al. "Pain-related attentional processes: A systematic review of eye-tracking research." Clinical Psychology Review 80 (2020): 101884.

[12] Ma et al. "Whether ambulatory electroencephalogram and visual tracking system could be the new strategy for pain assessment?" Frontiers in Neuroscience 17 (2023):1122614.