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ORIGINAL ARTICLE

Impairment in anticipatory cognitive brain processing in frail older adults

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Abstract Frailty of the elderly is a condition that incorporates multisystem physiological age-related impairments with poor clinical and functional outcomes. Literature shows that this condition could be associated with cognitive deterioration due to the degeneration of brain structures and functions, especially in the prefrontal cortex (PFC). Despite the interest in this condition, research on cognitive performance and brain activity in frailty remains limited. The purpose of the present study was to use the event-related potential (ERP) method to investigate the frontal and prefrontal brain activity of frail elderly people during the anticipatory phase of a cognitive task. ERPs of 38 frail and pre-frail participants (Frail group) aged ≥ 65 years, and a group of 38 matched robust individuals were compared. Cognitive functions were also assessed using the Montreal Cognitive Assessment (MoCa); anxiety was evaluated with the State-Trait Anxiety Inventory (STAI). Results showed that in the Frail group, the activity from the PFC was lower than in the Robust group. This reduction of top-down cognitive control may have produced, in the frail participants, greater response errors and anxiety levels higher than those of the Robust group. Results suggest that PFC degeneration may reduce the cognitive readiness preceding a cognitive task, which is necessary for accurate task performance. This PFC hypoactivity may also lead to increased anxiety levels in frail people. Considering that this effect was of similar magnitude in frail and pre-frail participants, the anticipatory ERP activity of the PFC could be a potential neuromarker of frailty.

Keywords EEG · ERP · Frailty · Cognitive and motor anticipation

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Introduction

The demographic rate of the population over 65 is continually increasing and is estimated to grow exponentially, thus highlighting the need to provide health services for the maintenance of independence and prevention of disability in this population [e.g., 1]. Frailty in older adults can be defined as a syndrome or as a condition induced by the build-up of multiple health dysfunctions [2], leading to multisystem dysregulations, including chronic inflammation and cardiovascular disorders [3]. Frailty is also connected with exogenous environmental factors, low levels of education, isolation or loneliness, inadequate nutrition, and physical [4]. It is a stage of transition from independence in daily life to functional decline and

disability [e.g., 5]. According to the frail phenotype classification by Freid and colleagues [6], an older individual is considered frail if three or more of the following criteria are present: unintentional weight loss, self-reported exhaustion, muscle weakness (grip strength), slow walking speed, and low physical activity levels. The presence of one or two criteria categorises older people as Pre-frail, whereas if none of these criteria are present, older adults are considered Robust. In Brazil, a recent cross-sectional study on 335 older adults over 60 showed that more than half of the participants were frail (12%) and/or pre-frail (43%), with physical inactivity and low gait speed as the most prevalent criteria [7].

Frailty-related brain changes have not been fully investigated, although several studies have highlighted a reduction in both white and grey matter, particularly in the frontal cortex [e.g., 8, 9]. For this reason, the construct of cognitive frailty refers to physical frailty in concurrence with mild cognitive impairment [10]. A study on 504 subjects [11] with a mean age of 80 years found similar cognitive dysfunctions in frail and pre-frail participants, highlighting the importance of adding early cognitive markers to frailty assessment [for similar conclusions, see 12. In addition, research utilising neuroimaging techniques has demonstrated an association between frailty and a reduction in the volume of grey and withe matter and altered functions within the prefrontal cortex (PFC) [13], which is among the brain regions most susceptible to age-related changes [14–16]. In particular, a relationship between the loss of PFC volume and impaired gait performance was identified and attributed to slower cognitive processing [17]. In support of this, Robertson et al. [12] showed that pre-frail and frail individuals had worse performance on cognitive tasks compared to healthy age-matched peers. Processing speed, executive functions, and attentional performance showed a robust correlation with walking and grip strength performance. Rosado-Artalejo et al. [18] evidenced a potential relationship between cognitive dysfunction and frailty, showing that cognitive functions were predictors of gait performance and grip strength. Even in the absence of cognitive impairment, executive functions in physically frail individuals have been shown to be impaired compared with a sample of robust individuals. These results indicate that the integrity of cognitive functions should be used as early markers for the condition of frailty. Already in late midlife, reduced response times in cognitive tasks were more likely to predict future frailty [19]. However, using less demanding tasks such as a visuomotor detection task, a large sample study including 284 over-65 people [20] could not find consistent response time differences among frail, pre-frail, and robust people. Anxiety is also a psychological condition associated with frailty. In a recent systematic review conducted on 21 studies, a clear association was found between pre-frailty/frailty and anxiety in older adults [21]. Therefore, individuals who were positive to frailty criteria are expected to be categorised as psychologically frail, as they were more prone to emotional disturbances [22]. In addition, it is known that reduced PFC activity is associated with elevated levels of anxiety [e.g., 23, 24].

Some studies have tried to identify neuromarkers to characterise frail people using electroencephalography. Event-related potential (ERP) studies found effects on the P3 and mismatch negativity components evoked in cognitive tasks, indicating post-perceptual cognitive deterioration during the processing of task-relevant information in parietal areas [for reviews, see 25, 26]. These anomalies have been associated with dysfunctional attention and reduced memory skills [27, 28]. No ERP studies investigated the frontal and prefrontal cortex activity in frail people, as the activity that is produced by the brain during the anticipatory phase in a cognitive task. This preparatory brain activity can be measured by two anticipatory components known as the Bereitschaftspotential (BP) and the prefrontal negativity (pN). The BP originates in premotor brain areas and is linked to motor readiness before any voluntary movement and can be detected in sensory-motor tasks before the imperative stimulus onset. A larger BP has been associated with faster response time. The pN, rising from the PFC, is linked to top-down attentional and inhibitory regulation and has also been used as an indicator of cognitive readiness. A larger pN has been associated with a higher response accuracy [e.g., 29] and low anxiety levels [24].

In this study, we aimed to find possible neuromarkers of frailty by inspecting the electrophysiological correlates of frontal cortex dysfunction in frail older adults. This has been done by investigating the preparatory ERP components during the anticipatory phase of a visuomotor discrimination response task (DRT) before the onset of an imperative event. In

addition, we evaluated the anxiety level and the general cognitive status as possible neuropsychological markers.

According to the literature, we expect that a decreased pN component should index reduced PFC activity and, consequently, be associated with reduced response accuracy and increased anxiety. Considering the lack of effect on response time [20], we expect to confirm that data and find no difference in the BP amplitude. Given that frail phenotype assessment is based on physical function parameters, the general cognitive function should not necessarily be impaired in frail people. Considering that pre-frail and frail people were found comparable for several psychological parameters [11, 12, 20], pre-frail and frail participants were merged in the same group to increase the sample size and then compared to robust peers.

Methods

Participants

The study involved a group of older adults aged ≥ 65 years classified as either frail or pre-frail (Frail group) and a group of age and sex-matched robust older adults (Robust group). The sample size was calculated by a power analysis conducted using G*Power 3.1.9.7 software [30]. Based on Cohen-d statistics, a medium–high effect size of d = 0.70 was fixed for independent (two-tailed) t-test analysis [31]. The alpha level was set to 0.05 and the power to 0.85. This resulted in a minimum sample size of 76. Thus, the sample consisted of 38 frail (19) or pre-frail (19) older adults (age mean (years) ± standard deviation (SD): 75.1 ± 5.7; 68% females), and 38 robust older adults (matched for age and sex) (age mean (years) ± standard deviation (SD): 74.8 ± 5.4; 67% females). All participants were right-handed, according to the Edinburgh Handedness Inventory. Preliminary comparisons between frail and prefrail participants did not find significant differences (all t-values were lower than 1) in all tests used (see below).

Participants were recruited from local senior centres and were initially screened by qualified geriatricians to assess the general clinical status, the pharmacological history, and the presence of frail/pre-frail phenotype. Inclusion criteria were: age ≥ 65 years and absence of dementia (Mini-Mental State Examination > 25/30). Exclusion criteria were: history of neuropsychiatric or neurological disorders, head trauma, any substance abuse or addictive disorder (except those involving nicotine) in the previous 6 months, and severe vision problems. Participants voluntarily participated in the study. All participants provided informed consent for the study and were naïve of the purposes of the experiments. The project was conducted in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and authorised by the research authorisation committee of the University of Rome "Foro Italico".

Procedure and measures

To screen for frailty, we used the *Linda Fried Frail Phenotype* criteria [5], which includes an assessment of 5 criteria (unintentional weight loss, exhaustion, low levels of physical activity, slow gait speed, and weak grip strength). For the presence or absence of these criteria (with a score equal to 1 for presence and 0 for absence), we used the reference values proposed by Fried et al., [5]. For the assessment of "Weight loss" we asked the participants if they had lost more than 4.5 kg unintentionally during the previous year, for self-reported "Exhaustion", according to the Fried criteria, we used two items from the Center for Epidemiological Studies Depression Scale (CES-D) [32]: "I felt that everything I did was an effort" and "I could not get going.": participants were asked, "How often in the last week did you feel this way?" and responses indicating a frequency of 3 or more days were scored as positive for exhaustion (score = 1) [6]. For the assessment of physical activity levels, we used the Italian Short Version of the International Physical Activity Questionnaire (IPAQ-SF) [33]. The IPAQ-SF includes four specific questions that assess the frequency (in days) and duration (in minutes) of vigorous and moderate physical activity, walking, and time spent sitting during the previous seven days. Responses were used to estimate participants' total physical activity by MET/week. We used a cut-off value of < 600 MET/week for low physical activity [34]. For the assessment of "Slowness" we asked the participants to walk at their usual speed on a linear path of 4.6 m, collecting the time for two attempts: we registered the best time of the two and used Fried cut-off values by gender and standing height for scoring positive [6]. For the assessment of

"Weakness" grip strength was measured by a Grip Strength Dynamometer (GRIP_D Takei Ltd., Tokyo, Japan) twice on both sides; the best of the four values was used as the grip strength measure to be compared to Fried cut off values by gender and body mass index [6]. The score of each of the five criteria was then summed up. Participants with a total score of 0 were defined as robust, while those with a total score from 1 to 2 were defined as pre-frail, and a total score ≥ 3 defined participants as frail.

Subjective psychological tests

To measure the level of anxiety, Spielberg's State-Trait Anxiety Inventory (STAI) form Y questionnaire [35] was used. STAI is the "gold standard" for measuring anxiety, and it includes two self-report scales for measuring state and trait anxiety. State anxiety is characterized as an unpleasant emotional state of apprehension that is temporary. On the other hand, trait anxiety is a personal trait associated with a propensity to continuously react to different situations with concern, agitation, and restlessness [35]. The scores range from 20 to 80 and are commonly classified as "no or low anxiety" (20–37), "moderate anxiety" (38–44), and "high anxiety" (45–80).

The Montreal Cognitive Assessment (MoCA) [36] was employed to test the general cognitive functioning of the participants. The MoCa is a common test for detecting mild cognitive impairment (MCI). The scores range from 0 to 30 and are commonly classified as "normal cognition" (25–30), "MCI" (18–25), "moderate cognitive impairment" (10–17), and severe cognitive impairment "under 10" [e.g., 37].

Participants completed the STAI by themselves, while the MoCA test was administered by the geriatrician or by trained personnel.

Objective cognitive test

To evaluate the visuomotor cognitive brain functions of participants, a discriminative response task (DRT), i.e., assimilable to a common Go/No-go paradigm, was administered to all participants during electroencephalographic (EEG) recording. For this task, participants sat in a low-lit, sound-attenuated room after the EEG cap was fitted to the scalp. Participants were in front of a 32″ monitor at a distance of 114 cm. The task required responding (pressing a key) to target stimuli and avoiding responding to non-target stimuli. The response was provided by pressing a button that participants held in their right hand, resting on their right leg. Two kinds of target stimuli and two non-target stimuli individually appeared in rapid succession and random order on the screen, with equal probability ($p = 0.25$), alternating with a black screen with a yellow fixation point, which was always displayed in the centre. The duration of each stimulus was 250 ms, while the interstimulus time varied from 1500 to 2500 ms to avoid a learning effect. The stimuli comprised grey squares containing vertical and horizontal black lines. The non-target stimuli contained the same combinations of lines as the target stimuli but were rotated by 90° (Fig. 1). Participants performed 10 runs of this task, including a total of 800 trials (400 targets and 400 non-targets). Each run consisted of 80 trials interspersed with a few seconds of rest. Participants were encouraged to respond as quickly as possible, without omitting accuracy. In the middle of the session, participants were offered the opportunity to take a break for a few minutes. The total duration of the EEG recording was 35–40 min. For data on a large sample using this task and parameters, please see Di Russo et al. [29].

EEG data recording and analysis

The EEG signal was recorded using the BrainAmp™ system (BrainProducts GmbH, Munich, Germany) with 64 scalp electrodes mounted according to the 10–10 International system. All electrodes were referenced to the left mastoid and then re-referenced to both mastoids. The horizontal and vertical electrooculograms (EOG) were also recorded with bipolar montage using electrodes at the right external canthi and below the left eye, respectively. Electrode impedances were kept below 5KΩ.

The EEG was digitized at 250 Hz, amplified, filtered (band-pass of 0.01–80 Hz including a 50 Hz notch filter), and stored for offline averaging. A correction of the eye-movement artifacts was then performed using the common regression-based method. Then, artifact rejection was performed to discard the remaining epochs contaminated by signals exceeding the amplitude threshold of ± 60 μV to remove possible non-ocular artefacts. The EEG was segmented into 1300 ms epochs synchronised with stimulus onset from 1100 ms before to 200 ms after it. The

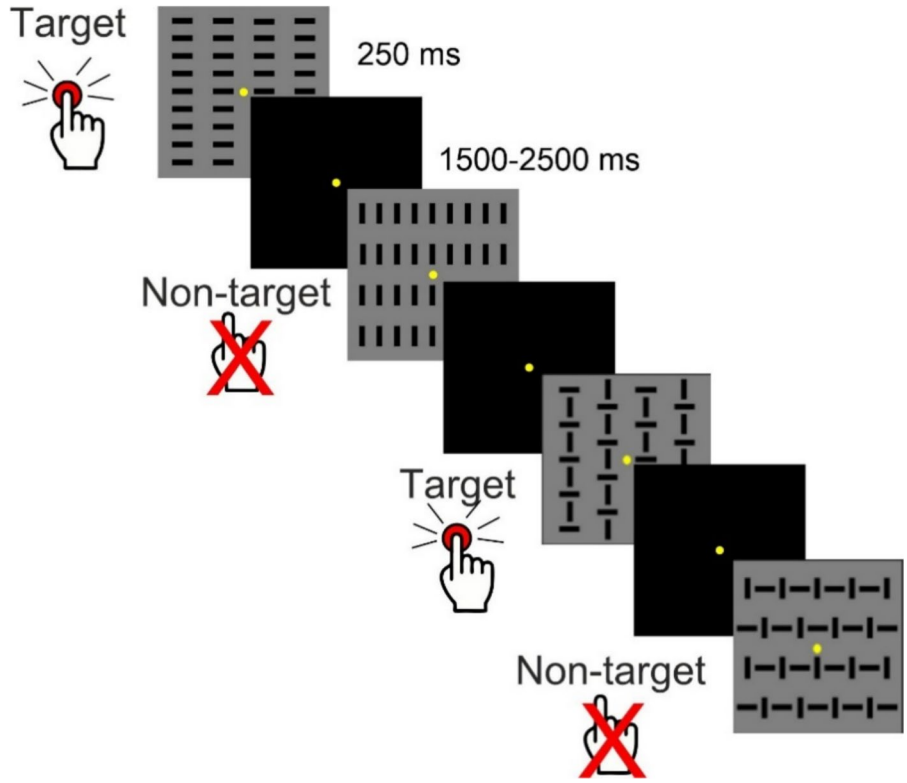

Fig. 1 Representation of the cognitive task, with features and timing of the stimuli

baseline was set from −1100 to −900 ms. This time window was chosen according to the literature on the used DRT showing that the earliest onset of any preparatory activity is no earlier than −800 ms [e.g., 29] The artifact-free trials were finally averaged. To identify scalp sites and the interval to consider for successive statistical analyses, a spatiotemporal cluster permutation analysis based on the Wilcoxon test was used [38]. This analysis was computed by averaging the ERP data across all participants, regardless of the group. Then the waveform was statistically tested against zero using a non-parametric cluster-based permutation test based on the Wilcoxon signed-rank test [38]. This analysis was carried out using the following parameters: time window: −900 to 0 ms, number of permutations: 10,000, initial alpha threshold: 0.01, minimum spatial cluster size: 3 electrodes, minimum temporal cluster duration: 10 samples (~120 ms), cluster-level alpha: 0.01 This procedure revealed one significant temporal cluster (from −604 to 0 ms), which included two spatially distinct clusters: a prefrontal cluster (Fp1, Fpz, Fp2, AF7, AF3, AFz, AF4, AF8), consistent with the prefrontal negativity (pN) component; a central cluster (C1, Cz, C2, CP1, CPz, CP2), consistent with the Bereitschaftspotential (BP).

Behavioural data were obtained by measuring the mean response time (RT) for target trials. Accuracy was measured as the error rate summing the missed responses (i.e., omitted responses to target stimuli) and false alarms (i.e., responses to non-target stimuli).

Statistical analysis

Before statistical analyses, the normality assumption for all variables was assessed using the Shapiro–Wilk test. None of the distributions deviated significantly from normality. T-test for independent samples was used to compare the two groups' RT, accuracy in the DRT, anxiety using the STAI, general cognition using the MoCA, and the pre-stimulus ERP components (pN and BP) amplitude. The Cohen's d value was also reported to quantify the effect size of significant differences. The overall alpha level was fixed at 0.05. The statistical analyses were conducted using Statsoft Statistica (StatSoft, Inc., Tulsa, OH, USA, version 12).

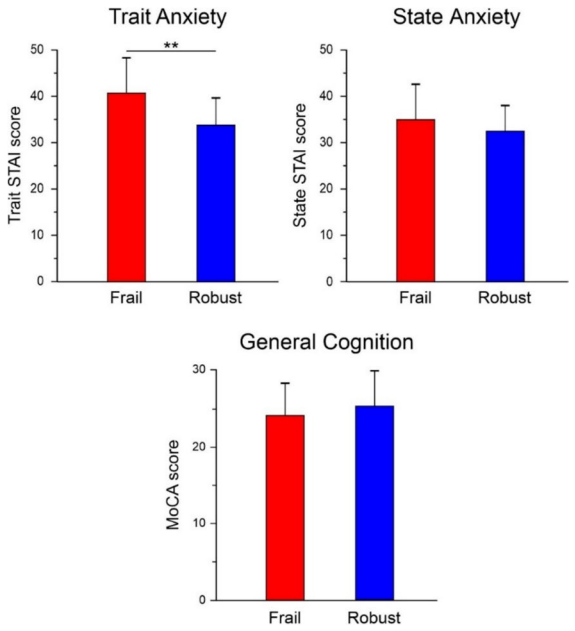

Fig. 2 Psychological status and cognitive screening of the two groups. The vertical lines represent the 95% confidence interval. Significant group differences are also indicated ($^{**}p<0.01$)

Results

Subjective anxiety and cognitive tests

As shown in Fig. 2, the level of trait anxiety was higher ($t_{(74)}=3.06$, $p<0.01$, $d=0.72$) in the Frail (40.7, SD = 9.4) than in the Robust group (33.8, SD = 9.9). The state anxiety and general cognition were comparable between groups ($t>1$), obtaining a mean state STAI score of 33.6 (SD = 8.1) and a mean MoCa score of 24.9 (SD = 2.9) indicating initial signs of MCI.

Objective cognitive test

The t-test on the response time (RT) showed a non-significant effect ($t>1$) with a mean response time of 582 ms, SD = 47. The t-test on the accuracy was significant ($t_{(74)}=4.99$, $p<0.01$, $d=1.13$) with a larger error rate in the Frail (38.3%, SD = 14.5) than in the Robust (25.1%, SD = 7.6) group. Figure 3 graphically represents these results.

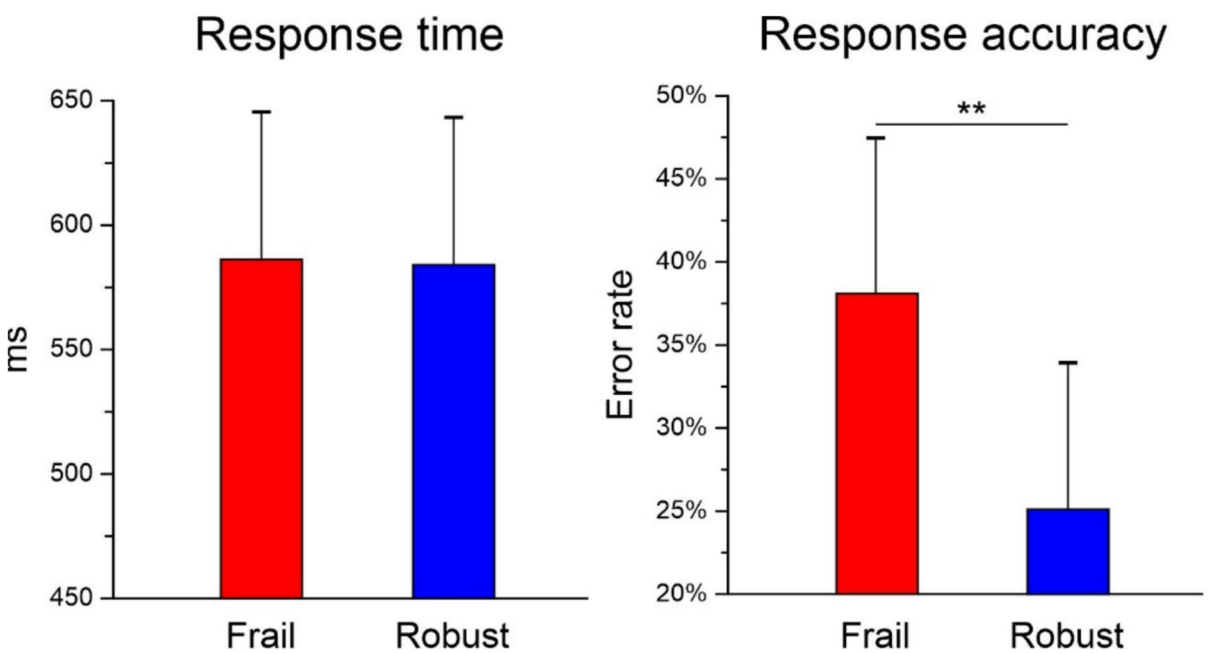

Fig. 3 Behavioural data of the two groups in the visuomotor cognitive test. The vertical lines represent the 95% confidence interval. The significant group differences are also indicated ($^{**}p<0.01$)

ERP data

The left side of Fig. 4 shows the group-averaged ERP waveforms of the two groups in the two clusters of electrodes representing the pN and BP components. The right side of Fig. 4 shows the current source density (CSD) and voltage scalp topography showing the two possible prefrontal and central current and voltage sources. CSD maps, using a Laplacian transformation of the voltage scalp distribution, remove the influence of the reference electrode, identifying more precise areas of neural activity and current flow.

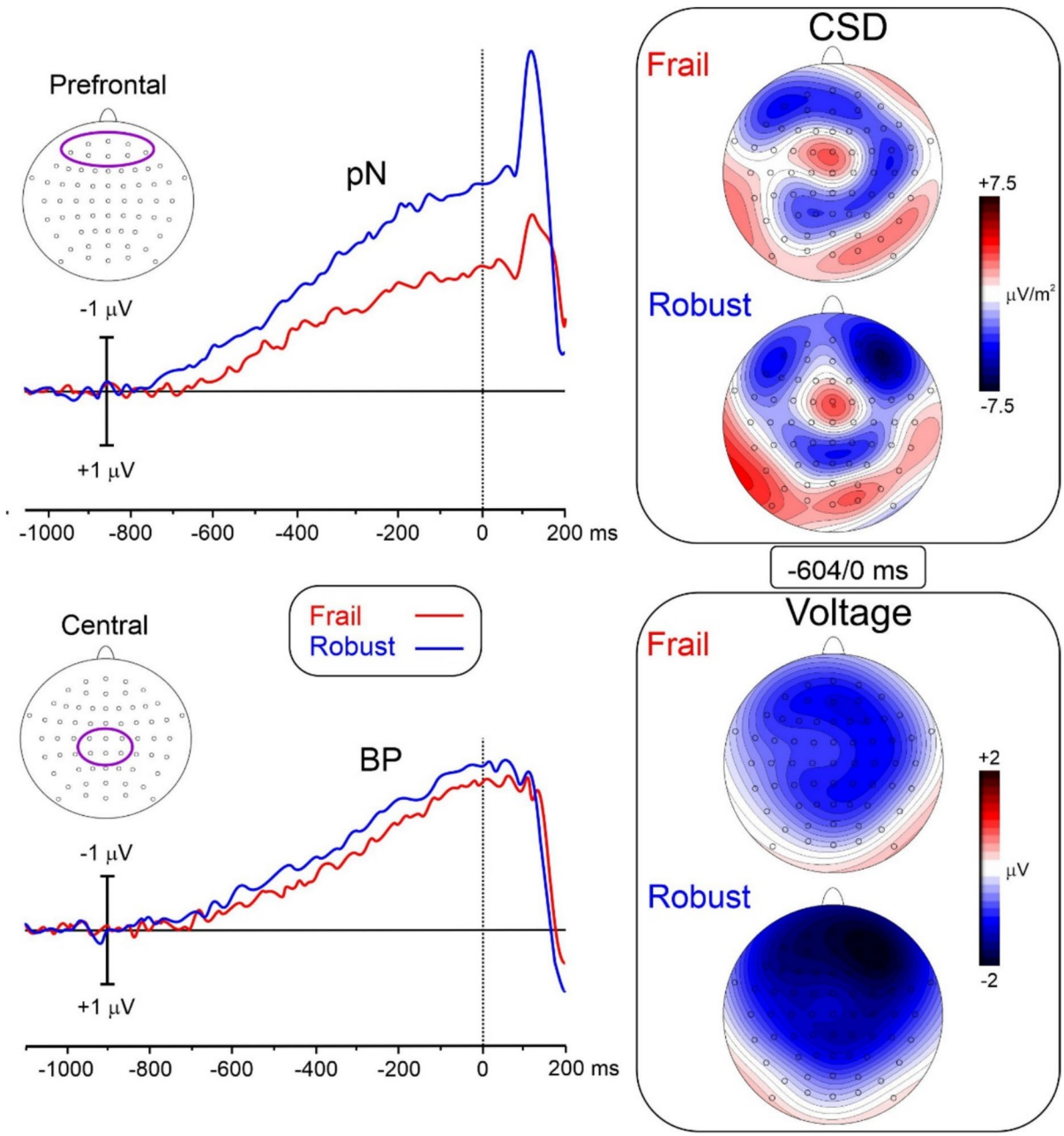

Fig. 4 Left: Pre-stimulus ERP waveforms of the two groups. The circles within the head figures indicate the electrodes included in the waveforms. Right: current source density (CSD) and voltage scalp topography (top-flat view) in the −604/0 ms intervals

The t-test carried out between the mean amplitude in the −604 to 0 ms interval was significant for the prefrontal clusters (pN component) ($t_{(74)} > 8.64$, $p < 0.01$, $d = 1.76$), indicating lower amplitudes in the Frail (1.52 µV, SD = 0.32) than the Robust (2.59 µV, SD = 0.56) group. The t-test on the central cluster (BP component) was non-significant with a mean amplitude of 1.67 µV, SD = 0.41.

To describe group differences over the whole scalp, differential activity and t-test comparisons were also performed on all electrodes. Figure 5a shows the scalp maps of CSD and the voltage differential activity between the two groups (Robust minus Frail) in the interval from −604 ms to 0 ms. Figure 5b shows the whole scalp distribution of the t-test on all 64 electrodes in the same interval. In addition, the channels with $p < 0.05$ and $p < 0.01$ (after Bonferroni

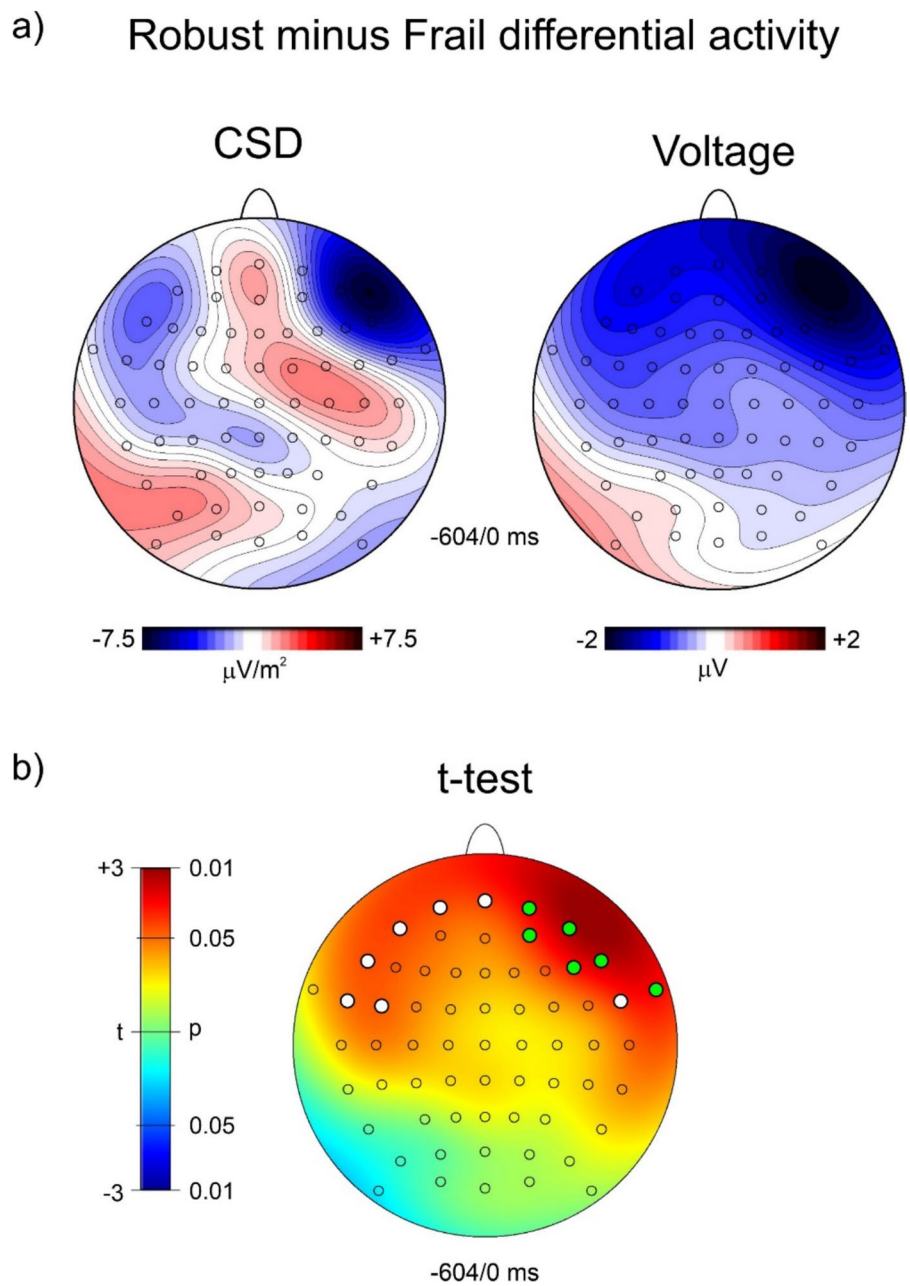

Fig. 5 Comparison between the brain activity of the Frail vs. Robust groups: **a**) current source density (CSD) and voltage scalp differential topography in the −604/0 ms intervals; **b**) a statistical comparison of the whole scalp. The electrodes filled with white and green indicate $p > 0.01$ and $p = 0.01$ significant differences, respectively

correction for multiple comparisons) are highlighted in white and green circles, respectively. This analysis confirmed the reduction of prefrontal preparatory activity in the Frail group but also showed a stronger effect in the right hemisphere.

Pearson correlation between the pN amplitude and the trait-anxiety level measured with the STAI of all participants was significant ($F_{(1,74)} = 14.31$, $p < 0.01$), obtaining an $R = 0.40$. Individual data and linear regression are presented in Fig. 6a. Robust, frail, and pre-Frail participants are coded with distinct colours showing a clear distinction between the robust and the other participants, but a similarity between the frail and pre-frail participants. Correlation analysis for each group separately was also significant (Bonferroni corrected $p < 0.05$) for Frail and Pre-frail

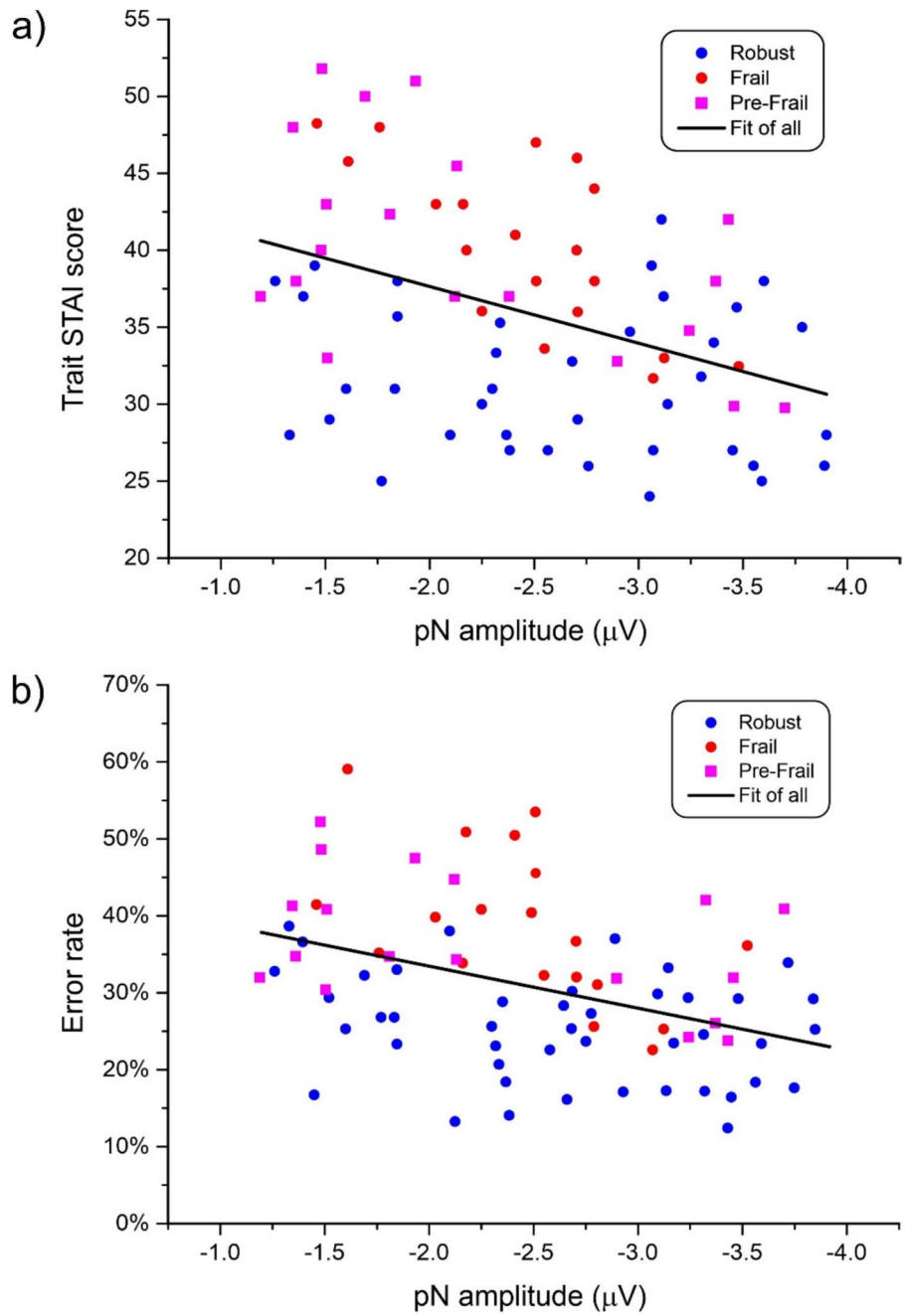

Fig. 6 Correlation between the pN amplitude and the **a**) trait-anxiety level (STAI), and **b**) Response accuracy expresser as percentage of errors. Robust, Frail, and Pre-Frail participants are coded with distinct colours, but the linear regression fits all points

groups (R = 0.48 and 0.36, respectively), but not for the Robust group (R = 0.14).

Pearson correlation between the pN amplitude and the response accuracy in the DRT of all participants was significant ($F_{(1,74)} = 15.56$, $p < 0.1$), obtaining an R = 0.42. Individual data and linear regression are presented in Fig. 6b. The figure shows a clear distinction between the robust and the other participants, while frail and pre-frail participants were less distinguishable. Correlation analysis for each group separately was also significant (Bonferroni corrected $p < 0.05$) showing a Pearson's r value of 0.62, 0.53 and 0.38, for Frail and Pre-frail and Robust groups, respectively).

Discussion

The present study aimed to characterise the neurocognitive and emotional condition of frail elderly adults using electroencephalography, cognitive and psychological testing. To this aim, frail and pre-frail individuals were compared to robust controls. As a preliminary result, frail and pre-frail participants showed comparable neuropsychological impairment, as repeatedly found in the literature [e.g., 7, 39, 40]. This means that neurocognitive dysfunctions could be an early sign of frailty. As indicated by Aguilar-Navarro et al. [10], these cognitive signs may not necessarily impact physical functioning at this stage, as they could represent an early accumulation of progressive brain damage without clinical symptoms. Therefore, it is important to implement timely detection strategies aimed at an early diagnosis.

Regarding the general cognitive functioning, both groups showed signs of mild cognitive impairment, with non-significant differences likely because the MoCa test is a good screening tool to test general cognition, but it does not deeply evaluate the different cognitive domains as a complete neuropsychological assessment [e.g., 41]. On the other hand, we found between-groups differences in the anxiety level. The tests for anxiety showed that trait anxiety was 17% higher in the Frail group compared with the Robust group. This result is supported by Honzawa et al., [40], showing that both pre-frail and frail individuals exhibited higher trait and state anxiety than robust older adults. Our study did not show between-group differences in state anxiety levels, likely because we excluded individuals with acute clinical conditions, while Honzawa et al. [40] included individuals during cardiac rehabilitation. The association between frailty and anxiety is in line with the systematic review of Tan et al. [21]. Specifically, mental disorders, including anxiety, are associated with worse physical health, the presence of medical comorbidities, and lower life expectancy [e.g., 39, 42]. Additionally, Zhao et al. [43] found that the anxiety condition may elevate the risk of developing frailty. Higher levels of anxiety are associated with lower levels of physical activity, reduced social support, and a poorer diet of nutrients or unhealthy behaviours. Individuals with higher levels of anxiety appear to have a lower propensity to seek help or support [e.g., 44].

Regarding the behavioural data associated with the visuomotor cognitive task, the Frail group showed a 34% worse response accuracy compared with the Robust group. This is in line with the results of the study by O'Halloran et al. [45] where it is argued that the frail population is characterised by dysfunctions in sustained attention that could reduce response accuracy. On the other hand, the response time was not significantly different between the two groups although it was 6% slower on average in the Frail group. The lack of effect in response time confirms previous studies that compared robust, pre-frail, and frail elderly and found no response time differences in cognitive tasks such as sustained attention and choice response tasks [12, 20].

The most important result of the present study arose from the investigation of the neural correlates of the observed visuomotor cognitive dysfunctions using electroencephalographic measures of anticipatory brain processing in prefrontal and premotor areas. In the Frail group, anticipatory brain processing in prefrontal areas, indexed by the pN component, showed a drastic amplitude reduction (70%) in comparison to the Robust group. In contrast, anticipatory brain processing in premotor areas, indexed by the BP component, showed no differences between groups, indicating intact anticipatory excitability of the premotor cortex, explaining the unaffected response time and confirming literature on this relation [e.g., 29].

The pN component has been associated with cognitive anticipation of an upcoming complex task, intended as top-down cognitive control (mainly attention and inhibition) for the impending action. The pN, localized in PFC, has been described as a proactive brake used to avoid false alarms in discrimination response tasks. Accordingly, as confirmed here,

the pN amplitude has been associated with response accuracy [e.g., 29, 46, 47]. The present study supports this functional interpretation of the pN, showing concomitant reduced pN and response accuracy. Reduced activity in the prefrontal regions was also found in pre-frail people by [48] using functional near infrared spectroscopy (fNIRS) during a complex cognitive task and comparing them to healthy peers. Reduced PFC activity has been associated with several cognitive and emotional dysfunctions such as MCI, Alzheimer's, and Parkinson's diseases [e.g., 49], post-traumatic stress disorder [e.g., 50, and excessive anxiety [e.g., 51]. Associations between excessive anxiety and reduced anticipatory PFC functions indexed by the pN have been specifically provided in both young individuals [24] and older adults [52]. Here we confirm this data showing that higher preparatory activity over the PFC is associated with lower anxiety levels.

Considering the present result and the mentioned studies, the assessment of cognitive function using visuomotor discrimination tasks, analysis of the associated pN ERP component, and anxiety assessment could be used among early determinants of frailty. In particular, the use of EEG recording and ERP analysis of the pN component may detect functional deterioration of the PFC and could be used as an early neuromarker of frailty.

The present study has a limitation in that it adopted a cross-sectional experimental design, which did not permit the identification of any causal relationship linking frailty, anxiety, and cognitive brain functions. Future studies will need to use longitudinal designs to investigate these relationships. However, this study is one of the first to include clinical, psychological, and neurophysiological variables within the same experimental design. In addition, the present study is the first to investigate anticipatory brain processing through electroencephalographic recording and, therefore expanding our knowledge of brain functions in elderly frail individuals.

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Author contribution Conceptualization: LB, MS, RB, AM, CF, FG, FDR. Data acquisition and curation: LB, MS, RB, CF, FG. Formal analysis: LB, FDR, CF. Methodology: LB, MS, RB, AM, CF, FG, FDR. Writing – original draft preparation: LB, CF, FDR. Writing – review & editing: LB, MS, RB, VC, CF, FG, AM, FP, SP, AZ, FDR. Software development: FDR, AM, SP, VC. Supervision: VC, FP, AZ, AM, SP, FDR, Funding acquisition: FDR, FP, AZ, AM.

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Data Availability The data belong to the University of Rome "Foro Italico".

Declarations

Ethics approval The study was authorised by the research authorisation committee of the University of Rome "Foro Italico" (date Oct. 6, 2023, code CAR 171/2023).

Competing interests The authors declare no competing interests.

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