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Exploring neurofeedback as a therapeutic intervention for subjective cognitive decline

Véronique Paban¹ | Lewis Feraud¹ | Arnaud Weills¹ | Fabien Duplan²

RESEARCH REPORT

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Abstract

Impact statement: This study addresses the pressing issue of subjective cognitive decline in aging populations by investigating neurofeedback (NFB) as a potential early therapeutic intervention. By evaluating the efficacy of individualised NFB training compared to standard protocols, tailored to each participant's EEG profile, it provides novel insights into personalised treatment approaches. The incorporation of innovative elements and rigorous analytical techniques contributes to advancing our understanding of NFB's modulatory effects on EEG frequencies and cognitive function in aging individuals.

Abstract: In the context of an aging population, concerns surrounding memory function become increasingly prevalent, particularly as individuals transition into middle age and beyond. This study investigated neurofeedback (NFB) as a potential early therapeutic intervention to address subjective cognitive decline (SCD) in aging populations. NFB, a biofeedback technique utilising a brain-computer interface, has demonstrated promise in the treatment of various neurological and psychological conditions. Here, we evaluated the efficacy of individualised NFB training, tailored to each participant's EEG profile, compared to a standard NFB training protocol aimed at increasing peak alpha frequency power, in enhancing cognitive function among individuals experiencing SCD. Our NFB protocol incorporated innovative elements, including the implementation of a criterion for learning success to ensure consistent achievement levels by the conclusion of the training sessions. Additionally, we introduced a non-learner group to account for individuals who do not demonstrate the expected proficiency in NFB regulation. Analysis of electroencephalographic (EEG) signals during NFB sessions, as well as before and after

Abbreviations: BNT, Boston Naming Test; CCI-S, Cognitive Change Index (Self-report); EEG, electroencephalography; FFT, fast Fourier transformations; fMRI, functional magnetic resonance; GDS, Geriatric Depression Scale; MCI, mild cognitive impairment; MCQ-30, Meta-Cognitions Questionnaire 30; NFB, neurofeedback; PAF, peak alpha frequency; SES, Self-Esteem Scale; SCD, subjective cognitive decline; SMR, sensorimotor rhythm; STAI Y, State Trait Anxiety Inventory.

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training, provides insights into the modulatory effects of NFB on EEG frequencies. Contrary to expectations, our rigorous analysis revealed that the ability of individuals with SCD to modulate EEG signal power and duration at specific frequencies was not exclusive to the intended frequency target. Furthermore, examination of EEG signals recorded using a high-density EEG showed no discernible alteration in signal power between pre- and post-NFB training sessions. Similarly, no significant effects were observed on questionnaire scores when comparing pre- and post-NFB training assessments.

KEYWORDS

electroencephalography, memory complaints, neurofeedback, subjective cognitive decline

1 | INTRODUCTION

In the aging field, it is commonplace for individuals to express concerns regarding their memory, particularly as they transition into middle age and beyond. This phenomenon becomes more prevalent with advancing age, as noted in empirical studies (Jonker et al., 2000). Such self-reported memory issues may serve as early indicators of cognitive decline or the onset of neurodegenerative conditions like dementia (Jessen et al., 2014). Additionally, these complaints can be linked to manifestations of depression or anxiety (Balash et al., 2013). To address this complex interplay of factors, the subjective cognitive decline (SCD) initiative, comprising an international consortium of researchers and clinicians, introduced the term SCD in 2014 (Jessen et al., 2014). It is noteworthy that various terminologies exist to describe this perceived cognitive decline, including subjective memory complaints, subjective cognitive impairment, subjective memory impairment and functional memory disorder. What is interesting is that individuals experiencing SCD often perform within normal ranges on standard neuropsychological assessments of memory and attention (Jonker et al., 2000). Despite this, they commonly encounter everyday memory lapses such as forgetting names or experiencing difficulties in word retrieval, alongside challenges in maintaining concentration (Metternich et al., 2009; Snitz et al., 2012). SCD has gained attention as a potential early indicator of dementia, particularly Alzheimer's disease (AD), based on findings from numerous clinical and neuroimaging investigations (Jessen et al., 2020; Liew, 2020). Occasional inconsistencies in research outcomes have been noted, which could be attributed to variations in the types of subjects recruited. Indeed, the methods utilised for sampling and recruitment are critical factors in SCD research (Rodríguez-Gómez et al., 2015). It is worth noting that individuals sourced from memory clinics often present with more

pronounced cognitive impairments compared to those sampled from broader population cohorts (Kuhn et al., 2019). Several pharmacological and nonpharmacological interventions are currently being investigated to enhance cognitive functioning and psychological well-being in individuals with SCD. Several systematic reviews and meta-analyses suggested that education programs, physical interventions, and cognitive training can lead to improvements in psychological wellbeing and memory performance in individuals with SCD, but with modest effects (Bhome et al., 2018; Roheger et al., 2021; Smart et al., 2017). However, consensus on the optimal treatment for SCD remains elusive, regardless of whether they are related to preclinical or nonpreclinical dementia types (Chiasson et al., 2023).

Neurofeedback (NFB) is a biofeedback technique that utilises a brain–computer interface to monitor brain activity, analyse it and deliver specific brain features back to the participant in real time (Gaume et al., 2016; Lubianiker et al., 2022; Micoulaud-Franchi et al., 2014; Wood et al., 2014). In other words, during NFB training sessions, individuals receive continuous real-time feedback signals derived from particular aspects of their brain activity, obtained from electroencephalography (EEG) recordings taken from the scalp. Participants are encouraged to regulate their brain activity according to a prescribed NFB protocol. NFB shows promise as a therapeutic method due to its active selfneuromodulation approach, integrating learning mechanisms and neuroplastic effects (Ros et al., 2014; Sitaram et al., 2017). NFB training has demonstrated effectiveness as a treatment for individuals with a broad spectrum of deficits, encompassing various neurological conditions such as pain (Roy et al., 2020), traumatic brain injury (Gray, 2017), epilepsy (Walker & Kozlowski, 2005), attention-deficit hyperactivity disorder (Rubia et al., 2021), Parkinson's disease (Ubeda Matzilevich et al., 2024), mild cognitive impairment (Lavy et al., 2019;

Marlats et al., 2020) and AD (Luijmes et al., 2016) as well as psychological disorders including major depression (Dobbins et al., 2023) and schizophrenia (Gandara et al., 2020). NFB can also be used in adult healthy individuals in order to enhance cognitive functions (Agnoli et al., 2018; Jiang et al., 2022; Zoefel et al., 2011). In healthy aging, Bielas and Michalczyk (2021) reported the efficacy of NFB as a method for enhancing executive functioning in the elderly. Campos da Paz et al. (2018) demonstrated that individuals, on average 70 years old, improved their working memory performance after NFB training, suggesting that NFB can benefit brain reserve in an aging population. However, Lecomte and Juhel (2011) found no improvement in memory performance following NFB training in subjects over 65. Electrophysiological NFB holds significant promise for individuals with SCD, as increasing evidence indicates alterations in neural oscillations within this population. Hence, Gouw et al. (2017) identified associations between abnormal delta, theta, and alpha power, as well as alpha peak frequency, and the clinical progression of the disease. Furthermore, abnormalities in the amplitudes of delta, theta and alpha rhythms have been observed in individuals with SCD when compared to healthy controls, indicating an atypical pattern of dominant cortical alpha rhythms (Babiloni et al., 2010). However, consensus regarding this association remains elusive due to the high heterogeneity among SCD subjects, which is notably influenced by variations in subject recruitment methods. The methodologies employed in sampling and recruitment play a pivotal role in SCD research (Rodríguez-Gómez et al., 2015). Notably, patients recruited from memory clinics often exhibit higher levels of cognitive impairment compared to those from general population samples (Kuhn et al., 2019). Additionally, discrepancies in the results may also be partly attributed to differences in the diagnostic criteria used for defining the study groups (clinical or biomarkerbased). To the best of our knowledge, only two studies have investigated NFB therapy's impact on cognitive performance in individuals with SCD to date. Andrade et al. (2022) employed NFB protocols targeting three biomarkers: peak alpha frequency (PAF), gamma-band synchronisation and the theta/beta ratio. Conversely, Pei et al. (2020) utilised NFB training focused on auditory mismatch negativity. However, in both cases, the training demonstrated limited efficacy in improving cognitive performance among SCD subjects, as assessed through various neuropsychological measures (Andrade et al., 2022) and working memory tests (Pei et al., 2020). One possible explanation for these modest outcomes could be attributed to the utilised NFB protocols. As of now, there remains no consensus on the optimal NFB protocols. Various protocols have been investigated in both healthy and unhealthy elderly populations, including those with mild cognitive impairment (MCI) and AD, encompassing alpha and alpha peak frequency, theta and theta peak frequency, sensorimotor rhythm (SMR) and beta bands (Jirayucharoensak et al., 2019; Laborda-Sánchez & Cansino, 2021; Marlats et al., 2020; Meeuwsen et al., 2021).

The present study contributes to the advancement of early therapeutic intervention for self-reported cognitive decline in memory or other cognitive domains, such as executive function or attention. To achieve this goal, we have concentrated on employing an individualised protocol, specifically tailored for each subject based on their EEG profile. The underlying premise is that EEG oscillation alterations in individuals with SCD are not standard but may be subject-dependent. Therefore, NFB training based on an individualised protocol should address the specific EEG power anomalies of each individual, potentially yielding greater efficacy. The advantage of using an individualised NFB protocol is that targeting specific EEG power anomalies is likely to be more effective than a one-size-fits-all approach, as it directly focuses on the areas where the individual needs the most improvement while avoiding the inefficiencies of training brain frequencies that may not be relevant or problematic for the participant. One could argue that such individualised training can more effectively harness the brain's capacity for neuroplasticity, leading to more significant and lasting changes in brain function and behaviour. The effects of this individualised training were assessed using EEG measurements and various questionnaires evaluating their subjective cognitive state. These effects were then compared to those of a standard protocol based on alpha band that was adjusted to the individual PAF. PAF corresponds to the discrete frequency with the highest magnitude within the alpha range. It is known to be slower in the elderly (Scally et al., 2018) and to vary across individuals (Bazanova, 2012; Klimesch, 1999), making it essential to consider. The Pz location was chosen for PAF power training because it is a region where alpha activity is typically robust and stable especially when a person is in a relaxed state. This makes it an ideal site for detecting and modulating alpha activity. In addition to the standard NFB training group, an extra group was included in our analysis: a non-learner group. It has been repeatedly found that not everyone who receives NFB can regulate their brain signals in the desired direction, regardless of the NFB techniques used, such as EEG NFB and realtime functional magnetic resonance (fMRI) NFB (Haugg et al., 2021; Kadosh & Staunton, 2019). These participants, when indicated by the authors, are often referred to as non-responders, non-performers or non-regulators and represent up to 30%–50% of the population (Alkoby

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et al., 2018). The reasons for these inabilities still need to be identified. Given the non-negligible proportion of nonlearners, there is a strong need to include them in the analysis of our results. This group constitutes an interesting subset, as participants were subjected to exactly the same experimental conditions, with no associated ethical problems unlike participants subjected to sham-NFB. Sham-NFB involves a placebo or simulated NFB intervention, where participants believe they are receiving genuine NFB training but are actually receiving a fake or inert treatment. We hypothesised that SCD trained with an individualised NFB protocol would demonstrate superior regulation of EEG power control and self-reported cognitive enhancement compared to those in groups subjected to standard NFB training.

2 | MATERIALS AND METHODS

2.1 | Participants

The current study is part of a broader project investigating SCD in aging. The performances obtained in neuropsychological tests, questionnaires and EEG recordings of healthy elderly controls have been previously published (Paban et al., 2023). These data were utilised in the present study for comparisons with those obtained from the 36 SCD subjects specifically recruited for this study. Recruitment of these SCD individuals was conducted through general population advertisements. To be eligible, participants had to meet several inclusion criteria including independence in daily living, absence of medical, psychiatric or neurological conditions impacting brain structure or function, absence of depression (evaluated with the Geriatric Depression Scale [GDS]), absence of anxiety (assessed using the State Trait Anxiety Inventory forms Y-A and Y-B [STAI Y]), normal cognitive test performance, no use of psychoactive medications and no sensory impairments affecting cognitive testing. Exclusion criteria comprised clinical diagnoses of MCI or dementia, self-reported cognitive decline attributed to psychiatric or neurological disorders, history of head injury or relevant medical conditions, medication use impacting cognitive function or substance abuse. The classification of individuals as having SCD was determined based on their scores on the Cognitive Change Index (Self-report) (CCI-S), as described in Paban et al. (2023). Specifically, if their score on the first 12 items of the CCI-S, which pertain to memory concerns, was 20 or higher, they were classified as having memory concerns.

The present study was carried out in accordance with the Declaration of Helsinki and obtained approval from the 'Comité de Protection des Personnes Sud

Méditerranée' (agreement no. 19.09.12.44636-AF). Written informed consent was obtained from all participants. Initially, the 36 French subjects with SCD were randomly assigned to either the individualised NFB (Ind-NFB) training group ($n = 18$) or the Standard NFB (St-NFB) training group ($n = 18$). Both participants and the research assistant conducting the NFB sessions were unaware of the experiment's design.

2.2 | Experimental design

The experiments included NFB training, EEG resting state acquisition, neuropsychological tests and self-report questionnaires before and after the training. A pipeline is illustrated in Figure 1.

2.2.1 | NFB

NFB training consisted of two sessions per week until participants achieved a predefined success criterion, as outlined below. Each session started with a 3-min eyesopen baseline assessment, serving as a reference point for subsequent training phases. This baseline was succeeded by eight 3-min training intervals. The equipment employed for NFB training consisted of a ProComp Infiniti differential amplifier and software (Thought Technology Ltd., Montreal, Quebec). Electrodes were positioned either on participant-specific zones of interest for the Ind-NFB group or on the Pz location based on the international 10-20 system for the St-NFB group. The reference electrode was affixed to the left earlobe, while the ground electrode was attached to the right earlobe. Electrode sites were prepared with abrasive conductive gel (Nuprep, Weaver and Company, Colorado), and conductive gel (Ten 20 conductive paste, Weaver and Company, Colorado) was applied to electrode cups to maintain electrode impedance below 5 kV. The raw EEG signal was sampled at 256 Hz and online A/D converted for feedback processing. Using the BioGraph Infiniti software, an IIR (infinite impulse response) filters were applied to the recorded signal to extract frequency-domain information. Spectral amplitude estimates were calculated for the active site on raw 1-s EEG segments with a frequency resolution of 1 up to 30 Hz. Bandpass filters were used to extract the reward EEG frequency bands (Ind-NFB group: subject-specific frequency bands; St-NFB group: PAF \pm 1 Hz) through fast Fourier transformations (FFT). Participants received audio–visual feedback via customisable videos (e.g. rollercoaster, facial animations, landscapes) accompanied by preferred pleasant sounds upon goal attainment. We employed this variety in feedback format

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FIGURE 1 Schematic representation of the experimental design. EEG, electroencephalography; NFB, neurofeedback.

in order to overcome boredom and maintain participants' engagement in modulating their target frequencies. The participants were encouraged to let the video progress and sustain the production of sound for as long as possible. Participants were not instructed on specific strategies; instead, they were encouraged to actively explore mental strategies in a trial-and-error fashion. These strategies aimed to elicit various mental content involving perceptual, imaginative, cognitive or metacognitive components, leading to a defined neural change. At the end of each NFB training session, three additional 3-min sessions were included. During these sessions, no feedback was provided; however, the EEG signal was still recorded to assess whether the subject achieved the training goals or not. Participants sat in front of a computer screen that displayed no information. They were instructed to keep their eyes open and to replicate the mental strategies they had used to achieve the training goals. Lastly, in each session without NFB, participants were asked to self-assess their ability to voluntarily control their brain waves on a 6-point Likert scale: 0% (absolutely no control), 20%, 40%, 60%, 80% and 100% (complete voluntarily control). The measure used to assess this subjective evaluation was the prediction error. This measure (expressed in absolute value) consisted of subtracting the judgment score from the actual performance score. The judgment score was the mean of the response given to the question divided by 100. The actual performance corresponded to the mean number of successful sessions. Prediction error varies between 0 and 1, with 0 indicating perfect agreement between the judgment and the actual performance and 1 indicating that the subject's judgment does not correspond at all to the actual performance.

To ensure that all participants achieved the training goals, the number of sessions was not predefined. Instead, the training continued until subjects reached a learning criterion, which was arbitrarily set at achieving three consecutive successful sessions. The criteria for determining whether a NFB session is successful is a topic of ongoing debate in the literature, with no clear consensus. In the present study, we define a session as successful if the power of the targeted frequency band exceeds or falls below the baseline power, depending on the specific NFB protocol used for each subject. Based on this criterion, 12 subjects were classified as nonlearners as they did not meet this requirement, with seven belonging to the Ind-NFB group and five to the St-NFB group. These subjects abandoned the task before achieving the success criterion. The reasons for abandonment are various, including fatigue from attending the laboratory, additional health issues and difficulties with transportation. Consequently, we analysed the results with three groups of subjects: the Ind-NFB group $(n = 11)$, the St-NFB group $(n = 13)$ and the non-learner group ($n = 12$). The inclusion of the non-learner group serves as a control measure, as these participants received identical instructions and experienced the same interactions as those in the two NFB training groups.

The EEG signals recorded with BioGraph Infiniti were analysed offline using homemade software, which includes Welch's method to compute the power spectral density (PSD), converted to amplitude (μ V²/Hz), and Hilbert's method to elaborate the frequency-time distribution of signal amplitude. This software was written in Python and is available upon request. This distribution indicates the percentage of time a given frequency is **6 WILEY-EN** EIN European Journal of Neuroscience **FENSIER**

present in a signal, allowing determination of the duration spent by the subject above or below the baseline at each frequency considered. These two analyses were assessed during each session with and without NFB at the site of interest for the frequency band target, as well as for three other frequency bands named (1) Band of frequency 1 (Bf1), defined as the frequency band target \pm 2 Hz; (2) Band of frequency 2 (Bf2), defined as Bf1 \pm 3 Hz; and (3) band of frequency 3 (Bf3), defined as the frequency bands beyond Bf2. The underlying idea was to evaluate whether the voluntary control of waves was specific to the frequency band of interest or not. The results are expressed as the percentage change in signal between the last NFB training session and the baseline. Therefore, regardless of the NFB protocols used (whether increasing or decreasing specific frequency bands), the data remain comparable.

The analysis of EEG signals (spectral amplitude and time-frequency) was conducted using analysis of variance (ANOVA) with post hoc Newman–Keuls paired comparisons. Additionally, the comparison between pre- and post-training was performed using parametric t-tests for paired samples (within subjects) and independent samples (between groups) processed with XLSTAT 2019. 3.2 software. Two-tailed *p*-values were reported for all analyses, with correction for multiple comparisons (by using the Benjamini–Hochberg procedure).

2.2.2 | Pre-and post-training EEG acquisition and signal processing

For EEG acquisition pre- and post-training, two 5-min EEG recordings were collected for each assessment, one with eyes closed and one with eyes open. EEG data were collected using a 64-channel Biosemi ActiveTwo system (Biosemi Instruments, Amsterdam, The Netherlands), following the standard 10–20 system montage. Additional bilateral electro-oculogram electrodes were included to monitor horizontal eye movements. Anatomical measurements at the nasion-inion and preauricular points were taken to locate each participant's vertex site. Data were digitised at 1024 Hz sampling rate, with electrode impedance maintained below 20 kΩ. EEG post-training acquisition was conducted 10 days after the final NFB session.

EEG data preprocessing was conducted using the EEGLAB software (Delorme & Makeig, 2004). Recordings were bandpass filtered (.5–70 Hz) and offline downsampled to 256 Hz. Data preprocessing followed the PREP pipeline outlined by Bigdely-Shamlo et al. (2015). Segmentation into consecutive 2-s epochs was performed, and independent component analysis (ICA) was applied to remove artifacts from eye blinks, movement and

motion. The SASICA plugin was used for IC classification to guide artifact IC selection (Chaumon et al., 2015). The number of rejected ICs varied across participants (3 to 10). PSD analysis was conducted on an average of 100 artifact-free segments per participant. For each SCD subject, PSD was assessed in 1 Hz bins from 1 to 30 Hz at every electrode location. Only PSD assessed at the electrode of interest and the frequency band targeted during NFB sessions was compared between pre- and posttraining phases. The statistical analysis of these PSD results was conducted using the XLSTAT software. An one-sample ANOVA was utilised to compare the three groups: Ind-NFB, St-NFB and the non-learner group. Two-tailed p-values were reported, with correction for multiple comparisons.

The EEG signals recorded during the pre-training phase were utilised to develop individualised NFB protocols. Specifically, the EEG signal assessments for each subject were analysed using the Neuroguide 3.2.4 software (Applied Neuroscience, Inc.) and visually inspected by a clinician certified by the Biofeedback Certification International Alliance [\(https://www.neuroconnexion.fr/](https://www.neuroconnexion.fr/)). This process aimed to identify the most suitable NFB protocol based on the unique findings observed in each individual. Briefly, Neuroguide is a sophisticated software tool designed for analysing EEG power and connectivity measures. It allows for the importation of previously recorded EEG data and processes it into topographical images of the brain. Additionally, it provides a Z-score standardised database, which is instrumental in comparing and analysing brainwaves. Neuroguide is the most commonly used analytics tool in the field due to its stability and practical application (Thatcher et al., 2003). The NFB protocol used for the 11 subjects in the Ind-NFB group is illustrated in Table S1. The pretraining EEG signal assessments were also used to establish standard NFB protocols. Specifically, the individual alpha frequency ranges were determined based on the subject's PAF, which is the frequency showing the highest spectral amplitude within the 7 to 13 Hz band. Therefore, for each subject, the alpha frequency band trained was PAF \pm 1 Hz. The EEG signals recorded during the post-training phase were intended to assess whether the EEG profile was restored by the NFB training. During this recording, the subject was instructed to be in a similar mental state as during the pre-training phase; that is, they should not replicate the strategy acquired during NFB sessions.

2.2.3 | Pre- and post-training psychological evaluation

In the pre-training assessments, participants underwent a battery of neuropsychological tests and completed selfreport questionnaires, as previously described (Paban et al., 2023). The neuropsychological tests included the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), the RL/RI-16 Test (Grober & Buschke, 1987), the Boston Naming Test (BNT) (Kaplan et al., 2001), the Stroop Color Word Test (Scarpina & Tagini, 2017), the Digit Span backward (Wechsler, 2018), the Trail Making Test forms A and B (Tombaugh, 2004), the Letter and Category Verbal Fluency test (Benton, 1968) and the Rey-Osterrieth Complex Figure Copy (Berry et al., 1991). The questionnaires included the Cognitive Change Index (Self-report) (CCI-S) assessing memory performance, executive function, and language (Rattanabannakit et al., 2016); the State Trait Anxiety Inventory form Y-A (STAI Y-A) (Spielberger et al., 1983); the Meta-Cognitions Questionnaire 30 (MCQ-30), covering five domains: Positive Beliefs; Beliefs about Uncontrollability and Danger; Cognitive Confidence, Beliefs related to Superstition, Punishment and Responsibility; and Cognitive Self-Consciousness (Dethier et al., 2017); the French version

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of the Rosenberg Self-Esteem Scale (Gana et al., 2005); and the WHOQOL-OLD, encompassing six domains: Sensory Abilities; Autonomy; Past, Present and Future Activities; Social Participation; Death and Dying; and Intimacy (Leplège et al., 2013).

In the post-training assessments conducted 10 days after the completion of NFB training, participants completed only the aforementioned five questionnaires. CCI-S scores were the primary outcome in this study, while all other measures constituted the secondary outcomes. Participants were also asked to self-assess the beneficial effects of their NFB training using a 10-point scale, ranging from 0 (absolutely no benefits) to 10 (full of benefits). The question asked was: 'On the scale below, indicate to what extent you believe the NFB training sessions have been beneficial to you?'

Demographic measures, neuropsychological tests and self-report questionnaires were analysed using the XLSTAT software. A one-sample ANOVA was used to compare the three groups: Ind-NFB, St-NFB and the nonlearner group. Paired t-tests were employed for pre- and

TABLE 1 Group means and standard deviation (SD) of demographical and neuropsychological characteristics of individuals with subjective cognitive decline (SCD) ($N = 36$), categorised into three neurofeedback (NFB) groups: individualised NFB (Ind-NFB) training group, standard NFB (St-NFB) training group and non-learner group. Data from the non-SCD group have been previously published in Paban et al. (2023) and are included here as a control group for the present study. MMSE: Mini-Mental State Examination. CCI-S: Cognitive Change Index (Self-report).

post-training comparisons. Two-tailed p-values were reported, with correction for multiple comparisons.

3 | RESULTS

3.1 | Neuropsychological analysis

The 36 individuals with SCD ranged in age from 60 to 81 years, with a mean age of 70.53 ± 7.51 years; 27 were women. They were divided into three NFB groups: individualised NFB (Ind-NFB) training group, standard NFB (St-NFB) training group and non-learner group. All participants completed a battery of neuropsychological tests and questionnaires. Education levels varied from 8 years of schooling to a PhD degree. Table 1 summarises the main demographic and neuropsychological characteristics of all subjects. Note that data from the non-SCD group were previously published in (Paban et al., 2023). There were no significant differences among the four groups (non-SCD, Ind-NFB, St-NFB and non-learners) regarding age, gender and years of education. Individuals with SCD exhibited a CCI-S score above 29.77 ± 5.28 on the first 12 items, surpassing the cutoff value established in the Alzheimer's Disease Neuroimaging Initiative (ADNI) study (see <http://www.adni-info.org>). Furthermore, they demonstrated normal results on neuropsychological evaluations, consistent with the expected performance range for SCD individuals on such tests.

3.2 | NFB data analysis

3.2.1 | Analysis of sessions with NFB

The analysis of the number of training sessions completed by each group revealed a significant difference between the non-learner group and the other two groups (Ind-NFB and St-NFB) ($p \leq .02$, post hoc analysis) (Figure 2). Non-learner participants completed an average of 5 more sessions than those in the Ind-NFB and St-NFB groups (ANOVA, $F[2, 36] = 4.16$; $p = .02$).

The changes in signal amplitude assessed between the last NFB session and the baseline are depicted in Figure 3. An ANOVA performed among the three groups revealed a significant difference when the changes in signal amplitude were assessed at the frequency band target (Figure 3a) $(F[2,36] = 49.99; p < .0001)$. Post hoc analyses indicated that the non-learner group differed from the other two groups ($p \leq .0001$), as the percentage of signal changes was null or decreased instead of increased. In the Ind-NFB and St-NFB groups, participants exhibited an average performance alteration of 16%, with some

FIGURE 2 Number of sessions of NFB training in the individualised NFB (Ind-NFB) training group, standard NFB (St-NFB) training group and non-learner group. NFB, neurofeedback.

subjects showing changes exceeding 25% compared to baseline levels, including one subject with approximately 43%. It is worth noting that there was no difference between these two groups; both groups exhibited similar changes in signal amplitude. The results of the changes in signal amplitude at the other frequency bands are shown in Figure 3b. One-sample ANOVA yielded no significant effect in the Ind-NFB group $(F[3,30] = 1.29)$; $p = .28$), indicating that a modification of the amplitude of the EEG signal was observed in individuals with SCD subjected to an individualised training protocol, regardless of the frequency bands analysed. In the other two groups of subjects, a significant effect was observed (F $[3,36] = 8.29$; $p < .0001$ in St-NFB and $F[3,33] = 3.20$; $p = .03$ in non-learner groups), suggesting that the NFB training affected the frequency bands differently. Specifically, in the St-NFB group, Bf3 was not affected compared to the other frequency bands (post hoc, $p \leq .003$). The changes in signal amplitude were comparable between all the other bands; that is, the target frequency band was altered similarly to the closest frequency bands (Bf1 and Bf2).

The time-frequency analysis performed to determine the duration spent by the subject above or below the baseline revealed results consistent with the spectral amplitude analysis. These results are illustrated in Figure 4. In the target frequency band, both the Ind-NFB and St-NFB groups spent approximately 60% of their time above the baseline, whereas the non-learner group spent less than 40% (Figure 4a) $(F[2,36] = 20.56; p < .0001)$. Figure 4b demonstrated that subjects, regardless of their group, spent an equal amount of time in the frequency

FIGURE 3 Signal amplitude changes between the last NFB session and the baseline in the individualised NFB (Ind-NFB), standard NFB (St-NFB) training groups and non-learner group. Changes were assessed (a) at the target frequency band and (b) at three additional frequency bands: band of frequency 1 (Bf1), defined as the target frequency band \pm 2 Hz; band of frequency 2 (Bf2), defined as Bf1 \pm 3 Hz; and band of frequency 3 (Bf3), encompassing frequency bands beyond Bf2. NFB, neurofeedback.

band they need to learn to modulate voluntarily, as they did in the other bands ($p \geq .35$).

3.2.2 | Analysis of sessions without NFB

After completing each NFB training session, three extra 3-min sessions were incorporated, during which no feedback was provided. Results obtained on the changes in signal amplitude between the last session without NFB and the baseline are presented in Figure 5. An ANOVA conducted among the three groups unveiled a significant

FIGURE 4 Time-frequency analysis in the individualised NFB (Ind-NFB), standard NFB (St-NFB) training groups and non-learner group. Analysis was performed (a) on the target frequency band and (b) on three additional frequency bands: band of frequency 1 (Bf1), defined as the target frequency band \pm 2 Hz; band of frequency 2 (Bf2), defined as Bf1 \pm 3 Hz; and band of frequency 3 (Bf3), covering frequency bands beyond Bf2. NFB, neurofeedback.

difference when analysing the changes in signal amplitude at the target frequency band $(F[2,36] = 8.89;$ $p = .001$). Post hoc analyses revealed a distinction between the non-learner group and the other two groups $(p \leq .001)$. Within the Ind-NFB and St-NFB groups, participants exhibited an average performance increase of 13%, with some individuals showing over 30% augmentation compared to the baseline. Notably, no disparity was observed between these two groups; both demonstrated similar alterations in signal amplitude. The results

FIGURE 5 Signal amplitude changes were assessed during sessions without NFB. The data depict the percentage of alteration between the last session without NFB and the baseline in the individualised NFB (Ind-NFB), standard NFB (St-NFB) training groups and non-learner group. Changes were evaluated at the target frequency band. NFB, neurofeedback.

FIGURE 6 Prediction error evaluated in the individualised NFB (Ind-NFB), standard NFB (St-NFB) training groups, and nonlearner group. NFB, neurofeedback.

concerning changes in signal amplitude at other frequency bands were not showed.

At the end of each session without NFB, participants were asked to self-assess their ability to voluntarily control their brain waves using a 6-point scale. A measure of prediction error was calculated, and the data are presented in Figure 6. An ANOVA revealed no statistical difference between the three groups: Ind-NFB, St-NFB and non-learners ($p \geq .54$), suggesting that all groups had a similar prediction error of approximately .2. This low score indicates that both learners and non-learners had a good understanding of their performance even without NFB. Learners, regardless of the NFB protocol used, knew they were capable of achieving the training goals.

Non-learners recognised that they had not succeeded in reaching the NFB objective.

3.3 | Pre- and post-training evaluations

3.3.1 | EEG signal analysis

To investigate changes in the EEG data acquired with the 64-electrode cap 10 days after the last NFB training session, paired t-tests were performed on the EEG signal between the post-training EEG acquisition and the pretraining EEG acquisition for each group. Results are shown in Figure 7 and Figure S1. No statistical difference was demonstrated regardless of the group considered $(p \ge .61)$, indicating that the EEG signal did not change after NFB training for any of the groups. The PAF values in the St-NFB group did not show any changes following the NFB training (Table 2).

3.3.2 | Questionnaires score analysis

Pre-post comparisons of the questionnaire scores revealed no statistical differences regardless of the questionnaire used (Table 3), indicating similar performance across the three groups before and after the NFB training.

Interestingly, when asked to self-assess the beneficial effects of their NFB training using a 10-point scale, all participants reported experiencing benefits, including those in the non-learner group. However, an ANOVA conducted on the three groups revealed a statistical effect $(F[2,34] = 3.95; p = .03)$. Post hoc paired comparisons indicated that both the Ind-NFB and St-NFB groups had significantly higher scores than the non-learner group $(p \le .02)$.

4 | DISCUSSION

The theoretical foundation of NFB training suggests that altering brain activity in accordance with targeted changes in the EEG signal can induce plastic reorganisation within the relevant brain networks, potentially resulting in improved performance on specific behavioural tasks. This assumption underlies the use of NFB training as a potential therapeutic intervention for individuals with SCD. To date, various interventions for SCD, including psychological, cognitive, lifestyle or pharmacological approaches, have been attempted with limited noticeable effects (Bhome et al., 2018; Roheger et al., 2021). Pereira-Morales et al. (2018) demonstrated

 (a)

 (b)

FIGURE 7 Pre- and post-training EEG power spectral density (PSD, μ V²/Hz) for (a) individualised NFB, (b) standard NFB training subjects and (c) non-learner subjects. Changes were measured for each participant at both the electrode of interest and within their target frequency band. The cross indicates the group mean. EEG, electroencephalography; NFB, neurofeedback.

improvements in cognitive functioning, particularly in short-term memory, in SCD participants following complex cognitive training programs comprising computerised and traditional exercises. The findings of our study indicate that despite an average age of 70.53 \pm 7.51 years, SCD subjects were able to voluntarily regulate their brainwaves in terms of signal amplitude and time spent above or below the baseline. This effect was observed in approximately two-thirds of the participants, with no significant difference between the two NFB protocols. Individuals who underwent either individualised or standard NFB training were able to modulate the power of their target frequency relative to their baseline. In a recent meta-analysis, Lin et al. (2024) suggested that NFB may enhance memory (both general and episodic) in both healthy elderly individuals and those with MCI.

These findings support previous evidence indicating that the aging brain can undergo training and improvement despite anatomical and pathological constraints (Jiang et al., 2017). Numerous studies on the aging brain have suggested the presence of plasticity, with continuous structural and functional reorganisation (Kanishka & Jha, 2023).

The data from the current study were analysed following the recommendations outlined by Enriquez-Geppert et al. (2017) and Ros et al. (2020). Specifically, the analysis focused on EEG signals during NFB sessions, as well as before and after training. Additionally, consideration was given to other EEG rhythms. This rigorous analysis revealed that the ability of individuals with SCD to modulate EEG signal power and duration targeted at specific frequencies was not specific to the goal **12 WILEY-EIN** Einopean Journal of Neuroscience **FENS**

TABLE 2 Peak frequency within the alpha band (8–12 Hz) in participants of the standardised-NFB group before and after NFB training.

Subject no.	Before training	After training
$\mathbf{1}$	10	10
$\overline{2}$	11	11
3	9	9
$\overline{4}$	9	9
5	8	9
6	10	11
$\overline{7}$	9	9
8	8	8
9	11	10
10	12	12
11	8	8
12	9	9
13	10	9

frequency. The analysis of EEG signals recorded using an advanced EEG cap indicated no discernible alteration in signal power between pre- and post-NFB training sessions, regardless of the NFB protocols used. It is noteworthy that, following the individualised protocol, the specific EEG power anomalies in each individual were not corrected. Moreover, no significant effects were noted on questionnaire scores when comparing pre- and post-NFB training assessments.

The protocol of NFB training used in the present study incorporated various innovative aspects to address several issues. One crucial aim was to ensure consistent levels of achievement by the conclusion of the NFB training. This is particularly significant as it could potentially account for the heterogeneity observed in NFB's outcomes (Thibault et al., 2016). To address this concern, we established a success criterion, selected arbitrarily but grounded in learning paradigms observed in animal studies (Paban et al., 2005). Regardless of the chosen criterion, its utilisation enables us to assert confidence in the participants' accomplishment of their training objectives. Thus, the effect attributed to the NFB training can be more accurately assessed and understood within the context of the established success criterion. This approach is crucial as it provides a standardised measure for evaluating participant progress and ensures consistency in assessing the efficacy of the NFB intervention. To our knowledge, no study in the literature has reported the use of such a success criterion in their NFB training paradigm. However, Lin et al. (2024), in their meta-analysis, introduced the notion of an adequate training time,

defined as 300 min or more of NFB training, to achieve successful outcomes in memory in the elderly.

A second criterion was employed to assess participants' abilities to regulate their brainwaves. This involved the introduction of additional 3-min sessions without NFB at the end of each training session. During these sessions, participants were instructed to replicate their strategies to achieve training goals while no feedback was provided. Interestingly, the EEG signal recorded during these sessions corroborated the subjects' performances during the training phase. In other words, subjects who had acquired the ability to voluntarily regulate their EEG rhythm during training with NFB exhibited good performances during sessions without NFB. The subjective evaluation conducted at the end of these extra sessions yielded similar conclusions. Participants, regardless of the group they belonged to, demonstrated a good understanding of their performance even without NFB. Learners were aware of their ability to achieve the training goals, whereas non-learners acknowledged their failure to attain the NFB objective. Interestingly, Fassi et al. (2024) discussed in their review the significance of individuals' subjective beliefs in assessing treatment efficacy. Specifically, they emphasised the importance of considering participants' subjective perceptions and how they interact with objective treatment measures when evaluating the effectiveness of treatments, in both clinical and non-clinical studies. Another important objective behind incorporating these three sessions without feedback was to facilitate the transfer of participants' acquired skills to real-life situations. It is crucial for participants to be able to effectively apply these newfound abilities in various contexts, beyond the controlled setting of the training sessions. This ensures that the skills learned during the training program have practical relevance and can positively impact participants' everyday lives.

The number of sessions necessary to meet the success criterion ranged from 4 to 22. Consequently, certain participants demonstrated a remarkable ability to develop strategies for regulating the power and duration of the targeted EEG signals. Although not systematically assessed in the current study, informal discussions with participants suggest that individuals familiar with practices such as meditation, mindfulness, yoga and tai chi may have found it easier to acquire the mental strategies required for voluntary regulation of brainwaves (Friedrich et al., 2014).

The implementation of a success criterion has enabled us to identify individuals who did not meet this criterion. Such participants are commonly referred to in the NFB literature as non-responders, non-performers or non-regulators (Jackson et al., 2023; Kadosh & Staunton, 2019). However, for the purposes of the present

TABLE 3 Group means and standard deviation (SD) of pre- and post-scores assessed in the individualised NFB (Ind-NFB) training group, standard NFB (St-NFB) training group and non-learner group for the five questionnaires used as outcome measures: Cognitive Change Index (Self-report) (CCI-S), the State Trait Anxiety Inventory form Y-A (STAI Y-A), the Meta-Cognitions Questionnaire 30 (MCQ), the French version of the Rosenberg Self-Esteem Scale (SES) and the WHOQOL-OLD (p: two-tailed p-values).

study, the term 'non-learners' appeared more fitting. This choice was based on the observation that these subjects exhibited difficulties in achieving the training objectives, indicating an inability to effectively acquire the strategies taught during the training sessions. In contrast, the term 'non-responders' typically denotes individuals who did not demonstrate the desired outcomes from the NFB training. When reviewing factors influencing interindividual differences in NFB performance, Kadosh and

Staunton (2019) highlighted the significance of various factors, including psychological, learning dynamics and neurophysiological factors. In our study, non-learners underwent, on average, a slightly higher number of training sessions than learners, though not significantly more (only five additional sessions). This suggests that session quantity alone may not be the decisive factor in achieving successful outcomes. Non-learners discontinued their participation in the experiment due to various reasons,

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such as fatigue from frequent laboratory attendance, additional health concerns, transportation difficulties and other personal challenges. Further exploration into factors contributing to successful skill acquisition and learning outcomes is warranted. Non-learners comprised approximately one-third of the participant pool, a proportion previously documented in the literature (Alkoby et al., 2018; Enriquez-Geppert et al., 2017; Weber et al., 2020). However, as highlighted in Jackson et al. (2023), the majority of studies did not provide information on the number of non-learners, which raises concerns about the reliability of this statistic. Additionally, the identification of these individuals lacks consistency in definition, further complicating the matter. Indeed, some authors have used the power of the target band as a criterion for success, requiring it to increase by at least 5% between the baseline and the last session of NFB (Rozengurt et al., 2017). In this study, we did not account for this factor. Some participants altered their EEG signal of interest by up to 25%, while others achieved only a 4% change in EEG signal. Previous authors, such as Smit et al. (2023), categorised participants as responders or non-responders to NFB training based on the regression slope calculated from a complex composite score. They demonstrated that the analysis conclusions varied depending on the inclusion of non-responder participants.

Two protocols of NFB training were utilised. The standard protocol aimed to instruct participants in increasing their PAF power. PAF represents a specific frequency at which alpha waves reach their maximum amplitude (Klimesch, 1999), typically observed in the posterior regions of the scalp and during closed-eye conditions. In the context of healthy elderly individuals or those with dementia, such NFB protocols have been implemented with varying degrees of success. Pioneering work by Angelakis et al. (2007) demonstrated that PAF power NFB training enhanced cognitive processing speed and executive function but did not yield significant improvements in memory among healthy aging participants. More recently, Lavy et al. (2019) observed significant enhancements in memory performance following PAF power training, with these improvements sustained at a 30-day follow-up. However, they noted that PAF power returned to baseline levels by this evaluation in subjects with MCI. Conversely, Andrade et al. (2022) found no significant effects of PAF power feedback training on subjects' cognition as assessed by neuropsychological tests in those with SCD. The individualised NFB protocol was specifically tailored for each subject based on their EEG profile. EEG signal alterations in individuals with SCD are not standardised but rather subjectdependent. Therefore, we found it compelling to employ

an NFB training based on an individualised protocol, as it could address the specific EEG power anomalies of each individual, potentially leading to greater efficacy. This factor appears significant and could potentially explain the heterogeneous data reported with NFB training (Thibault et al., 2016). Interestingly, among the 13 subjects who underwent the individualised protocol, the majority (nine subjects) focused on frequency bands between 12 and 18 Hz, corresponding to the beta band. Beta oscillations are known to play a significant role not only in sensorimotor functions but also in cognitive processes, particularly due to their association with attentional mechanisms (Gola et al., 2013). In aging, a reduction in beta frequency power has been observed across various brain regions (Babiloni et al., 2016). Individualised protocols have not been widely utilised previously. In Alzheimer's patients, Luijmes et al. (2016) demonstrated memory improvement in patients who received NFB treatment, as measured by the Cambridge Cognitive Examination (CAMCOG) test. Successful utilisation of quantitative EEG-guided NFB training has been reported in dementia patients. Surmeli et al. (2016) observed an increase in MMSE scores for all subjects, irrespective of dementia type (AD, vascular, or multiinfarct dementia), with an average MMSE score increase of 6 points. Additionally, Collura et al. (2010) showed in a series of clinical case studies that individualised NFB training effectively addressed EEG abnormalities.

In our study, the analysis of EEG signals acquired during NFB training revealed that regardless of the protocol used, the majority of SCD subjects were able to voluntarily modulate the power and duration of their EEG signal at the site of interest for the target frequency band. However, examination of other frequency bands indicated alterations in the EEG signal, suggesting a lack of specificity. It is worth noting that analysis of frequency bands other than the target one is rarely reported in the literature. Eschmann et al. (2020) showed that NFB training aimed at upregulating the theta band in young subjects is highly specific to that band, as no alterations in EEG signal were observed in other bands such as alpha and beta. In contrast, Chikhi et al. (2023) demonstrated that while trainability of high alpha amplitude during a single training session was possible, analysis of other frequencies revealed alterations in those bands, particularly an increase in the amplitude of the low alpha frequency while decreasing the amplitudes of delta, beta and gamma frequencies. In our analysis, we also aimed to examine the entire spectrum, analysing both adjacent frequencies (defined as the frequency band target ± 2 Hz) and non-adjacent frequencies (defined as the frequency band target \pm 5 Hz and beyond). Indeed, it is well known that EEG is an intricate, composite signal, consisting of a

superposition of many signals stemming from different sources. Therefore, it is not surprising that in this frequency interplay, acting on one frequency band affected the others. At a behavioural level, as suggested by Klimesch (2018), it is the interaction between different 'frequency domains' that constitutes the basis of cognitive and bodily functions. These results underscore the importance of considering the entire EEG spectrum in analyses of the electrophysiological effects of NFB training as well as behavioural outcomes.

When considering behavioural outcomes, regardless of the NFB protocol used, we did not observe any significant pre/post changes in EEG signals or self-report questionnaires. One possible explanation is that the targeted brain regions or frequencies may not have been optimal for inducing changes in self-reported outcomes, which could apply to both protocols. For instance, the use of the PAF power protocol at Pz might not have been the best choice, and in the individualised protocol, the clinician's decision, despite their expertise, may not have been ideal. The lack of transparency regarding the selection of individualised protocols raises concerns about the replicability of the study, highlighting the challenges associated with such tailored approaches. Future studies should address this issue in order to make the development of NFB protocols more standardised and reproducible. Another consideration regarding the absence of differences between pre- and post-training in EEG signals or self-report questionnaires is that combining NFB training with other interventions, such as cognitive training, mindfulness exercises or physical activity, could create a synergistic effect, potentially enhancing brain plasticity and improving self-reported outcomes. Additionally, a limitation of the present study may lie in the outcome measures used. Relying solely on self-reports might have overlooked meaningful effects that could have been detected through objective cognitive tasks, such as memory tests. Objective measures provide a more comprehensive understanding of cognitive changes and their impact on training outcomes. However, because individuals experiencing SCD do not exhibit discernible cognitive changes on objective assessments, it becomes arduous to pinpoint suitable outcome measures. This intricacy underscores the importance of refining evaluation strategies to accurately capture nuanced cognitive changes.

5 | CONCLUSION

This study demonstrated that individualised NFB training, tailored to each participant's EEG profile, did not result in more beneficial effects compared to a standard NFB protocol focused on increasing PAF power. While

participants in both protocols were able to voluntarily modulate their EEG signal power and duration, these effects were not specific to the targeted frequency band and did not lead to significant improvements in behavioural outcomes among individuals with SCD. Further research is needed to optimise NFB protocols and explore complementary approaches that may enhance the therapeutic potential of NFB interventions.

AUTHOR CONTRIBUTIONS

V. P.: conceptualisation, formal analysis, funding acquisition, writing—original draft. L. F.: investigation. A. W.: data curation. F. D. is a certified NFB expert by the Biofeedback Certification International Alliance.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data used in this manuscript are available from the corresponding author upon request and after approval by institutional authorities.

PEER REVIEW

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