Cognitive rehabilitation in a case of traumatic brain injury using EEG-based neurofeedback in comparison to conventional methods

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Severe traumatic brain injury residual cognitive impairments significantly impact the quality of life. EEG-based neurofeedback is a technique successfully used in traumatic brain injury and stroke to rehabilitate cognitive and motor sequelae. There are not individualized comparisons of the effects of EEG-based neurofeedback versus conventional neuropsychological rehabilitation. We present a case study of a traumatic brain injury subject in whom eight sessions of a neuropsychological rehabilitation protocol targeting attention, executive functions, and working memory as compared with a personalized EEG-based neurofeedback protocol focused on the electrodes and bands that differed from healthy subjects (F3, F1, Fz, FC3, FC1, and FCz), targeting the inhibition of theta frequency band (3 Hz–7 Hz) in the same number of sessions. Quantitative EEG and neuropsychological testing were performed. Clear benefits of EEG-based neurofeedback were found in divided and sustained attention and several aspects related to visuospatial skills and the processing speed of motor-dependent tasks. Correlative quantitative EEG changes justify the results. EEG-based neurofeedback is probably an excellent complementary technique to be considered to enhance conventional neuropsychological rehabilitation.

Keywords

Traumatic brain injury; Neurorehabilitation; Cognition; Neurofeedback; Virtual reality; Quantitative electroencephalography

1. Introduction

Severe traumatic brain injury (TBI) has a worldwide incidence of 73 cases per 100,000 people, a more significant burden in undeveloped countries [1]. Besides motor deficits, residual cognitive impairments significantly impact the quality of life of affected subjects [2]. It is estimated that between 10–20% of young people who have suffered TBI have residual long-term cognitive problems [3].

Rehabilitation and compensation of the affected cognitive processes are crucial to regain independence but require costly and intensive professional neuropsychological assistance.

EEG-based neurofeedback (EEG-NFB) is a technique in which, through brain-computer interfaces (BCI), subjects are trained to regulate the amplitude of a specific frequency band and are rewarded for doing so. This technique has been successfully used in TBI and stroke to rehabilitate learning and memory [4, 5], attention [6], and even as part of motor rehabilitation [7]. The effects of the therapy are reflected in the changes of neuropsychological scale scores and some characteristics of the EEG at rest [8, 9].

When designing an EEG-NFB protocol it is crucial to identify the target band associated with the specific cognitive deficit to treat. The selected band characteristics are transformed in visual or auditive real-time feedback. The subject can associate changes in the feedback coinciding with mental activities such as concentration or imagination. In this way, subjects can train self-identified actions leading to produce greater changes in the feedback. The changes produced in the selected EEG band are supposed to enhance or normalize the altered function [10].

Alpha and theta bands synchronization usually respond in opposite ways. In the resting state, the alpha band decreases and theta increases, when cognitive tasks are initiated; their variations opposite those described in the resting state. On one hand, Alpha band (8–12 Hz) is usually divided into high alpha and low alpha. Training in increasing desynchronization of the high alpha band in the frontoparietal region has led to improvements in working memory [11], desynchronization in the low alpha band is related to memory changes, and the high alpha band is related to attention [12]. On the other hand, Theta band (3.5–7.5 Hz) has been described as overexpressed in TBI, its variations have been associated with several cognitive functions, its increase is correlated with decreased attention [12], and its inhibition leads to improvement in working memory and verbal fluency [13, 14].

Besides, Beta band (12.5–30 Hz) is usually divided into high beta, mid beta and low beta. Within the low beta range,

we can differentiate the sensorimotor rhythm (SMR) (13–15 Hz), the activation of the SMR is correlated with movement inhibition [4], and improvement of concentration, sustained attention [15], semantic memory [16], working memory [17], and information processing facilitation [4]. Beta and theta band fluctuations have been correlated with memory and attention.

Given the heterogeneity of the TBI structural and network damages, EEG-NFB design needs to be individualized. Due to the frequency of impairment of these functions in TBI and the importance of these essential functions for the performance of more complex cognitive tasks, some authors have selected the increase of the beta band and the inhibition of theta as a primary objective to rehabilitate [17–20].

The use of virtual reality (VR) increases the immersion in EEG-NFB tasks in patients with low attention span, and this combination has been previously used to improve motor function after stroke [21, 22]. Still, there are no published protocols to our knowledge using VR and EEG-NFB to rehabilitate cognitive processes in TBI.

The main objective is to present a case of a TBI subject in whom a neuropsychological rehabilitation (NPS-R) protocol targeting attention, executive functions and working memory were compared with a personalized EEG-NFB protocol targeting the inhibition of theta frequency band (3 Hz–7 Hz) in frontal areas. We look for changes produced by both approaches on quantitative EEG (QEEG) and neuropsychological assessment of visuospatial and visuoconstructional skills, attention, visual learning, verbal learning, and executive function.

2. Participant and methods

This manuscript has been prepared using the CARE guidelines [23].

2.1 Clinical case description

A 20-year male with no past medical history presented for alternate rehabilitation interventions, 9-months post TBI. He was diagnosed with type III axonal damage using magnetic resonance imaging and received extensive cognitive and physical rehabilitation therapy. Since the family was looking for different choices, we proposed EEG-NFB as an option for rehabilitation. Baseline neurological examination revealed preserved consciousness with good orientation and apparently normal language skills interfered with moderate dysarthria. Cranial nerves exploration revealed left homonymous hemianopia. The patient was not taking any medication at the moment of the intervention.

2.2 A complete neuropsychological evaluation

A basal complete Neuropsychological evaluation was performed by an expert neuropsychologist (DDN). An operative and concise neuropsychological evaluation protocol were designed, based on the objectives of this study, to be iteratively applied in the same order in each evaluation. The battery of test included the following tests: Rey-Osterrieth Complex Figure (ROCF) [24] (copy, immediate and delayed recall); Trail Making Test (TMT-A and TMT-B) [25]; Stroop test [26]; FAS word fluency test [27]; Brief Test of Attention (BTA) [28]; Wechsler Intelligence Scale III (WAIS-III) (forward and reverse digit span, symbol search and digit-symbol coding tests) [29]; verbal learning test España-Complutense (TAVEC) [30] and Bells test [31].

2.3 Quantitative EEG (QEEG)

EEG was acquired in a resting state for one minute while the subject remained comfortable sited with eyes open.

An actiCHamp amplifier (Brain Vision LLC, NC, USA) was used to amplify and digitize the EEG data at a sampling frequency of 512 Hz. The EEG data were stored in a PC running Windows 7 (Microsoft Corporation, Washington, USA). EEG activity was recorded from 64 positions with active Ag/AgCl scalp electrodes (actiCAP electrodes, Brain Vision LLC, NC, USA) following the 10-20 system: Fp1, Fp2, AF7, AF3, AF4, AF8, F7, F5, F3, F1, Fz, F2, F4, F6, F8, FT9, FT7, FC5, FC3, FC1, FCz, FC2, FC4, FC6, FT8, FT10, T7, C5, C3, C1, Cz, C2, C4, C6, T8, TP9, TP7, CP5, CP3, CP1, CPz, CP2, CP4, CP6, TP8, TP10, P7, P5, P3, P1, Pz, P2, P4, P6, P8, PO9, PO7, PO3, POz, PO4, PO8, O1, Oz, O2. Ground and reference electrodes were placed on Fz and FCz, respectively.

EEG signal processing was carried out using MATLAB functions (The Math- Works Inc., Natick MA, USA), concretely the EEG Lab toolbox [32]. The continuous EEG signal for each channel was artifact-corrected by the Artifact Subspace Reconstruction (ASR) algorithm [33], disabling all parameters except the high-pass filter bandwidth (0.25–0.75) and the burst repairing (kurtosis >5). The signal was then band-pass filtered between 3 Hz and 31 Hz with a Finite Impulse Response (FIR) filter (order 846). After that, channels beyond five standard deviations of the average channel kurtosis were automatically rejected and spherically interpolated. Next, Independent Component Analysis (ICA) was performed, and artifact-related components were removed according to the Multiple Artifact Rejection Algorithm (MARA) [34].

The eLORETA algorithm [35] for source reconstruction was applied to the one-minute segment of the processed signal. The algorithm provided the source power for each of the 6239 voxels in which the algorithm divides the cortex, for six frequency bands: theta (4 Hz–7 Hz), low alpha (7 Hz–10 Hz), high alpha (10 Hz–13 Hz), low beta (13 Hz–18 Hz), mid beta (18 Hz–25 Hz) and high beta (25 Hz–30 Hz). The average source power standardized the source power of each voxel in the participant.

Besides, the Power Spectral Density (PSD) over the whole one-minute interval was extracted from the processed signal for each of the frequency bands mentioned above.

2.4 Intervention

The study comprised 3 phases over six weeks. During the first phase, the EEG-NFB intervention was applied in eight
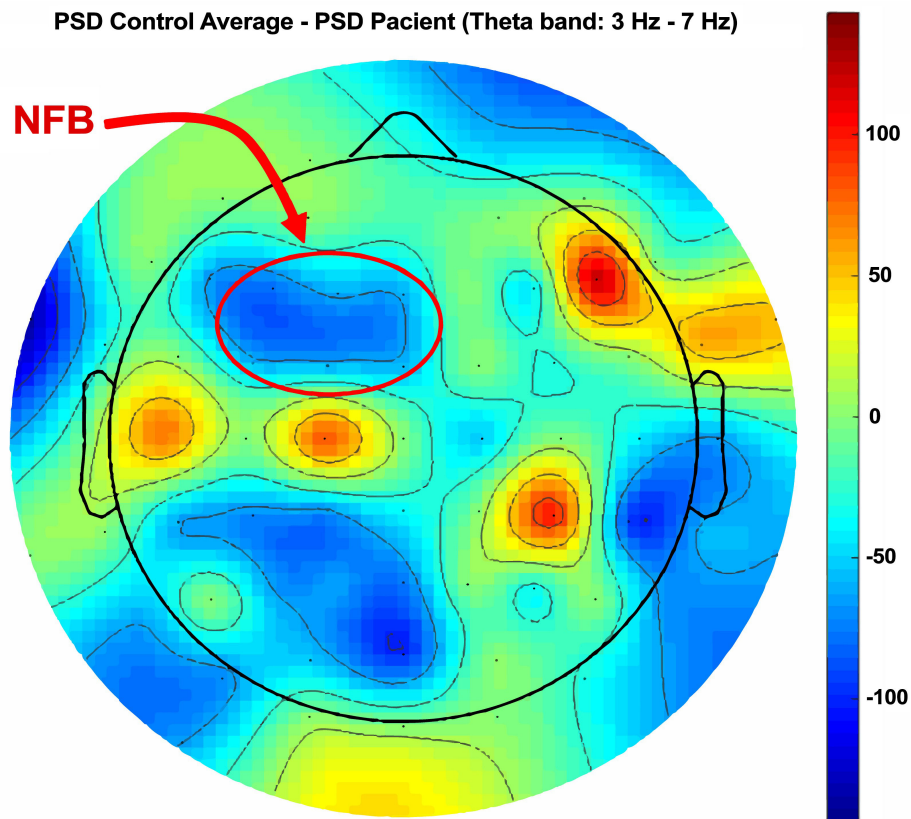
Fig. 1. Power Spectral Density (PSD) differences between the average of control participants and the patient participant in the theta frequency band (3 Hz–7 Hz). The circle comprises de electrodes targeted for neurofeedback (EEG-NFB) modulation in the theta band.

sessions along the two first weeks (four consecutive days each week). The second phase consisted of 2 weeks rest period without any type of cognitive rehabilitation. The third and last phase consisted of eight sessions of conventional neuropsychological rehabilitation (NPS-R) on four consecutive days each week.

2.4.1 EEG-NFB intervention

The EEG resting activity was recorded from the subject and three healthy controls (non-demented, non-depressed, not previous neurologic diseases, and currently not taking any medication) paired in age and education level with the subject.

The average PSD of the EEG of the healthy participants was contrasted with the PSD of the patient. After that, the channels and frequency band that presented the highest difference compatible with the patient dysfunction were targeted for the subsequent EEG-NFB intervention. Neuromodulation was based on theta band inhibition at the F3, F1, Fz, FC3, FC1 and FCz electrodes (Fig. 1).

In each EEG-NFB session, the patient intended to move an object in different virtual environments through immersive virtual glasses (Oculus DK2) with no explicit instruction. The goal was set to produce a normalization of the electrophysiological signal captured from the channels and frequency band identified by contrast with healthy participants. Before each

session, the EEG signal of these electrodes is captured at one-minute resting EEG. The average and standard deviation of the PSD for all electrodes and the frequency band identified are calculated for this period.

During the EEG-NFB session, the patient interacted with three different virtual scenarios for ten minutes each. Each scenario has a virtual object that moves in the scenario when the average PSD in windows of 0.5 seconds with a window step of 3 samples for the identified electrodes in the identified frequency band is at least a standard deviation lower than the average resting PSD.

The virtual scenarios were designed with Unity Engine 2018.1.9 (Unity Technologies, USA). The online processing of the EEG signal was carried out with NeuroRT Studio (Mensia Technologies Ltd., France). The two software platforms are communicated by TCP/IP.

2.4.2 Neuropsychological intervention

Each session had a duration of 45 minutes distributed as follows: rush hour traffic jam board game (deductive reasoning and cognitive flexibility, visual-spatial skills) [36] for 10 minutes; digit symbol coding copy task for 10 minutes; number cancellation task (supervisory control and processing speed) for 10 minutes and performing mental mathematical operations (working memory) 15 minutes. The neuropsychologist supervised the patient's execution during the

sessions, providing feedback regarding the mistakes made, helping the patient generate and apply the most appropriate strategies for the task and helping him to improve awareness of cognitive deficits.

2.4.3 Follow up and outcomes

Four neuropsychological and QEEG evaluations were performed: The first evaluation was made previous to neurofeedback intervention (A), the second one immediately after neurofeedback (B), the third one two weeks after the end of neurofeedback intervention and previous to neuropsychological intervention (C). Finally, there was a final evaluation on the last day of neuropsychological intervention (D).

Intervention adherence was complete and there was good tolerability with no adverse or unanticipated events.

2.5 Statistical analysis of neuropsychological results

The neuropsychological results were analyzed by calculating the different reliable change indexes (RCIs) proposed by Jacobson and Truax in 1991 since it has been readily employable [37]. To calculate the RCI index, it is necessary to know the standard deviation of the test and the test-retest reliability index's standard deviation. These data have been obtained from the application manuals for each of the tests applied. The results of z with a confidence level greater than 95% (<1.96 or >1.96) are considered a significant difference. The learning effect of the tasks was eliminated by using test-retest reliability in the analysis of results [37, 38].

2.6 Statistical analysis of EEG results

Since only one subject from the patient group, no statistical test was applied. The results show the PSD differences between the average activity among the healthy participants and the activity of the patient and the source power difference in the patient between the different time points.

3. Results

3.1 Baseline neuropsychological evaluation

Basal neuropsychological evaluation of this patient didn't have orientation impairments; perception was impaired by left hemianopia without hemi-negligence. Moderate attentional problems and decreased processing speed were also evidenced. Executive functions were characterized by impaired working memory and reduced cognitive flexibility with a tendency to perseverate. On the other hand, planning and sequencing were preserved without marked impulsiveness. Verbal and visual learning were moderately impaired. Naming, comprehension and repetition were preserved but interfered with by mild spastic dysarthria.

3.2 Neuropsychological changes after interventions

Scores of each neuropsychological measure and statistical analysis can be found in Table 1.

3.2.1 Visuospatial and visuo-constructional skills

As it is evident in ROCF copy the patient significantly improved after EEG-NFB ($d = 0.85$). This change persisted even

after the resting period C ($z = 2.15$; $d = 0.68$) with a slight additional improvement after NPS-R intervention D ($d = 0.17$).

3.2.2 Attention

BTA task improved significantly after EEG-NFB intervention (A/B $z = 6.74$; $d = 4$), losing a part of its effect after the resting period between interventions (A/C $z = 3.37$ $d = 2$; B/C $z = -3.37$; $d = 2$). There was again a significant improvement in response to NPS-R intervention (C/D $z = 2.25$ $d = 1.33$). Bells test performance improves after EEG-NFB (A/C $z = -3.06$; $d = 2.24$) but worsens after NPS-R, even overcoming the basal value measured in A.

3.2.3 Visual learning

As reflected by ROCF, short term memory, worsens after EEG-NFB in B ($z = -5.38$; $d = -1.69$) but return to initial values in C (B/C $z = 5.91$; $d = -1.86$) and has a further improvement in D after NPS-R intervention (C/D $z = 3.76$). In ROCF delayed recall we found a significant improvement in B ($z = 6.45$; $d = 2.33$) that persists in C (A/C $z = 7.52$; $d = 2.37$) but does not experience a further improvement after NPS-R intervention (C/D $z = -3.22$; $d = -1.01$).

3.2.4 Verbal learning

TAVEC immediate recall reflects a non-significant tendency to worsen after EEG-NFB intervention that recovers in C and has a significant extra improvement after NPS-R intervention (C/D $z = 2.47$; $d = 1.15$). In short term recall, there is a significant delayed improvement after EEG-NFB evidenced in C maintained through D with no extra improvement after NPS-R intervention. Delayed recall shows improvement after EEG-NFB intervention and additional improvement after NPS-R.

3.2.5 Executive function

There are no significant changes in the TMT test in any intervention. In WAIS-III we can see a tendency to improve after EEG-NFB in digit symbol test, symbol search and digits but not in a significant amount. There were no significant changes in FAS in any intervention. Finally, there is a significant worsening in the Stroop word-color condition after EEG-NFB with recovery in C and the tendency to worsen again after NPS-R.

3.3 Quantitative EEG

QEEG changes in response to EEG-NFB intervention reflect a reduction in power of Theta, Low alfa and Low beta bands at left frontocentral electrodes corresponding to a supplementary motor area (SMA) in B. This reduction is maintained over time, as seen in C. It is not seen after NPS-R intervention which produces a marked increase predominantly in theta, high beta, and high alpha in the upper central frontal zone bilaterally (BA6, pre-SMA) (Fig. 2).

There is an increase in power of all bands in the visual area (BA19) bilaterally and left superior parietal lobule (BA7) after EEG-NFB intervention. These changes do not persist in C and are not produced by NPS-R intervention.

Table 1. Neuropsychological results.

		A	B	C	D	A/B		A/C		B/C		C/D	
						z	d	z	d	z	d	z	d
	Copy SD: 2.95; r_{xx}: 0.95	26 (161 sc)	28.5 (119 sc)	28 (86 sc)	28.5 (83 sc)	**2.69***	0.85	**2.15***	0.68	−0.54	−0.16	0.54	0.17
Rey–Osterrieth complex figure test	Immediate memory SD: 2.95; r_{xx}: 0.95	25.5 (117 sc)	20.5 (66 sc)	26 (87 sc)	29.5 (92 sc)	**−5.38***	−1.69	0.53	0.17	5.91	−1.86	**3.76***	1.19
	Delayed memory SD: 2.95; r_{xx}: 0.95	21 (94 sc)	27 (90 sc)	28 (81 sc)	25 (65 sc)	**6.45***	2.33	**7.52***	2.37	1.07	0.33	**−3.22***	−1.01
TMT	A SD: 14.6; r_{xx}: 0.81	49	37	50	28	−1.33	−0.82	0.11	0.07	1.44	0.89	−2.15	−1.51
	B SD: 58,4; r_{xx}: 0.83	141	109	119	99	−0.94	−0.54	−0.65	−0.38	0.29	0.17	−0.59	−0.34
	Word SD: 18; r_{xx}: 0.88	34	46	43	40	1.36	0.67	1.02	0.5	−0.34	−0.33	−0.34	−0.33
Stroop	Color SD: 14; r_{xx}: 0.79	40	34	36	40	−1.32	−0.42	−0.44	−0.29	−0.02	−0.14	0.44	0.29
	Word-Color SD: 10; r_{xx}: 0.71	34	23	34	28	**−2.68***	−1.1	0	0	**−2.68***	−1.1	−0.79	−0.6
FAS	SD: 10.4; r_{xx}: 0.72	13	16	13	4	0.38	0.29	0	0	−0.88	−0.38	−1.15	−0.29
BTA	SD: 1.5; r_{xx}: 0.82	13	19	16	18	**6.74***	4	**3.37***	2	**−3.37***	−2	**2.25***	1.33
WAIS III: Digit-Symbol	SD: 17.48; r_{xx}: 0.81	37	45	42	34	0.74	0.46	0.46	0.28	−0.28	−0.17	−0.74	−0.46
WAIS III: Symbol search	SD: 8.17; r_{xx}: 0.76	21	25	15	17	0.72	0.49	−1.08	−0.73	−1.80	−1.22	0.35	0.25
WAIS III: Digits	Direct SD: 0.9; r_{xx}: 0.88	6	6	5	8	0	0	**−2.27***	−1.11	**−2.27***	−1.11	**6.81***	3.33
	Reverse SD: 1.8; r_{xx}: 0.88	3	5	4	4	**2.27***	1.11	1.13	0.55	1.13	0.55	0	0
TAVEC	Immediate SD: 5.19; r_{xx}: 0.89	29	25	30	36	−1.65	−0.77	0.41	0.19	**2.06***	0.96	**2.47***	1.15
	TAVECB SD: 1.71; r_{xx}: 0.89	3	3	4	3	0	0	1.25	0.58	1.25	0.58	−1.25	0.58
	Short term SD: 1.41; r_{xx}: 0.89	8	7	10	11	−1.54	−0.71	**4.61***	1.41	**3.07***	2.13	1.54	0.70
	Delayed memory SD: 1.20; r_{xx}: 0.89	7	9	9	11	**3.51***	1.67	**3.51***	1.67	0	0	**3.51***	1.67
Bells test	Time (omissions) DE: 2.9; r_{xx}: 0.73	149 (1)	120 (3)	84 (2)	155 (0)	−1.36	1	**−3.06***	−2.24	−1.69	−1.24	**3.34***	2.46

Note: SD, standard deviation; r_{xx}, reliability coefficient; TMT, Trail Making Test Parts A and B; FAS, F, A, S Word Fluency Test; BTA, Brief Test of Attention; WAIS III, Wechsler Intelligence Scale III; TAVEC, Verbal Learning Test España-Complutense; TAVECB, Verbal Learning Test España-Complutense Part B. A, B, C, D: measurements A, B, C and D respectively; z A/B value of z between measurements A and B, z B/C value of z between measurements B and C, z A/C value of z between measurements A and C and z C/D value of z between C and D measurements; d A/B value of d Cohen between measurements A and B, z B/C value of d Cohen between measurements B and C, d A/C value of d Cohen between measurements A and C and d C/D value of d Cohen between C and D measurements. * $p < 0.05$.

Bilaterally In the superior frontal cortex (BA8, 9), EEG-NFB intervention produces an increase in activity in Theta, Alfa and Low beta bands; this change does not persist in C. Still, a similar change is evidenced after NPS-R intervention.

In the left BA7, BA40 areas, in response to EEG-NFB intervention, have a power reduction in B's mid beta and high beta bands in B. This reduction is not maintained in C. After NPS-R intervention (D), there is a similar reduction in power of mid beta and high beta bands in BA40, but a more significant reduction is also seen in Theta, low Beta and Alpha bands (Fig. 2).

4. Discussion

The aim was to evaluate whether using an EEG-NFB protocol using VR improved a patient's cognitive performance with TBI and its comparison with conventional NPS-R rehabilitation.

EEG-NFB strategy was focused on the electrodes and bands that differed from healthy subjects, specifically the theta band, because according to previous reports, it is the one that is more related to cognitive processing of attention and significantly impaired in TBI [39]. We found that the electrodes that differed the most in theta band potency (higher than healthy subjects) were F3, F1, Fz, FC3, FC1 and FCz, so they were selected for the neuromodulation (the goal was set for inhibition of theta in these electrodes). These electrodes comprise Brodmann areas 6, 8 and 9 in the left hemisphere, and all these areas have a clear implication in cognitive functions. EEG-NFB intervention effectively produced a reduction in power of Theta, Low alfa and Low beta bands at left frontocentral electrodes (SMA); these changes were not produced after the NPS-R intervention showing the success of the neuromodulation strategy in the production of QEEG changes. QEEG is a mathematical interpretation of EEGs in a specific format to demonstrate and analyze relevant data. The automated events, topographic displays, source, and frequency of EEG signals are statistically analyzed [40].

Bilateral increases in activity in Theta, Alfa and Low beta bands in the superior frontal cortex (BA8, 9) after EEG-NFB intervention justifies changes in the performance of divided, preparatory and sustained attention [41]. These changes are correlated with BTA and bells test scales performance (divided and sustained attention) in measurement B. These effects in BTA are also seen after NPS-R intervention with similar changes evidenced in QEEG. A residual effect cannot be ruled out due to the short cleaning period, but both approaches are likely to evoke equivalent mechanisms.

Visuospatial and visuo-constructional skills evaluation after the use of EEG-NFB shows an improvement in two components of the Rey–Osterrieth complex figure test (ROCF) (copying and delayed recall) stands out. This may correlate with the increase in power of all bands in the visual area bilaterally and left superior parietal lobule after EEG-NFB intervention. Paradoxically, there is a worsening in immediate recall of the same test. Perhaps this worsening may be due

to a difficulty in suppressing the content interference of the visuospatial sketch pad, which is also reflected in the worsening of the interference control, from which the patient subsequently recovers, in the rest period after the EEG-NFB.

Described QEEG changes in bilateral visual areas and left superior parietal lobule are involved in locating objects in space and may result from virtual reality usage for this purpose [42, 43]. This may have probably conditioned a greater ability to mentally manipulate information and justify the improvement seen in BTA after EEG-NFB.

The increase evidenced in occipital areas activity and BA 40 can be linked to selective attention and visual search [44], corresponding to the improvement seen in digit-symbol and symbol search of WAIS-III test. The benefit of EEG-NFB is evident in several aspects that are related to visuospatial skills.

Memory changes have also been seen in response to studied interventions. Theta activity reduction seen in BA40 (inferior parietal lobule—supramarginal gyrus) in response to EEG-NFB and its amplification to alpha and beta bands in NPS-R may justify the increase seen delayed recall improvement after EEG-NFB and the additive effect of NPS-R seen in verbal learning tests [45].

Information retrieval is linked to the oscillation of the theta band in sub-cortical areas and increased in alpha in frontoparietal areas [46]; these data agree with our long-term visual and verbal learning results. We have not obtained significant differences regarding working memory, although there is a slight improvement in retaining reverse digits after EEG-NFB. The decrease in the score of the immediate memory in ROCF could be justified by an increased speed (50%-time reduction) of the test performance after EEG-NFB that goes back to normal in C.

Executive function effects are reflected by the improvement evidenced in processing speed in some motor-dependent tests such as ROCF and TMT. This may be justified by increasing alpha activity and decreasing theta activity in frontal areas [12, 47]. The use of VR linked to EEG-NFB has been previously shown to improve motor function [22], associated with decreased theta activity in central regions linked to motor preprogramming (BA 6 and 8) [48].

Some limitations must be considered. First, the immediacy of the EEG recording after the last EEG-NFB session could have masked the changes produced by the use of virtual reality as maybe the activation of the occipital regions was so evident.

Second, neuropsychological rehabilitation and compensation protocols use to be longer than eight sessions in real-life clinical interventions. The washout period of 15 days may have been too short of ruling out an influence of EEG-NFB over NPS-R results [49].

Finally, the unique case study has the advantages of an individualized intervention and evaluation strategy and has drawbacks of not easily generalizable results.

On the other hand, the strength of a single case study is that it eliminates the loss of information due to the averaging
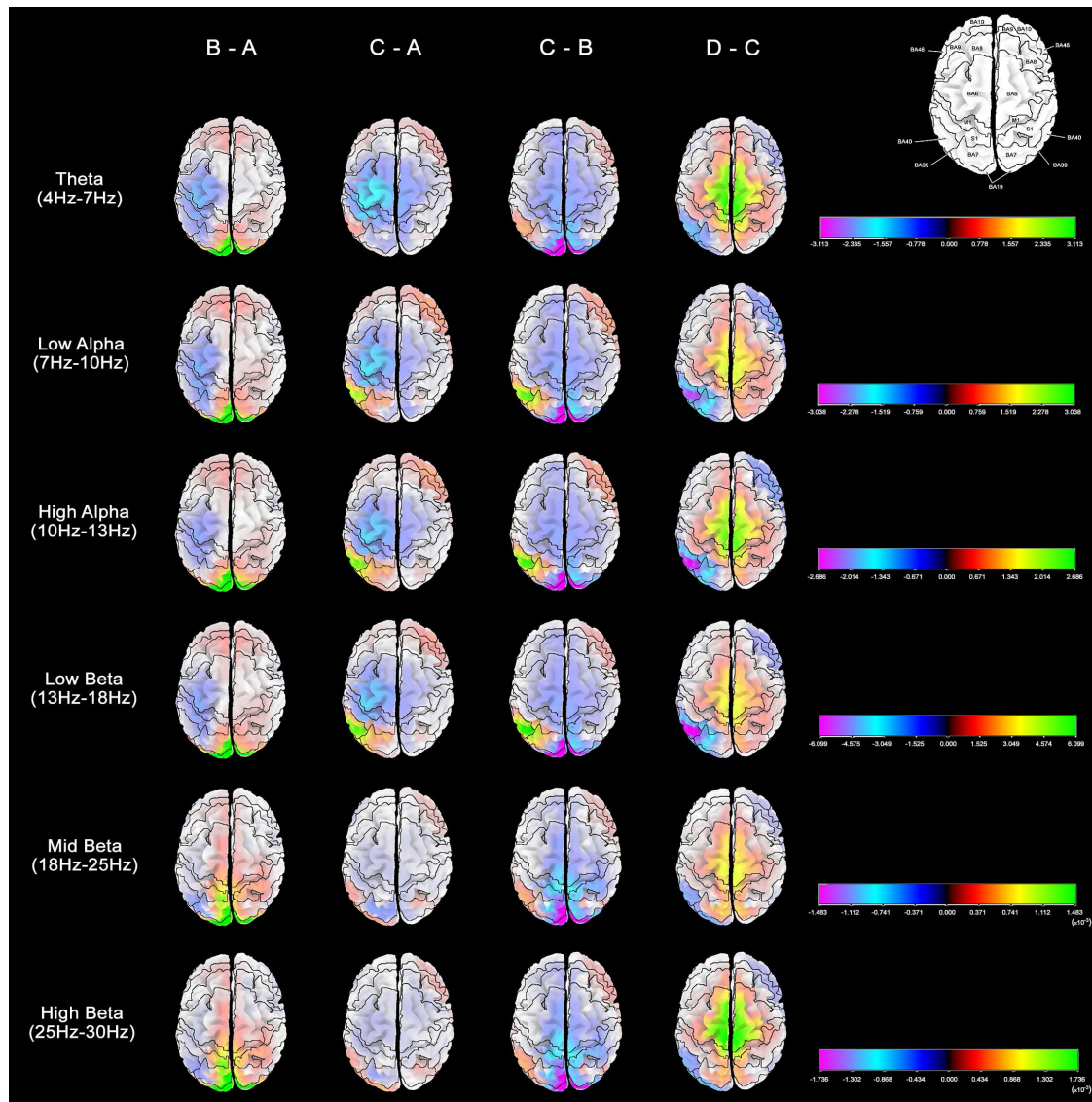
Fig. 2. The patient's source power differences at rest between time points (columns) in different frequency bands (rows). According to the legend in the top right corner, black lines over the cortex indicate Brodmann's area parcellation. (A) Before EEG-NFB intervention. (B) After EEG-NFB intervention. (C) Before NPS-R intervention. (D) After NPS-R intervention. Note: (X-X) indicates the EEG differences between two-time points.

of the scores in the group. In this way, the information in the present study is considered of interest since it makes it possible to correlate several variables and make it possible for these results to be compared with other single case studies in similar patients at different evolution stages. The calculation of the different reliable change indexes (RCIs) proposed by Jacobson and Truax gives more strength to our conclusions.

Knowing that neuropsychological evolution in response to the rehabilitation of some cognitive mechanisms can show different patterns of change that are not always linear and continuous throughout the treatment process. This study can only describe what happens in this time window.

Our results are consistent in neuropsychological and neurophysiological evaluations confirming previous reports on the efficacy of EEG-NFB in improving cognitive processes in TBI. Depending on selective sustained and divided attention

and long-term verbal and visual learning, the processes have been specially benefited from training in theta band inhibition. Both protocols used in this study (8 sessions EEG-NFB and NPS-R) have similar cognitive effects in long-term memory, processing speed, visual search and alternating and sustained attention. There is not enough evidence to support the use of EEG-NFB as a unique rehabilitation tool. Still, due to the similar evoked mechanisms and changes, it is probably an excellent complementary technique to be considered to enhance conventional neuropsychological rehabilitation.

It is worth noting that probably the EEG-NFB strategy may influence the most basic and automated tasks preferentially through the self-regulation of brain activity and due to the nature of NPS-R, the explicit guidance to improve specific behaviors may benefit the performance of more complex tasks.

Further research is needed to establish the duration and combination protocol of both therapeutic approaches.

Author contributions

Conceptualization, JPR and AAF; methodology, JIS and DdN; investigation, AAF and JPR; resources, JPR.; data curation, AAF, DdN; writing—original draft preparation, JPR, and AAF; writing—review and editing, JPR, AAF, DdN, MRL and JIS; visualization, JIS; supervision, JPR; project administration, JPR. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

The institution's bioethics committee approved the project. The patient's legal guardian and the patient were informed of the details of the evaluation. They signed their consent to participate in this study, in accordance with the declaration of Helsinki.

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Conflict of interest

The authors declare no conflict of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author [J.R.], upon reasonable request.

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