International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Innovative Approach: Facial Recognition and Event Related Potential for Early Detection of Alzheimer's Disease

Abhijeet Satani[1], David Kaiser[2], Param Barodia[3]

[1]Abhijeet Satani, Chief Scientific Officer- MemoryCareAI,
Email: *abhijeet.satani[at]memorycareai.com*

[2] David Kaiser, Chief Executive Officer- MemoryCareAI,
Email: *daivid.kasier[at]memorycareai.com*

[3]Param Barodia, Research Assistant- MemoryCareAI,
Email: *info[at]memorycareai.com*

Abstract: ***Alzheimer's disease frequently causes impairments in facial recognition, leading to significant consequences for patients' social well-being. In this study, we employed electroencephalography (EEG) and experimental methods to investigate how facial processing differs between AD patients and a healthy control group. Distinct face processing characteristics were associated with various Event-Related Potential (ERP) components, including N170, N250, and N400. The AD patient, PATIENT(A), exhibited a reduced N170 for faces compared to houses and scrambled objects, suggesting deficits in encoding face-specific configurations. Moreover, facial recognition impairments in PATIENT(A) might be attributed to specific difficulties in processing face configuration, as evidenced by the absence of the typical inversion effect at the neuronal level. Additionally, fear facial expressions elicited a disproportionately large N170 response, indicating that emotional stimuli may be processed implicitly. Familiarity manipulation did not modulate the N250 in PATIENT(A) but did reveal a clear modulation of the N400 component, suggesting that long-term memory traces may be implicitly preserved. This study demonstrates the potential for advancing scientific understanding of face processing deficits in AD through the combination of in-depth individual case studies and electrophysiology. The findings highlight the importance of using electrophysiological markers in clinical practice to improve patient management, classification, and the development of targeted rehabilitation protocols for face processing deficits in AD patients.***

Keywords: Alzheimer's disease, facial recognition, electroencephalography, event-related potentials, MemoryCareAI

1. Introduction

Alzheimer's disease (AD) is a neurodegenerative condition that causes the formation of amyloid-β plaques, neurofibrillary tangles, and neuronal atrophy [1-2]. AD patients have a neuropsychological profile that includes a variety of abnormalities, including as disorientation, language problems, and trouble recalling recent events. Cognitive performance gradually diminishes as the disease advances. While Alzheimer's disease manifests differently in each patient, caregivers frequently describe memory problems as one of the disease's early symptoms. Caregivers frequently report other dysfunctions, including apraxia, attentional dysfunctions, and/or behavioural and psychiatric problems [3]. Alzheimer's disease development is characterized by the expansion of impairment to diverse cognitive processes and the deterioration of cognitive domains. At the mild-to-moderate stage of Alzheimer's disease, the family frequently highlight an emotionally charged issue connected to visuospatial and perceptual difficulties, specifically the inability to recognize faces [4, 5]. Indeed, Alzheimer's sufferers are unable to recognize familiar faces, including those of their own families, and finally lose the ability to recognize themselves in the mirror. As the disease advances [6, 7], difficulty recognizing familiar faces is commonly attributed to memory issues.

This conclusion is obvious considering that recognition entails the retention of memory traces. However, a recent study [8] suggests that the cause of facial recognition deficiencies in AD could be different. The study included 25 mild-stage Alzheimer's patients who were given a perceptual test in which they had to match simultaneously presented unfamiliar faces (with vehicles as control stimuli). The stimulus could be presented upright or inverted. The use of inverted faces is justified by the well-known face inversion effect [9], which describes a decreased capacity to recognize unknown faces when shown upside-down.

This effect is assumed to represent the difference in perceptual processing between upright and inverted faces [10]. The greater the effect, the better the ability to process configurational information for specific faces. The researchers discovered that when it came to faces (but not cars), AD patients' accuracy and reaction times were lowered. Furthermore, AD patients performed worse with both upright and inverted faces, indicating that AD may result in a unique deficiency in the construction of a coherent perceptual picture of individual faces.

To further test this hypothesis, we employed electrophysiology, specifically event-related potentials (ERPs), which are a dependable source of brain markers capable of characterizing the neuropsychological architecture of cognitive disorders [11]. Face processing has been linked to the modulation of three ERP components: the N170 [12, 13], the N250 [14, 15], and the N400 [16, 17, 18]. Some studies have also suggested that the P100 may be

sensitive to face processing, reflecting either a difference in low-level visual features between faces and other complex visual stimuli, or a holistic face perception, however, the evidence for this is somewhat disputed [19, 20].

The N170 component was the first and most extensively studied negative face-sensitive ERP component. It is a right-lateralized component that is typically larger for faces than for other objects and can be detected at occipitotemporal electrodes 140-200 ms after stimulus onset. Furthermore, the N170 component is similarly regulated when the same face is presented again (the identity-dependent adaptation effect) [21]. Finally, it has been demonstrated that the N170 component is responsive to facial expression, with fear having the biggest influence when compared to other emotions [22]. These findings suggest that the N170 component serves as an electrical marker for the processing of configurational information and the perceptual structural encoding of individual faces.

Unlike N170, the N250 and N400 components are impacted by personal acquaintance [16, 23, 24, 18]. As a result, they are both regarded indices of face identification processing, albeit from distinct perspectives. The N250 component, in particular, is regarded as the first electrophysiological correlate of the face recognition process [25, 26, 27]. The N250 component has also been recorded in frontal regions at the same latency, however it is often seen at occipitotemporal electrodes with a bigger amplitude for famous faces. However, it exhibits the opposite pattern, namely, increased negativity for new faces relative to popular faces [28, 17]. Previous research has related this component to the ability to retrieve facial perceptual representations from visual memory without the use of semantic information [27, 29, 30]. Furthermore, repeated face presentation modulates the N250 in an experimental environment [31, 32, 30].

On the other hand, the N400 is a negative component that peaks around 400 ms after stimulus initiation and has a centroparietal distribution [16, 33, 17]. Based on existing findings, the N400 component is assumed to be associated with the post-perceptual representation of familiar faces, indicating a pure semantic processing stage [16, 34, 17]. This idea appears to be consistent with a stronger negative association with famous faces than with unfamiliar faces. In two separate electroencephalogram (EEG) experiments, we examined the existence and modulation of the three aforementioned ERP components considered to be important for face processing. We studied individuals to determine whether Alzheimer's patients who have difficulty recognizing familiar faces have mnestic or gnostic face processing abnormalities. Crucially, this technique could be the initial step in evaluating if electrophysiological indicators are appropriate for differential diagnosis and developing unique rehabilitation regimens for Alzheimer's patients with visuoperceptual abnormalities [8]

2. General Methods

2.1 Participants

PATIENT(A), a 69-year-old right-handed woman with nine years of education, was a participant in the study. At the time of admission, PATIENT(A) is a homemaker. She is alert, cooperative, spatially and temporally oriented, and aware of her cognitive condition; her main complaint appears to be related to difficulty recognizing familiar faces, such as those of distant relatives and, at times, neighbors. PET data, on the other hand, revealed hypometabolism in the right hemisphere's occipitotemporal and parietotemporal cortices, as well as the inferior temporal cortex bilaterally. Furthermore, the cerebrospinal fluid (CSF) examination, conducted during her evaluation at JK Hospital Sanand for AD, revealed a profile of biomarkers (tau and amyloid-β) consistent with AD. [2]

In experiment 1, participants had to indicate whether the stimulus was meaningful or not. In experiment 2, participants had to discriminate between an upright and an inverted stimulus. Examples of stimuli used in experiments 1 (faces, houses, and scrambled images), and 2 (faces with famous or unfamiliar faces, upright and inverted).

A control group of eight healthy right-handed female participants (age range: 62-74) with no history of neurological or psychiatric disorders was tested based on previous studies [35]. Both the healthy participants and the patient signed an informed consent form before taking part in the study, from which they could withdraw at any time.

2.2 Neuropsychological Testing

PATIENT(A) underwent an extensive neuropsychological assessment to evaluate cognitive functions. All tests were administered and scored according to standard procedures and guidelines. The neuropsychological assessment lasted about 40 minutes. The Montreal Cognitive Assessment (MoCA) [36] was used to assess general cognitive impairment, while ad hoc tests were employed to assess specific cognitive functions. The Trial Making Test [37] was used to assess attentional functions. The Clock Drawing Test [38], standardized specifically for Alzheimer's disease patients, was used to assess visuospatial and praxis abilities. Three tests were used to assess language functions: two verbal fluency tests to assess phonological [39] and semantic [40] access, and a short version of the Token Test [41] to assess language comprehension. The Rey Auditory Verbal Learning Test was used to assess memory impairment, both short- and long-term [42, 39]. The abstraction test was used to assess logical reasoning [41]. Two tests were used to assess ideational and ideomotor apraxia [41] and constructional apraxia [39]. Finally, when depression symptoms were assessed using the Geriatric Depression Scale (GDS) [43], a slight mood deflection was detected.

2.3 Neuropsychological assessment.

Based on the tests administered during the experiment and the data collected from those tests, it seemed that PATIENT(A) experienced difficulties with certain cognitive abilities. Specifically, PATIENT(A) showed lexical abilities that were within the expected range for semantic cues but were toward the lower end of the spectrum for phonemic cues. In contrast, however, PATIENT(A) demonstrated adequate autobiographical memory, a normal understanding

of verbal information, and fluency in spontaneous speech, which was both coherent and informative. PATIENT(A) also exhibited an ability to learn verbal stimuli as expected and showed a moderate capacity to retrieve previously learned information during delayed recall tasks.

All three words were retrieved at the MoCA incidental memory test. The Trial Making Test showed deficits in visual scanning, number recognition, sequencing, and the ability to reproduce numeric sequences with motor slowing. However, the ability to carry out mental backward tasks remained relatively preserved. The clock drawing's planning was adequate. The position of the clock's hands on the requested time was incorrect, indicating a slight mental representational error; the numeric sequence was correct, but there were slight errors in the spatial arrangement. Logical and deductive abilities, on the other hand, were within the norm. Finally, there was a significant impairment in the ability to reproduce geometric figures (constructional apraxia) as well as a deficit in ideational and ideomotor praxis.

According to the neuropsychological assessment, PATIENT(A) had difficulty recognizing familiar faces. To make a preliminary assessment of face recognition ability, PATIENT(A) was presented with photographs (faces only) of famous Indian personalities (10 males and 10 females; two images of the same character, one at a young age and one at an older age, were administered). Faces were presented one at a time, and PATIENT(A) was asked to name the person in the photograph and report any additional information she might have about them. Despite identifying the images as faces and reporting details about the faces (e.g., Mahatma Gandhi's glasses), she was unable to name any of the famous faces. She was also unable to decode the emotional expressions of the faces. In a second test, the same images were presented three at a time: two of the same person and one of a different person. PATIENT(A) had to identify the photograph that did not belong to the same identity. In this case, her inability to match the two photographs that belonged to the same identity prevented her from completing the task.

Furthermore, to assess the specificity of the agnosic deficit, an object recognition test was planned for the second visit. A standard set of 182 photographs of objects, including both living and non-living items, was used. The test lasted about 80 minutes. PATIENT(A) made a total of 35 identification errors (19.2%), with non-living objects (11.3%) being misidentified more frequently than living objects (7.9%). Even when she made identification errors, she was still able to identify the semantic category of the objects in each case because, in most cases, the reported name corresponded to an object in the same category and with similar physical features. These findings suggest minor object identification difficulties that are not comparable to the widespread face recognition deficit.

2.4 Experimental Design, Apparatus, and Stimuli

The participants of each trial were seated in a comfortable chair in front of a monitor to reduce head movements and keep the participant's distance from the monitor constant. Open-sesame (Software) was used to present visual stimuli on an LED panel. An infrared camera was used for the online monitoring of eye movements to ensure that fixation was maintained during stimulus presentation. Different stimuli were investigated in two different experiments. The two trials for PATIENT(A) were carried out on different days, while the trials for the healthy controls were carried out on the same day.

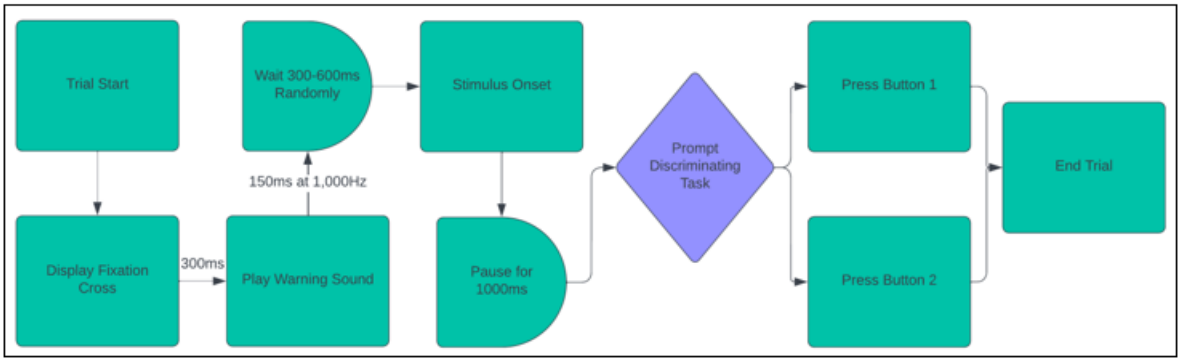

Figure 1: Experimental Procedure

Figure 1 depicts the experimental procedure. At the beginning of each trial, a central fixation cross appeared for 300 milliseconds and remained visible throughout the experiment. A 150 millisecond warning sound at 1,000 Hz preceded the presentation of stimuli. The time interval between the warning sound and the stimulus onset varied randomly between 300 and 600 milliseconds to avoid anticipation. After a 1000 millisecond interval, participants were asked to perform a discriminating task by pressing two different keyboard buttons. The stimuli presented in each trial were displayed for 300 milliseconds. Various stimuli were centrally presented in the visual field across the 2 experiments. The next trial started after a 1,000 millisecond inter-trial interval.

2.5 EEG Recording, Pre-processing, and Event-Related Brain Potential Analysis

The electroencephalogram (EEG) signal was continuously recorded using the RMS EEG system with wet electrodes mounted according to the 10-20 International System. Four additional electrodes were used to record blinks and eye movements. Electrodes placed above and below the right eye, and at the left and right canthi, respectively, were used to detect both vertical and horizontal eye movements. Two more electrodes served as an online reference (right mastoid,

RM) and a ground reference (AFz).

The continuous EEG signal was processed offline using RMS Maximus 32 software (version 2.0, Neuroinformatics Research Group, RMS Technologies). First, the data were high-pass filtered and down-sampled. Then, before using the Clean-Line plugin within RMS Maximus 32 [44], the scalp channels were re-referenced offline to the average of all electrodes to use adaptive multitaper regression to reduce power line noise (50 Hz and its harmonics). Independent Component Analysis (ICA) was performed on the segmented data (ranging from -1000 to 1000 milliseconds relative to the stimulus onset) using the enhanced FastICA algorithm [45].

After visual inspection, independent components identified as artifacts (e.g., eye movements, muscle activity, blinks) were removed. A low-pass filter with a cut-off frequency of 40 Hz was then applied. Baseline correction was performed using the pre-stimulus interval, with the epoch window adjusted from 300 milliseconds before stimulus onset to 800 milliseconds after stimulus presentation. Manual artifact rejection was performed to discard segments contaminated by residual isolated artifacts. Finally, the retained data were averaged across all electrodes and participants across experimental conditions for analysis.

3. Experiment 1 - Face Processing

The goal of this experiment is to investigate the N170 component and determine whether facial processing markers can be detected in the patient. As reported in the literature, we expect a larger N170 for faces in healthy participants compared to houses and scrambled images. If memory deficits are the cause of the patient's PATIENT(A) face recognition impairment, we should not expect any differences between the patient's and healthy participants' results. On the other hand, if her face recognition deficit is caused by gnosic problems, we should not expect to find a larger N170 for faces compared to houses and scrambled images, indicating an inability to form a coherent percept and to process perceptual information up to the level of the meaning of the percept itself.

3.1 Experiment 1 - Stimuli and Design

Three categories of stimuli were presented: faces (both male and female), houses, and scrambled images. Each stimulus identity was repeated twice. The stimuli were grayscale images with a background luminance of [8.56 cd/m2].

The experiment consisted of 14 blocks of 24 trials each (three faces, three houses, and eight scrambled images), for a total of 336 trials. For healthy participants, the total number of trials was reduced to 280, divided into 12 blocks of 24 trials each. The trials were performed in a fully randomized order within each participant.

Participants had to indicate whether the stimulus was meaningful (a face or a house) or not (a scrambled image) by pressing two different keys on the keyboard, the "m" and "z" keys, respectively.

Separate EEG averaging was performed for the three conditions (scrambled images, faces, and houses).

3.2 Experiment 1 - Results and Discussion

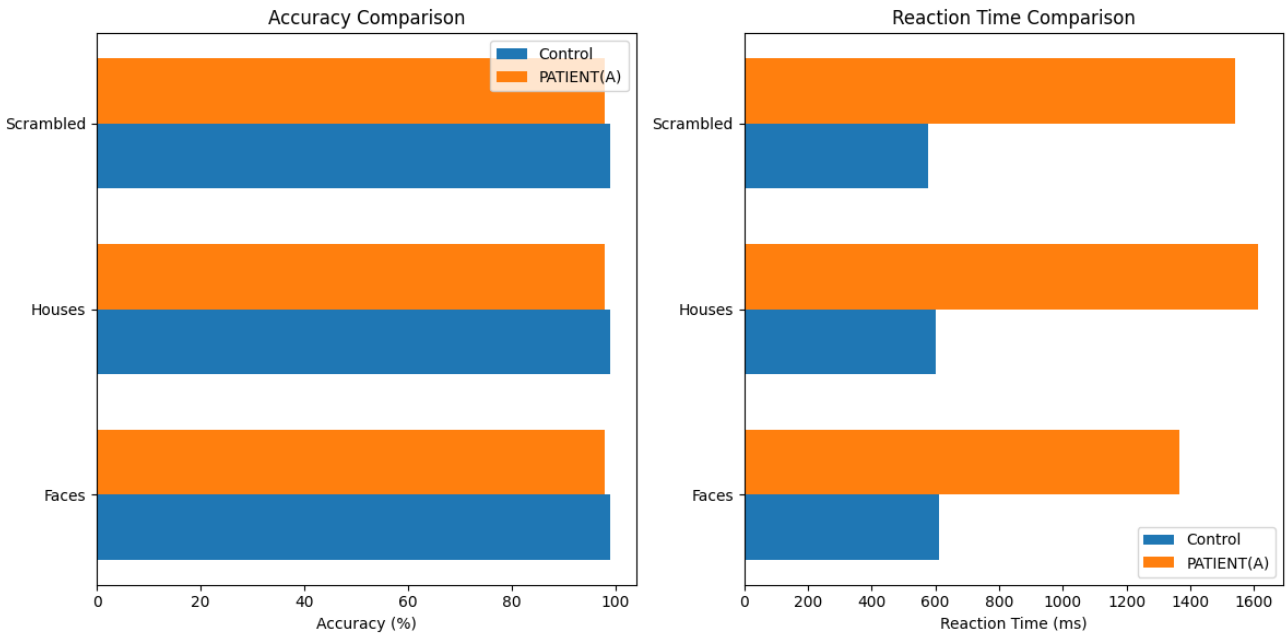

Figure 2 shows the accuracy and RTs for each stimulus category for PATIENT(A) and the controls. Importantly, both the PATIENT(A) and the controls were able to discriminate the category of the stimuli, distinguishing between meaningless (scrambled objects) and meaningful (faces and houses). This is shown by the high level of accuracy across conditions (overall >99% for the controls and 98% for the PATIENT(A)). The ($p > 0.05$) and controls (2, 14) = 0.542; $p = 0.593$] did not show significant differences in accuracy between conditions. While PATIENT(A)'s accuracy for scrambled stimuli was lower than that of controls ($t(7) = -4.148$; $p < 0.01$), face and house accuracy levels did not differ significantly from those of controls [faces $t(7) = -1.179$; $p = 0.277$; houses $t(7) =$

−0.404; p = 0.698]. For all conditions considered, the patient's RTs were slower than those of the control group (faces t(7) = 5.025; p < 0.01; houses t(7) = 6.250; p < 0.001; scrambled images t(7) = 7.052; p < 0.001). Moreover, the patient responded faster (p < 0.05) to faces (1,365 ms) compared to houses (1,611 ms) and scrambled images (1,541 ms), while healthy controls' RTs did not differ [F(2, 14) = 1.217; p = 0.326] (611 ms for faces, 603 ms for houses, and 579 ms for scrambled images). These results are not surprising, even in PATIENT(A), who during the neuropsychological assessment showed the ability to categorize a face as a face and a house as a house at a behavioural level. Her deficit, in fact, was not related to the ability to recognize a face as a configuration of parts, but rather to the ability to associate a specific identity with a familiar face.

Therefore, it becomes crucial to use Event-Related Potential (ERP) analysis to determine if the PATIENT(A)'s recognition deficiency is connected to the memory or perceptual aspects of information processing that ultimately lead to the recognition of a face. As anticipated, the N170 component's amplitude was larger for faces in the controls (Figure 2F) than for the other stimuli (electrode P8 from 120 to 236 ms, p < 0.05). On the other hand, while there was a drastically reduced N170 component for all the stimuli in PATIENT(A), there was an even smaller amplitude for faces (electrode T8 from 208 to 228 ms, p < 0.05) as opposed to houses and scrambled images (Figure 2E). These findings imply that issues with the structural encoding of certain faces--rather than faces in general--are connected to the recognition problem of PATIENT(A). In fact, systematic repetition of individual unfamiliar faces modulates the N170 component, even if long-term familiarity with the face has no effect on it [46, 21]. This suggests that the N170 component is an electrophysiological marker encoding the particular configuration of face elements that belong to individual people [47].

4. Experiment 2 - Effects of Face Inversion and Familiarity

This experiment aims to replicate the finding of Experiment 1 that there was no "inversion effect," that is, no enhanced N170 component for inverted faces in PATIENT(A). More importantly, though, it explores the possibility of identifying neural markers for an implicit "familiarity effect" (since she was unable to report the identities of the faces explicitly) by looking at the components that are typically modulated by familiarity, such as N250 and N400 [16, 28, 27, 18, 25, 26]. As previously mentioned, according to the literature, healthy participants should exhibit an augmentation of the N170 component for inverted faces, or the "inversion effect." Based on the outcomes of Experiment 1, PATIENT(A) should not exhibit this effect. Furthermore, we anticipate seeing an influence on the N250 or N400 components, as is generally observed in healthy individuals, if PATIENT(A) is able to understand the identity of the face, at least implicitly.

4.1 Experiment 2 - Stimuli and Design

In experiment 2, only faces were presented. Stimuli were selected from a database of famous and unfamiliar male and female faces (Figure 1E) in unpublished studies on fifty participants. The aim of the database was to assess familiarity. Moreover, [PATIENT(A)'s relative, her daughter, was presented with the faces of famous people to ensure the was familiar with them before the illness. The experiment included two photographs, each from a different angle, for each of the 36 identities (18 males and 18 females), half of whom were famous, and the other half were not. Each image was presented four times. The stimuli were black and white images.

The experiment consisted of 576 trials, divided into 24 blocks of 24 trials each, comprising six famous upright faces, six famous inverted faces, six unfamiliar upright faces, and six unfamiliar inverted faces. The trials were performed in a fully randomized order within each participant. Participants had to press two different keyboard keys, labeled "m" and "z," to indicate whether the stimulus was upright or inverted, respectively. Separate EEG averaging was performed for each of the four stimulus categories.

4.2 Experiment 2 - Results and Discussion

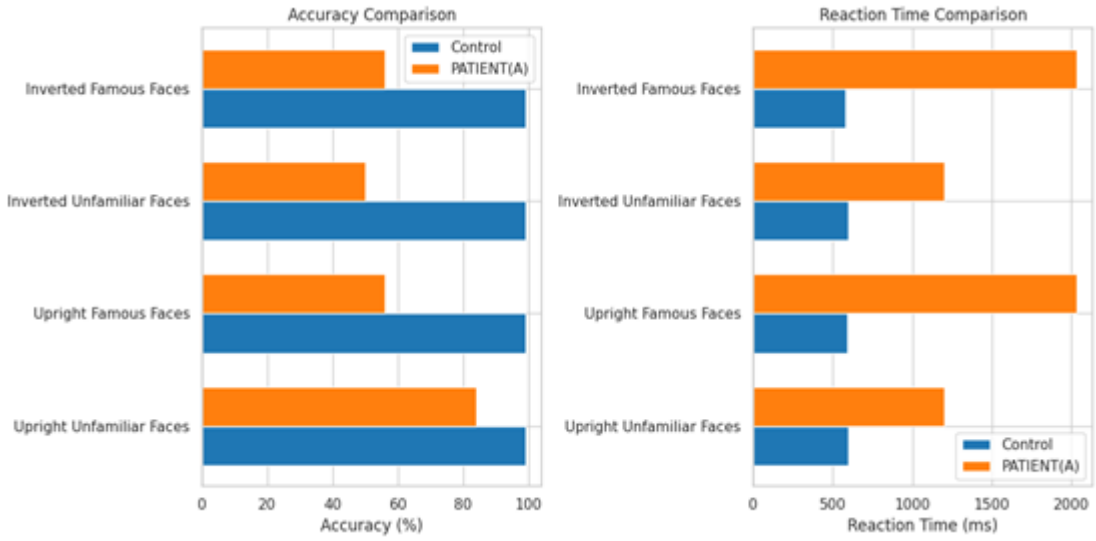

Figure 3 shows accuracy and RTs for each of the four stimulation conditions for PATIENT(A) and the control group. For each condition, the accuracy of the healthy controls was at ceiling: overall >99%; familiarity [$F(1, 7) = 0.090$; $p = 0.773$], orientation × familiarity [$F(1, 7) = 5.812$; $p < 0.05$]; orientation [$F(1, 7) = 0.576$; $p = 0.473$]. In contrast, PATIENT(A) showed better accuracy for upright faces (84%), similar to experiment 2, but reduced accuracy for inverted faces (56%), although all conditions were still above chance level (all ps < 0.05) except for the inverted unfamiliar faces (50%, $p = 0.934$).

PATIENT(A) showed significantly different accuracy levels compared to the control group [upright unfamiliar faces $t(7) = -10.999$; $p < 0.001$; upright famous faces $t(7) = -19.152$; $p < 0.001$; inverted unfamiliar faces $t(7) = -96.335$; $p < 0.001$; inverted famous faces $t(7) = -33.427$; $p < 0.001$]. Regarding RTs, PATIENT(A) was slower than the control group for all conditions considered [upright unfamiliar faces $t(7) = 3.915$; $p < 0.01$; upright famous faces $t(7) = 3.933$; $p < 0.01$; inverted unfamiliar faces $t(7) = 9.920$; $p < 0.001$; inverted famous faces $t(7) = 6.078$; $p < 0.001$]. The patient performed faster when the stimuli were presented upright (upright faces 1,203 ms, inverted faces 2,031 ms, $p < 0.05$), regardless of familiarity, although no significant main effect was found within the control group {upright famous faces 598 ms, upright unfamiliar faces 597 ms, inverted famous faces 590 ms, and inverted unfamiliar faces 578 ms; orientation [$F(1, 7) = 0.360$; $p = 0.567$], familiarity [$F(1, 7) = 0.190$; $p = 0.676$], orientation × familiarity [$F(1, 7) = 0.256$; $p = 0.628$]}. Similar to the results of Experiment 1, PATIENT(A) seems to have some difficulties in recognizing an upside-down face.

Similar to Experiment 1, ERP results show that the orientation of faces (electrode P8, time window from 188 to 200, $p < 0.05$) modulated the N170 component in healthy participants (Figure 4F), showing a larger amplitude for faces presented upside-down. Interestingly, healthy participants also showed a significant effect of familiarity (Figure 4H), with upright unfamiliar faces eliciting a larger frontal N250 component (fN250) than famous faces (electrode F2, time window from 292 to 328, $p < 0.05$), in line with previous studies [28, 17]. Although not reaching significance, the reversed effect (i.e., enhanced amplitude for familiar stimuli) was observed at posterior temporal regions [16, 27]. Furthermore, an additional analysis was conducted to validate the functional significance of our frontal N250. Additionally, an effect involving the N400 component emerged, indicating a higher amplitude for upright well-known faces compared to upright unknown faces in the 504-540 time window (electrode P2, $p < 0.05$).
In contrast, no inversion effect was detected in PATIENT(A): Experiment 1's findings were reproduced, indicating a generally lower N170 relative to controls, with no noticeable difference between upright and inverted faces . Interestingly, when analysing the N250 component, there was no implicit effect of familiarity, and there were no discernible differences between well-known and unknown faces across electrodes within the relevant timeframe. However, the familiarity with vertical stimuli (electrode P6, time frame from 504 to 540, $p < 0.05$) significantly altered the N400 component (see Figure 4I).

Taken together, these findings support the notion that PATIENT(A)'s facial recognition difficulties stem from gnostic rather than mnestic origins. Despite challenges in memorizing the structural characteristics of individual faces (absence of inversion effect on the N170 component), PATIENT(A) exhibited consistent modulation of the N400, suggesting implicit processing of facial identities. The interplay between these components offers an explanation for the observed results, highlighting the possibility of implicit face recognition processing even in the absence of reliable N170 responses. These findings are significant as they bolster the hypothesis that PATIENT(A)'s face recognition issues may be rooted in gnostic mechanisms rather than mnemonic processes. Previous research [48, 49, 50] suggests that prosopagnosia patients may have indirect access to memory traces, enabling covert face recognition. Although ongoing debates surround the neural underpinnings, various tasks and psychophysiological measures have been employed to probe distinct pathways underlying overt and covert face recognition mechanisms, including ERPs. Future studies could further investigate these mechanisms to elucidate the neural dynamics underlying face recognition deficits.

5. General Conclusions

In this study, we examined the facial processing abilities of an Alzheimer's disease (AD) patient and a control group utilizing EEG monitoring and experimental approaches designed to distinguish between perceptual and memory components of face processing and recognition. Modulation of several ERP components, such as N170 and N400, was discovered to be related with specific face processing properties.

PATIENT(A), an Alzheimer's patient, displayed the ability to identify meaningful stimuli (faces and houses) from meaningless ones on a behavioural level. However, ERP data revealed a much lower N170 component for faces compared to homes and scrambled items, indicating a problem encoding the unique configuration and structural components of individual faces.

In Experiments 1 and 2, PATIENT(A) demonstrated a partially retained capacity to detect face orientation by responding faster and more accurately to upright face stimuli. In contrast to the control participants, PATIENT(A) did not display the normal ERP inversion effect. This data lends support to the concept that PATIENT(A)'s face recognition issues are caused by selective face configuration processing deficiencies.

Experiment 2, which tested familiarity, produced no modulation in PATIENT(A), probably due to her inability to access stored facial representations in visual memory. However, both healthy controls and PATIENT(A) showed a clear modulation of the N400 component, with upright familiar faces having a higher amplitude than unfamiliar ones. This data suggests that long-term memory traces may still exist in PATIENT(A), albeit implicitly, given her inability to recognize faces explicitly.

The proposed approach sheds light on the nature of face processing abnormalities in Alzheimer's disease patients. This study has ramifications for both basic and clinical science, highlighting the possibility for expanding scientific understanding by in-depth examination of individual cases in conjunction with electrophysiology. Future study with larger patient populations is needed to assess if face processing abnormalities may be assigned to the perceptual stage in the general AD population, as well as to investigate potential distinctions between AD patients with posterior onset and those with various deficiency profiles.

References

[1] C. Duyckaerts, B. Delatour, and M.-C. Potier, "Classification and basic pathology of Alzheimer disease," Acta Neuropathologica, vol. 118, no. 1, pp. 5-36, 2009.
[2] C. R. Jack et al., "NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease," Alzheimer's & Dementia, vol. 14, no. 4, pp. 535-562, 2018.
[3] S. Weintraub, A. H. Wicklund, and D. P. Salmon, "The neuropsychological profile of Alzheimer disease," Cold Spring Harbor Perspectives in Medicine, vol. 2, no. 4, p. a006171, 2012.
[4] J. D. W. Greene and J. R. Hodges, "Identification of famous faces and famous names in early Alzheimer's disease: Relationship to anterograde episodic and general semantic memory," Brain, vol. 119, no. 1, pp. 111-128, 1996.
[5] J. R. Hodges and J. D. W. Greene, "Knowing about people and naming them: Can Alzheimer's disease patients do one without the other?" The Quarterly Journal of Experimental Psychology Section A, vol. 51, no. 1, pp. 121-134, 1998.
[6] J. T. Becker, F. Boller, O. L. Lopez, J. Saxton, and K. L. McGonigle, "The natural history of Alzheimer's disease: Description of study cohort and accuracy of diagnosis," Archives of Neurology, vol. 51, no. 6, pp.585-594, 1994.
[7] J. R. Hodges, "Alzheimer's centennial legacy: Origins, landmarks and the current status of knowledge concerning cognitive aspects," Brain, vol. 129, no. 11, pp. 2811-2822, 2006.
[8] M. M. Lavallée et al., "A qualitative impairment in face perception in Alzheimer's disease: Evidence from a reduced face inversion effect," Journal of Alzheimer's Disease, vol. 51, no. 4, pp. 1225-1236, 2016.
[9] R. K. Yin, "Looking at upside-down faces," Journal of Experimental Psychology, vol. 81, no. 1, pp. 141-145, 1969.
[10] B. Rossion and I. Gauthier, "How does the brain process upright and inverted faces?" Behavioral and Cognitive Neuroscience Reviews, vol. 1, no. 1, pp. 63-75, 2002.
[11] P. M. Rossini et al., "Early diagnosis of Alzheimer's disease: The role of biomarkers including advanced EEG signal analysis. Report from the IFCN-sponsored panel of experts," Clinical Neurophysiology, vol. 131, no. 6, pp. 1287-1310, 2020.
[12] K. Bötzel, S. Schulze, and S. R. G. Stodieck, "Scalp topography and analysis of intracranial sources of face-evoked potentials," Experimental Brain Research, vol. 104, no. 1, pp. 135-143, 1995.
[13] S. Bentin, T. Allison, A. Puce, E. Perez, and G. McCarthy, "Electrophysiological studies of face perception in humans," Journal of Cognitive Neuroscience, vol. 8, no. 6, pp. 551-565, 1996.
[14] S. R. Schweinberger, V. Pfütze, and W. Sommer, "Repetition priming and associative priming of face recognition: Evidence from event-related potentials," Journal of Experimental Psychology: Learning, Memory, and Cognition, vol. 21, no. 3, pp. 722-736, 1995.
[15] S. R. Schweinberger, E. C. Pickering, A. M. Burton, and J. M. Kaufmann, "Human brain potential correlates of repetition priming in face and name recognition," Neuropsychologia, vol. 40, no. 12, pp. 2057-2073, 2002.
[16] S. Bentin and L. Y. Deouell, "Structural encoding and identification in face processing: ERP evidence for separate mechanisms," Cognitive Neuropsychology, vol. 17, no. 1-3, pp. 35-55, 2000.
[17] E. I. Olivares, J. Iglesias, C. Saavedra, N. J. Trujillo-Barreto, and M. Valdés-Sosa, "Brain signals of face processing as revealed by event-related potentials," Behavioural Neurology, vol. 2015, Article ID 514361, 16 pages, 2015.
[18] M. J. Taylor, M. Shehzad, and K. A. McCarthy, "Electrophysiological correlates of face processing," in Oxford Handbook of Face Perception, A. J. Calder, G. Rhodes, M. H. Johnson, and J. V. Haxby, Eds., pp. 345-366, Oxford University Press, Oxford, 2011. (book chapter style)
[19] R. J. Itier and M. J. Taylor, "N170 or N1? Spatiotemporal differences between object and face processing using ERPs," Cerebral Cortex, vol. 14, no. 2, pp. 132-142, 2004.
[20] B. Rossion and C. Jacques, "Does physical interstimulus variance account for early electrophysiological face sensitive responses in the human brain? Ten lessons on the N170," NeuroImage, vol. 39, no. 4, pp. 1959-1979, 2008.
[21] S. Caharel, O. d'Arripe, M. Ramon, C. Jacques, and B. Rossion, "Early adaptation to repeated unfamiliar faces across viewpoint changes in the right hemisphere: Evidence from the N170 ERP component," Neuropsychologia, vol. 47, no. 3, pp. 639-643, 2009.
[22] M. T. Turano, F. Lao, D. Richoz, A.-R. Lao, J. Pascalis, O. Mento, and G. Caldara, "Fear boosts the early neural coding of faces," Social Cognitive and Affective Neuroscience, vol. 12, no. 12, pp. 1959-1971, 2017.
[23] S. J. Webb, E. Merkle, K. Murias, M. Richards, T. Aylward, and E. Dawson, "ERP responses differentiate inverted but not upright face processing in adults with ASD," Social Cognitive and Affective Neuroscience, vol. 7, no. 5, pp. 578-587, 2012.
[24] M. J. Taylor, R. J. Itier, T. Allison, and G. E. Edmonds, "Direction of gaze effects on early face processing: Eyes-only versus full faces," Cognitive Brain Research, vol. 10, no. 3, pp. 333-340, 2001.

[25] W. Huang et al., "Revisiting the earliest electrophysiological correlate of familiar face recognition," International Journal of Psychophysiology, vol. 120, pp. 42-53, 2017.
[26] S. J. Wuttke and S. R. Schweinberger, "The P200 predominantly reflects distance-to-norm in face space whereas the N250 reflects activation of identity-specific representations of known faces," Biological Psychology, vol. 140, pp. 86-95, 2019.
[27] L. J. Pierce, T. Khurana, J. Pressl, and C. Haenschel, "The N250 event-related potential reflects the activation of face representations," in Face Processing: Systems, Disorders and Cultural Differences, M. Bindemann and A. M. Megreya, Eds., pp. 207-224, Nova Science Publishers, New York, 2011. (book chapter style)
[28] Y.-J. Cheng and M.-C. Pai, "The N250 and event-related theta activity correlate with face identification in Alzheimer's disease: A single-trial analysis," Clinical Neurophysiology, vol. 131, no. 7, pp. 1433-1439, 2020.
[29] M. Eimer, A. Gosling, and B. Duchaine, "Electrophysiological markers of covert face recognition in developmental prosopagnosia," Brain, vol. 135, no. 2, pp. 542-554, 2012.
[30] S. R. Schweinberger and M. F. Neumann, "Repetition effects in human ERPs to faces," Cortex, vol. 80, pp. 141-153, 2016.
[31] S. R. Schweinberger, E. C. Pickering, I. Jentzsch, A. M. Burton, and J. M. Kaufmann, "Event-related brain potential evidence for a response of inferior temporal cortex to familiar face repetitions," Cognitive Brain Research, vol. 14, no. 3, pp. 398-409, 2002.
[32] M. F. Neumann and S. R. Schweinberger, "N250r and N400 ERP correlates of immediate famous face repetition are independent of perceptual load," Brain Research, vol. 1239, pp. 181-190, 2008.
[33] M. Eimer, "Event-related brain potentials distinguish processing stages involved in face perception and recognition," Clinical Neurophysiology, vol. 111, no. 4, pp. 694-705, 2000.
[34] B. Jemel, M. Pisani, M. Calabria, M. Crommelinck, and R. Bruyer, "Is the N170 for faces cognitively penetrable? Evidence from repetition priming of Mooney faces of familiar and unfamiliar persons," Cognitive Brain Research, vol. 17, no. 2, pp. 431-446, 2003.
[35] E. A. Prieto, S. Caharel, R. Henson, and B. Rossion, "Early (N170/M170) face-sensitivity despite right lateral occipital brain damage in acquired prosopagnosia," Frontiers in Human Neuroscience, vol. 5, p. 138, 2011.
[36] Z. S. Nasreddine et al., "The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment," Journal of the American Geriatrics Society, vol. 53, no. 4, pp. 695-699, 2005.
[37] A. R. Giovagnoli et al., "Trail making test: Normative values from 287 normal adult controls," The Italian Journal of Neurological Sciences, vol. 17, no. 4, pp. 305-309, 1996.
[38] T. Sunderland et al., "Clock drawing in Alzheimer's disease," Journal of the American Geriatrics Society, vol. 37, no. 8, pp. 725-729, 1989.
[39] G. A. Carlesimo et al., "The mental deterioration battery: Normative data, diagnostic reliability and qualitative analyses of cognitive impairment," European Neurology, vol. 36, no. 6, pp. 378-384, 1996.
[40] G. Novelli et al., "Tre test clinici di ricerca e produzione lessicale. Taratura su soggetti normali," Archivio di Psicologia, Neurologia e Psichiatria, vol. 47, no. 4, pp. 477-506, 1986.
[41] S. Mondini, D. Mapelli, A. Vestri, G. Arcara, and P. S. Bisiacchi, Esame Neuropsicologico Breve 2, Raffaello Cortina Editore, Milan, 2011. (book style)
[42] A. Rey, "L'examen clinique en psychologie," Presses Universitaries De France, Paris, 1958. (book style)
[43] J. I. Sheikh and J. A. Yesavage, "Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version," Clinical Gerontologist: The Journal of Aging and Mental Health, vol. 5, no. 1-2, pp. 165-173, 1986.
[44] S. W. Smith et al., "Adaptive extraction of time-frequency information from complex signals," in Time-Frequency Techniques for Radar Imaging of Moving Targets, F. Ahmad, Y. Zhang, and M. G. Amin, Eds., pp. 1-11, San Diego, 2014. (conference paper style)
[45] A. Hyvärinen and E. Oja, "Independent component analysis: Algorithms and applications," Neural Networks, vol. 13, no. 4-5, pp. 411-430, 2000.
[46] B. Jemel, M. Pisani, M. Rousselle, M. Crommelinck, and R. Bruyer, "Exploring the functional architecture of person recognition system with event-related potentials in a within- and cross-domain self-priming of faces," Neuropsychologia, vol. 43, no. 14, pp. 2024-2040, 2005.
[47] M. Eimer, "The face-sensitive N170 component of the event-related brain potential," in The Oxford Handbook of Face Perception, A. J. Calder, G. Rhodes, M. H. Johnson, and J. V. Haxby, Eds., pp. 329-344, Oxford University Press, Oxford, 2011. (book chapter style)
[48] R. Bruyer, "Covert face recognition in prosopagnosia: A review," Brain and Cognition, vol. 15, no. 2, pp. 223-235, 1991.
[49] E. H. F. De Haan, A. Young, and F. Newcombe, "Covert and overt recognition in prosopagnosia," Brain, vol. 114, no. 6, pp. 2575-2591, 1991.
[50] G. Avidan and M. Behrmann, "Implicit familiarity processing in congenital prosopagnosia," Journal of Neuropsychology, vol. 2, no. 1, pp. 141-164, 2008.