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CASE REPORT

Multimodal assessment of neuroplasticity in the neurorehabilitation process using virtual reality technology: a case study

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ABSTRACT

Aim: To evaluate neuroplastic changes during a neurorehabilitation protocol mediated by a serious video game in virtual reality using a multimodal assessment.

Methods: Case study with 18 serious video game sessions. The following were recorded: (i) clinical evolution using the Fugl–Meyer Assessment, (ii) in-game performance, (iii) task functional magnetic resonance imaging with motor paradigms (unilateral and bilateral), and (iv) resting state functional magnetic resonance imaging.

Results: The total Fugl–Meyer Assessment increased from 52 (T0) to 61 points (T2), with greater gains in 'upper limb' and 'coordination/speed.' Performance in the serious video game showed progression in line with clinically planned levels. In task functional magnetic resonance imaging, a significant difference was observed in the bilateral paradigm (Wilcoxon, $p=0.0016$), consistent with functional reorganisation. In resting state functional magnetic resonance imaging, there was evidence of increased interhemispheric connectivity between Precentral Gyrus, Postcentral Gyrus and Supplementary Motor Cortex and a more organised pattern of the somatomotor network compared to T0; connectivity approximated the normotypical reference pattern.

Conclusion: serious video game-mediated intervention is associated with clinical improvements and markers of neuroplasticity measured by functional magnetic resonance imaging; the proposed multimodal strategy is viable for quantifying functional reorganisation during rehabilitation and warrants further study in larger cohorts.

Keywords: Serious Game, fMRI, Neurorehabilitation, Neuroplasticity, Virtual Reality.

1. Introduction

Neurological disorders currently constitute one of the leading challenges for global public health, not only due to their high prevalence but also because of the magnitude of their impact on quality of life and on the sustainability of healthcare systems. According to the Global Burden of Disease study, in 2019 these conditions accounted for approximately 10 million deaths and 349 million disability-adjusted life years (DALYs), underscoring their weight in the global burden of disease[1]. It is further estimated that 43.1% of the world's population is affected by some form of neurological disorder, with stroke, dementias and idiopathic epilepsy being the main contributors[2]. In this context, the World Health Organization (WHO), through the Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders, has emphasised the need for a "neurological revolution" encompassing surveillance, prevention, acute care and, as a priority, rehabilitation processes[3]. This highlights the urgency of innovative, integrated and multidisciplinary strategies to improve neurological care and ensure equitable access[3,4].

Over recent years, digital technologies have gained increasing prominence as supportive tools in neurorehabilitation. In particular, the incorporation of serious games and virtual reality (VR) environments has shown considerable potential to complement traditional treatment methods[5–8]. Unlike conventional approaches—often characterised by repetitive routines that may induce demotivation and treatment abandonment—gamified interventions enhance therapeutic adherence by increasing the patient's intrinsic motivation. Moreover, several studies suggest that combining playful dynamics with immersive scenarios promotes neuroplasticity, supporting cortical reorganisation and functional recovery[9].

Recent literature provides solid evidence along these lines. For example, Pimentel-Ponce et al.[9] report that integrating game mechanics and VR optimises processes of neural plasticity and improves patient functionality. Complementarily, Saleh et al.[10] developed the Recover Me system—based on a mobile application and immersive games—which incorporates artificial neural networks to predict treatment evolution and personalise interventions, demonstrating significant improvements in motor performance. In addition, Vezér et al.[11], through a systematic review and meta-analysis, examined the effectiveness of video-game-based therapy (VGBT) in children with cerebral palsy, observing significant gains in hand function and grasping activities, while noting the need for studies with greater methodological rigour and longer follow-up. Finally, Muñoz-Novoa et al.[12] explored the combination of myoelectric pattern recognition, VR and serious games in patients with chronic stroke, confirming meaningful improvements in motor function, albeit highlighting the challenge of sustaining benefits over time.

Despite these advances, a major limitation persists: the lack of systematised protocols that clearly define how video games should be integrated into rehabilitation programmes[13]. Therapeutic planning ought to be grounded in objective evidence regarding how such interventions modulate brain reorganisation and support recovery processes[14]. In this regard, functional magnetic resonance imaging (fMRI) has become a reference tool for the study of neuroplasticity. By detecting blood-oxygen-level-dependent (BOLD) signals, fMRI enables the assessment of changes in brain activity associated with both damage and learning /rehabilitation[15–17]. This technique therefore offers a unique window onto the dynamic mechanisms of neuronal adaptation and stands as an indispensable method for scientifically validating new therapeutic strategies.

This work proposes a neurorehabilitation strategy based on the implementation of a motor-rehabilitation serious video game (SVG) designed by the research team[13]. Through a case study, we analyse the evolution of a person with a history of stroke who underwent a systematised rehabilitation protocol mediated by an SVG. The evaluation of progress combines the Fugl-Meyer Assessment (FMA), descriptive statistics of in-game performance, task-based fMRI (t-fMRI) focusing on voxel-wise activation in regions associated with motor function and resting-state fMRI (rs-fMRI) connectivity analysis. In doing so, we aim to contribute evidence on the value of serious games as complementary tools in neurological rehabilitation and to advance towards a multimodal assessment of neuroplasticity in recovery processes.

2. Diagnostic and therapeutic strategy

The study comprised three stages (Figure 1):

Baseline assessment (T0): a participant meeting the inclusion criteria was selected; a baseline functional evaluation was performed using the FMA, and an fMRI session was conducted to obtain brain-activity data at T0.

Systematised rehabilitation: the participant completed a structured programme mediated by the SVG, totalling 18 sessions.

Final assessment: upon completion of the sessions, a new evaluation (FMA and fMRI) was carried out following the same task paradigms established at T0.

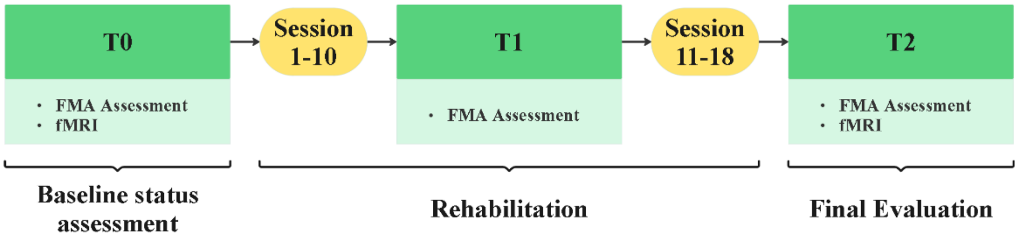


Figure 1. Schematic of the evaluation and rehabilitation plan.

2.1 PARTICIPANT

The study included a 44-year-old participant who had suffered a haemorrhagic stroke in the right hemisphere 18 months earlier. According to the medical record and patient report, the neurological event was characterised by a sudden loss of motor control on the left side of the body, without loss of consciousness or memory. Neuroimaging confirmed the presence of intracerebral bleeding, which required drainage of cerebrospinal fluid and subsequent medical stabilization. The participant remained in an induced coma for six days, followed by one month in intensive care and six months in a rehabilitation clinic. After discharge, outpatient therapy continued three times per week up to the time of this study.

Clinical characterization included upper-limb function, global mobility and balance; on the Berg Balance Scale, the participant scored 50, indicating low fall risk. In addition, an open-ended questionnaire was administered to gather information about activities of daily living in order to appraise quality of life.

2.2 CLINICAL CRITERIA FOR DESIGNING THE SYSTEMATISED TREATMENT PROTOCOL

A SVG focused on upper-limb motor rehabilitation was used, allowing the therapist to tailor game dynamics to the participant's functional capacity. The intervention was delivered by two physiotherapists, and the motor-rehabilitation protocol was structured around four components: (i) therapeutic objective; (ii) therapeutic activities; (iii) practice (dose and scheduling); and (iv) therapeutic progression. This organisation enabled a progressive, engaging and function-oriented experience aligned with the participant's needs. Figure 2 shows the implementation of the four components of the systematised treatment structure proposed for this patient.

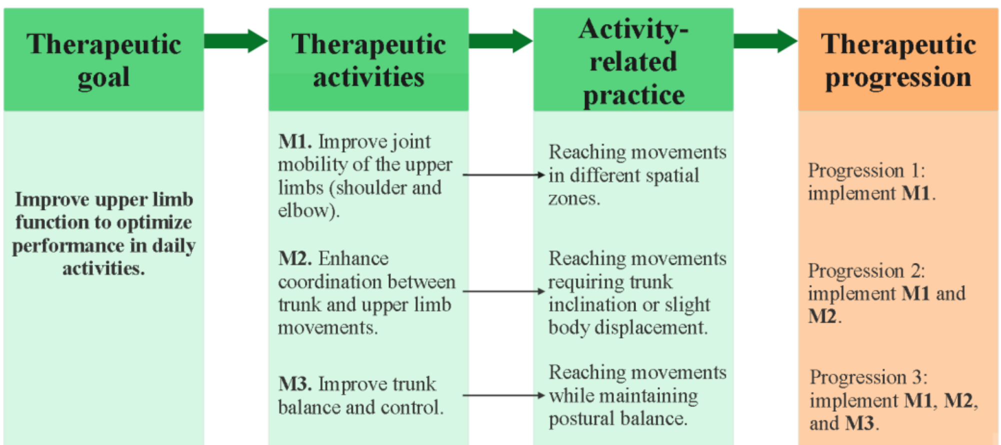


Figure 2. Flow of clinical criteria used to build the systematised treatment protocol.

2.2.1 Determination of the serious video game configuration based on the systematised rehabilitation protocol.

The SVG configuration was defined based on therapeutic progression, prioritising the location of the target areas in space, while parameters such as the speed of the impact objects, session time and the interval between object launches on the left and right sides were kept constant. Three levels were established, as shown in Figure 3 (purple box): level 1, focused on the shoulder and elbow joint range without compromising the trunk; level 2, incorporating trunk translation or inclination; and level 3, combining these demands with elements of postural instability.

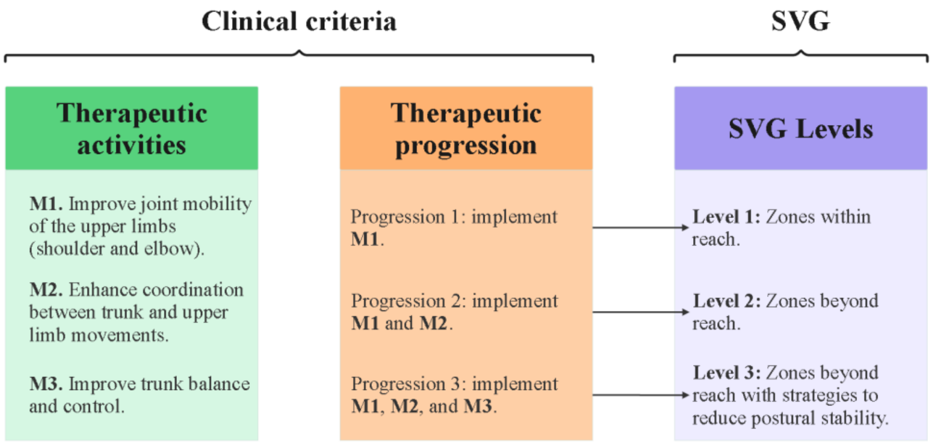


Figure 3. Determination of SVG levels based on clinically established 'therapeutic progression'.

In addition, to promote therapeutic variability and avoid monotony, each level included differentiated dynamics that kept the patient motivated, integrating specific strategies according to the healthy or affected side, which allowed for progressive, entertaining, and functional training (Figure 4).

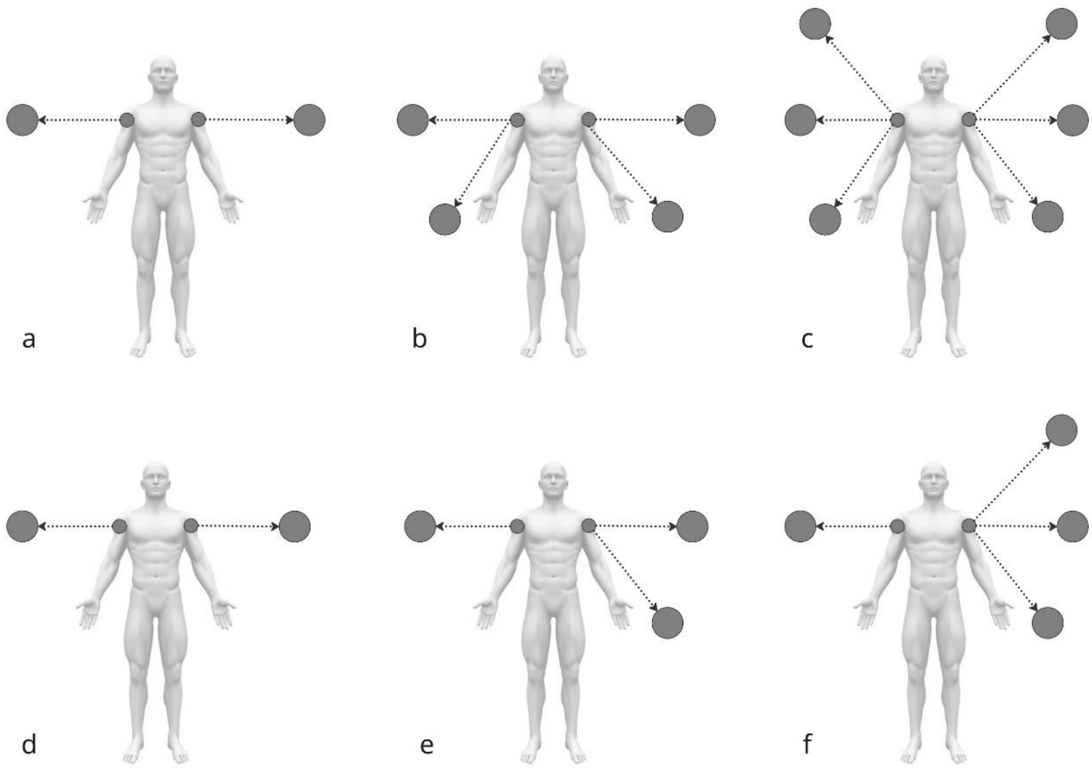


Figure 4. Dynamics implemented at the SVG levels. The larger grey circles are the coverage areas.

2.2.2 Structure and calculation of variables for score progression analysis.

For the analysis of score progression, the target areas were distributed variably in each SVG game (Table 1), which allowed the calculation of the average number of hits per area and upper limb based on the percentages obtained according to equation 1.

$$Mean = \frac{\sum correct\ responses}{\sum trials} \quad (1)$$

Two types of analysis were performed using these measures: (i) an inter-arm comparison considering the overall performance of the right and left arms, and (ii) an inter-dynamic and intra-arm comparison by stages, focusing on progression levels without discriminating between areas. This structure made it possible to characterise the patient's performance globally and specifically in terms of therapeutic progression.

Table 1. This table shows the selected zones (upper, middle, and lower) in each SVG game in a session.

Upper Limb	Areas Covered	SVG Matches per Session
Left (Affected)	Upper Area	3, 6, 7, 8, 9, 12
	Middle Area	1 to 12
	Lower area	2, 3, 5, 6, 7, 8, 9, 11, 12
Right	Upper Area	3, 6, 9, 10, 11, 12
	Middle Area	1 to 12
	Zona Inferior	2, 3, 5, 6, 8, 9, 10, 11, 12

2.3. ACQUISITION AND PROCESSING OF FUNCTIONAL MAGNETIC RESONANCE IMAGES

2.3.1 Acquisition of Images with Functional magnetic resonance images

Three t-fMRI paradigms with motor imagery were used for image acquisition[18], projecting SVG video blocks onto the resonator: one for the right upper limb, another for the left, and a third bilateral, complemented by a resting-state acquisition (rs-fMRI). The images were obtained at Dr. Guillermo Rawson Hospital with a Philips Multiva 1.5T resonator. T1-weighted anatomical images were acquired (256×256 matrix, FOV 256×231 mm², 1 mm³ voxel, TR 7227 ms, TE 3.33 ms, 180 slices) and functional images using a transverse EPI sequence (64×64 matrix, 3.59×3.59×4 mm³ voxel, TR 3000 ms, TE 50 ms, 80 volumes in 240 s) were acquired, with the patient instructed to remain still and pay attention to the evolution of the SVG in projection.

2.3.2 Functional magnetic resonance imaging processing

The analysis of fMRI data requires a series of pre-processing steps for accurate statistical interpretation. These include spatial realignment, co-registration, inter-subject normalisation, and spatial smoothing, with the aim of aligning functional and anatomical images and improving the signal-to-noise ratio. In addition, noise removal techniques are applied to minimise its influence on the BOLD signal time series, ensuring accurate spatial alignment and greater reliability in the results[18,19]. Once this preliminary processing is complete, the static data is analysed to identify the activation voxels, using the functional neuroimaging processing tool FMRIB Software Library (FSL)[20]. T1-weighted structural images were processed with FreeSurfer[21], using the Aparc+Aseg atlas to automatically segment the brain volume[22,23]. Once the activation areas and structural segments were obtained, the 3D Slicer application was used to visualise and extract metrics for statistical analysis[24-26].

2.3.3 Study Regions

The study regions were defined by grouping the segments obtained with the Aparc+Aseg tool according to their motor function. The segments included per region are identified in Table 2, where ctx refers to cortex, lh to left hemisphere, and rh to right hemisphere.

Table 2. Segments of the aparc-aseg brain atlas grouped by regions of interest.

Region	Main function	Included segments
Primary motor cortex (M1)	Corrections during motor actions and integration of sensory inputs[27].	ctx-lh/rh-paracentral, ctx-lh/rh-precentral, ctx-lh/rh-postcentral
Cerebellum	Regulation of the precision and rhythm of movements[28].	Left/Right Cerebellum-White-Matter, Left/Right Cerebellum-Cortex
Primary sensory cortex (S1)	Sensory feedback to M1 during motor execution[29].	ctx-lh-postcentral, ctx-rh-postcentral
Basal ganglia (subcortical)	Planning, modulation, and execution of voluntary movement[30,31].	Putamen, Pallidum, Caudate, Left and Right Thalamus
Premotor cortex	Preparation of movement and integration of the task; transmits information to M1 and the medulla[32].	ctx-lh/rh-parsopercularis, ctx-lh/rh-rostralmiddlefrontal, ctx-rh-rostralmiddlefrontal.

2.3.4 Resting state functional magnetic resonance imaging analysis methods: Hypothesis-driven

This is a hypothesis-driven functional connectivity technique, where a region of interest (ROI) is selected and its temporal correlation with other brain areas is analysed, generating maps that reveal functionally connected regions[33]. The seed can be defined in advance according to the objective of the study or derived from task-based fMRI results.

For this study, the seed-based method was used by implementing seed-to-voxel connectivity maps and the ROI-to-ROI-based method through connectivity matrices, using the CONN toolbox[27]. This choice seeks to focus on regions linked to motor functions. In principle, clusters of neighbouring voxels that exceeded an established statistical threshold ($p<0.005$) were generated from the maps. Subsequently, the areas belonging to the positive clusters were used for the ROI-to-ROI analysis, which is described in the following section.

For a better interpretation of the results obtained from the case, a preliminary study was conducted[34], which included 44 subjects with no detected neuropathologies. A first-level analysis (each subject independently) was performed, which yielded connectivity matrices for each subject (Figure 5) and their specific connectivity map.

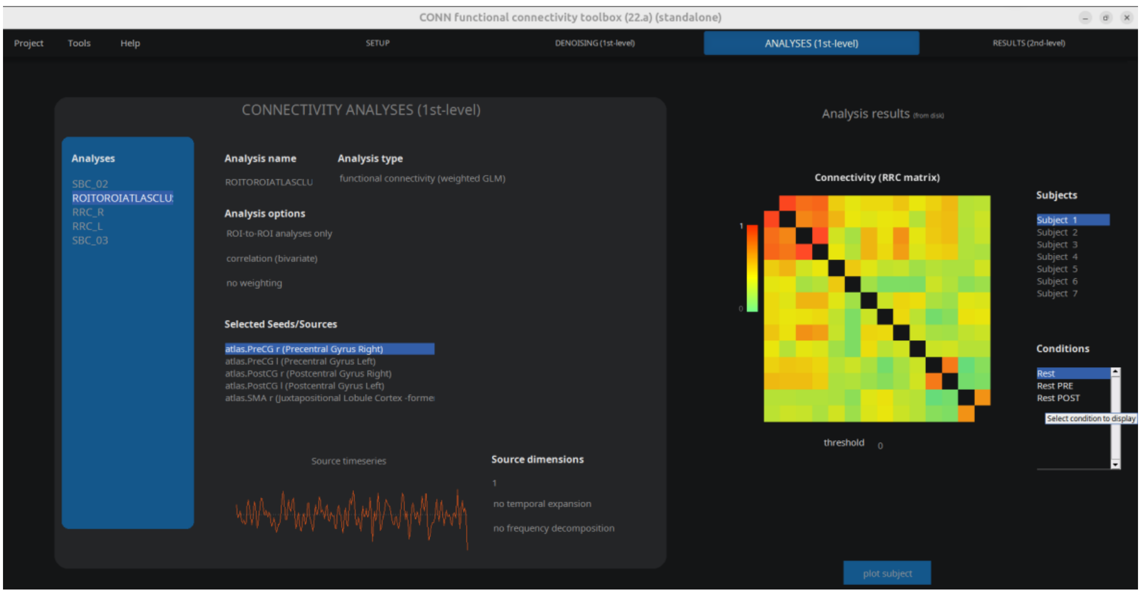


Figure 5. ROI-to-ROI analysis in the CONN graphical user interface of a subject without neuropathology.

For the latter, the CONN toolbox allows a second-level analysis to be performed, which averages the maps of all subjects into a single connectivity map (Figure 6)[27]. The latter was used as a reference for the evaluation of the case study.

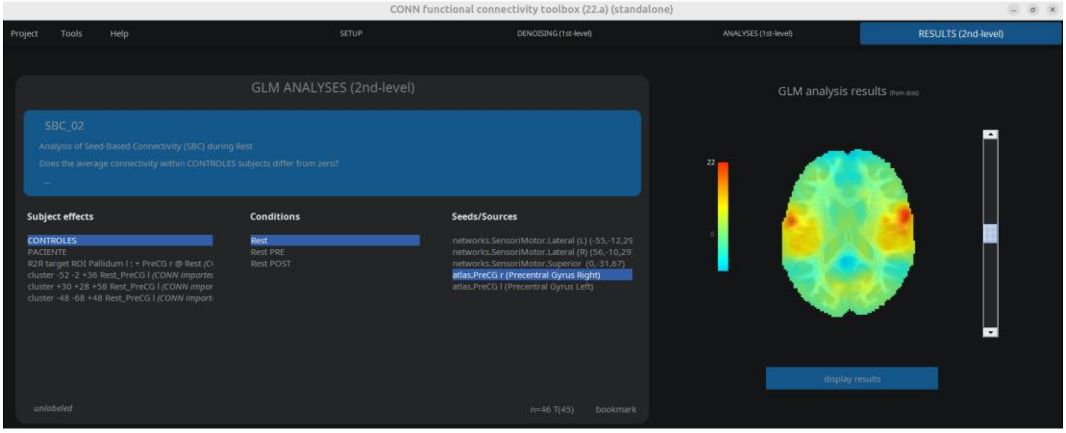


Figure 6. Second-level analysis in the CONN GUI

3 Results

This section will present the results obtained that validate the patient's progress, both with statistical assessment of performance linked to SVG and with statistical results related to T0 and T2, t-fMRI and connectivity assessed with rs-fMRI. Each of these results will be detailed in different subsections.

3.1 VIDEO GAME SCORES AND FUGL–MEYER ASSESSMENT PERFORMANCE

3.1.1 Overall interarm performance and Fugl–Meyer Assessment

The patient's clinical evolution was assessed using the FMA upper limb subscalethe result are summarized in Table 3.

Table 3. Clinical evolution shown with the FMA upper limb subscale assessment.

FMA Items	Maximum value for each item	T0	T1	T2
Upper limb	36	29	29	33
Wrist	10	5	9	9
Hand	14	14	14	14
Coordination/speed	6	4	5	5
Total	66	52	57	61

The temporal analysis of the subscale shows a progressive improvement in the total score: 52 points at T0, 57 at T1, and 61 at T2, approaching the theoretical maximum of 66. The most notable increases were recorded in the “upper limb” item (29 to 33) and in “coordination/speed” (4 to 5 points), consistent with the therapeutic focus on the shoulder and elbow.

The inter-arm session performance graph (Figure 7) reflects the average percentage of correct responses in interaction tasks for both sides. The affected side showed a positive trend throughout the sessions, with progressive improvement in response accuracy. Between sessions 1 and 4, both arms presented similar values (adaptation phase). From session 5 onwards, a noticeable difference emerged between the affected and healthy sides, which gradually narrowed until reaching comparable performance levels in the final sessions.

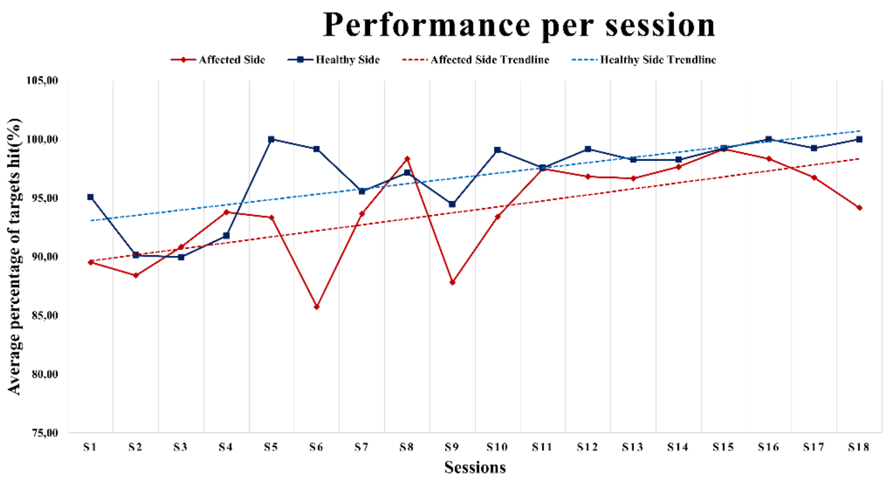


Figure 7. Performance of each limb during the sessions, with its trend line.

3.1.2 Intra-arm-level performance in the serious video game

Each level of the SVG was planned and designed according to the therapeutic activity and clinical progression. In terms of correct response percentage for the affected limb, the following changes were observed:

- Level 1: increase from ~92% to >95%.
- Level 2: improvement from ~87% to ≈94%.
- Levels 3* and 3** (greater motor and cognitive complexity): progression from 89% in the initial stage to >93% in the final stage.

These results confirm the gradual progression anticipated by the level design of the SVG and the therapeutic planning defined by the physiotherapy team.

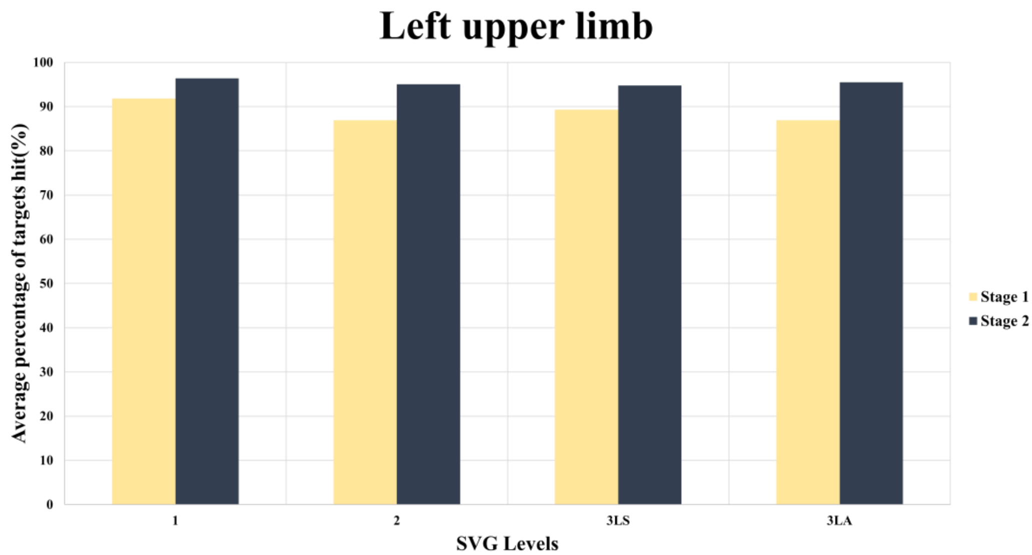


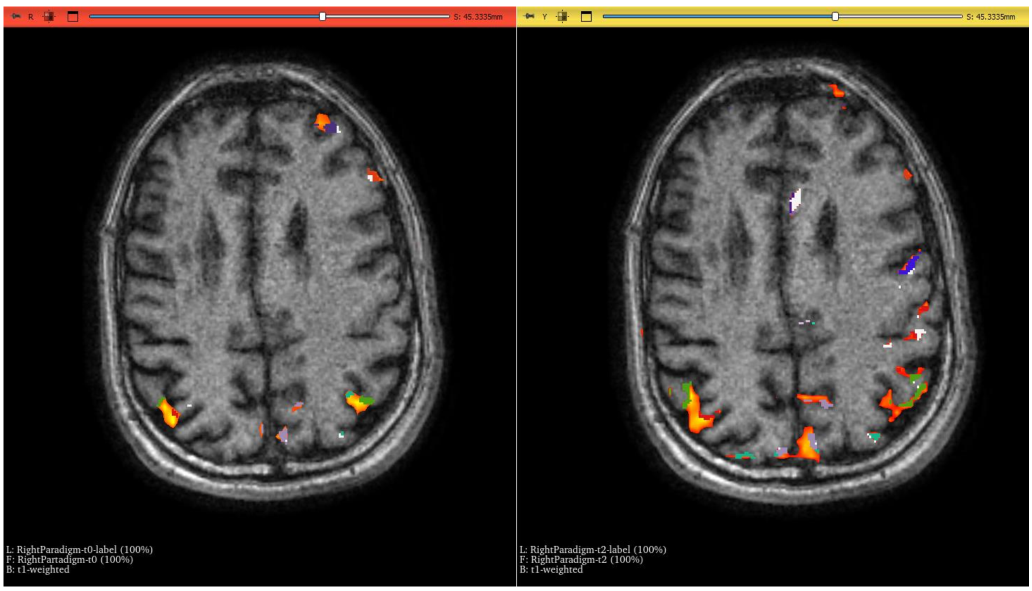
Figure 8. Evolution of the performance of the affected member at each level of the proposed SVG.

3.2 TASK FUNCTIONAL MAGNETIC RESONANCE IMAGING RESULTS

Segmented activation areas were visualised using 3D Slicer. Paradigm conditions are shown for the right upper limb (Figure 9), left upper limb (Figure 10), and bilateral movement (Figure 11). The segmentations were grouped by previously defined functional regions and verified by an imaging specialist.

Finally, statistical tests for paired samples were performed using Python[35] and the SciPy library[36]. The Shapiro–Wilk test indicated a non-normal distribution; therefore, the non-parametric Wilcoxon test was applied. Results are shown in Table 4.

a)



Right paradigm, T0 | Right paradigm, T2

b)

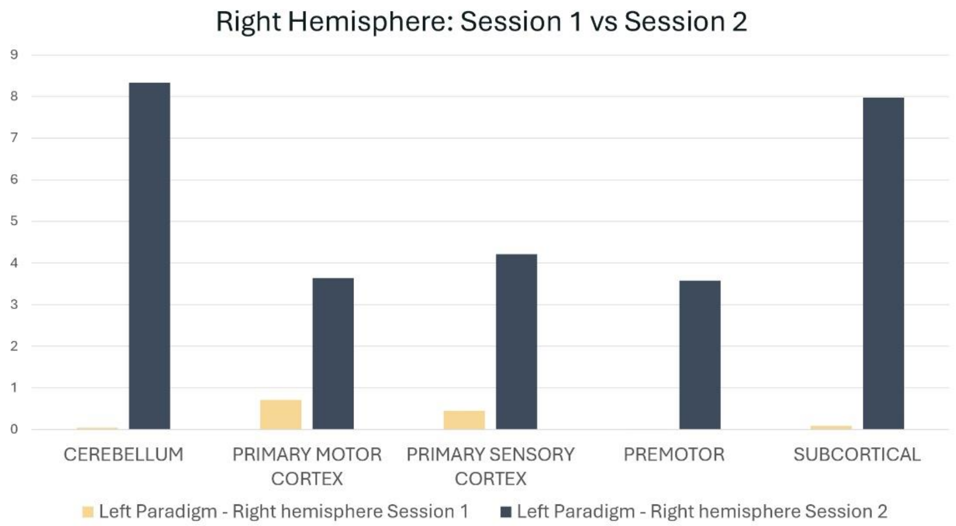
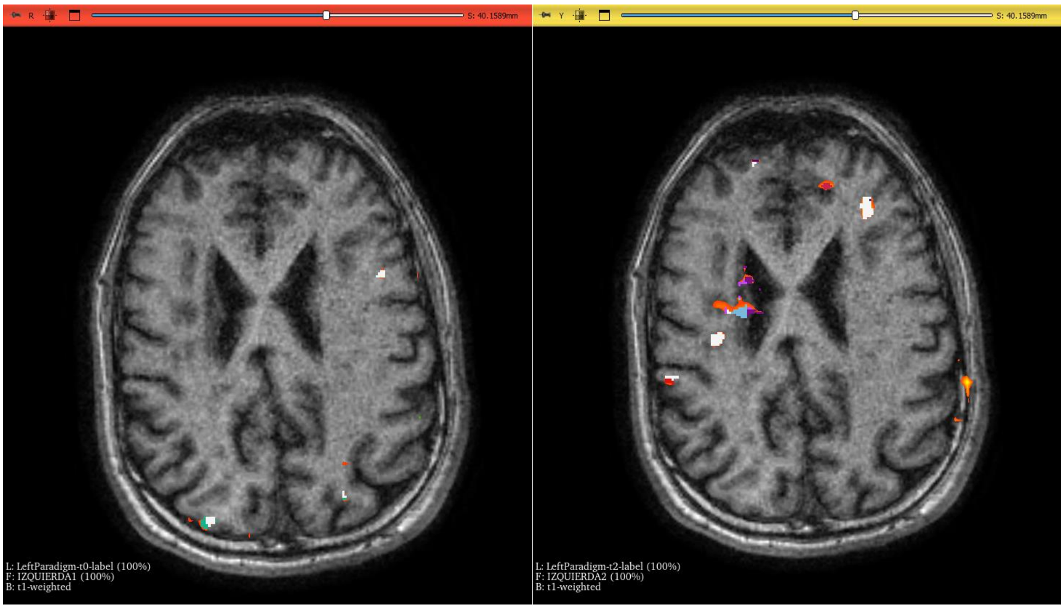


Figure 9. Right arm paradigm (Left hemisphere): T0 vs T2. a). Results of processing t-fMRI. b). Statistics for left hemisphere regions with right paradigm.

a)



Left paradigm, T0 Left paradigm, T2

b)

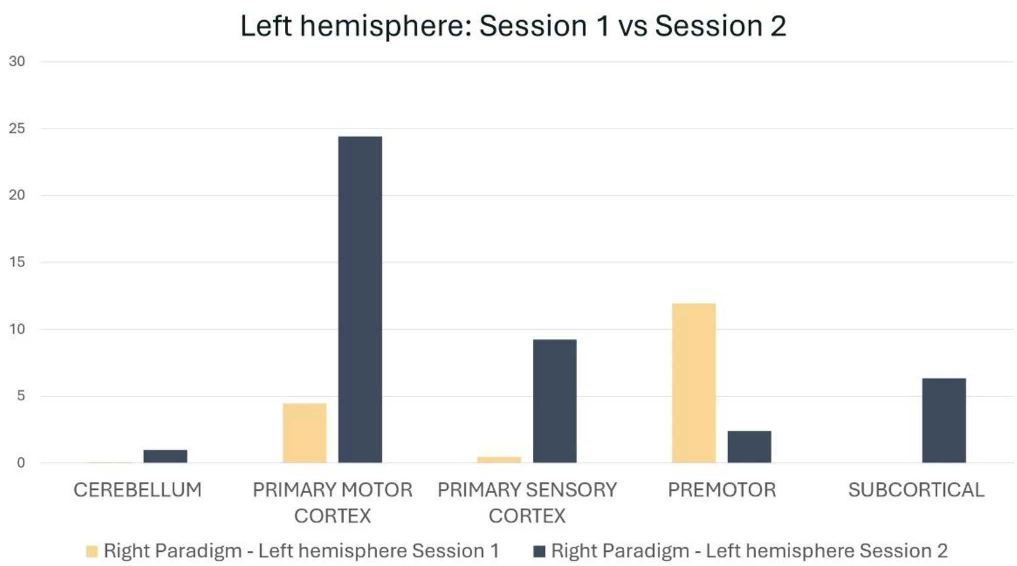
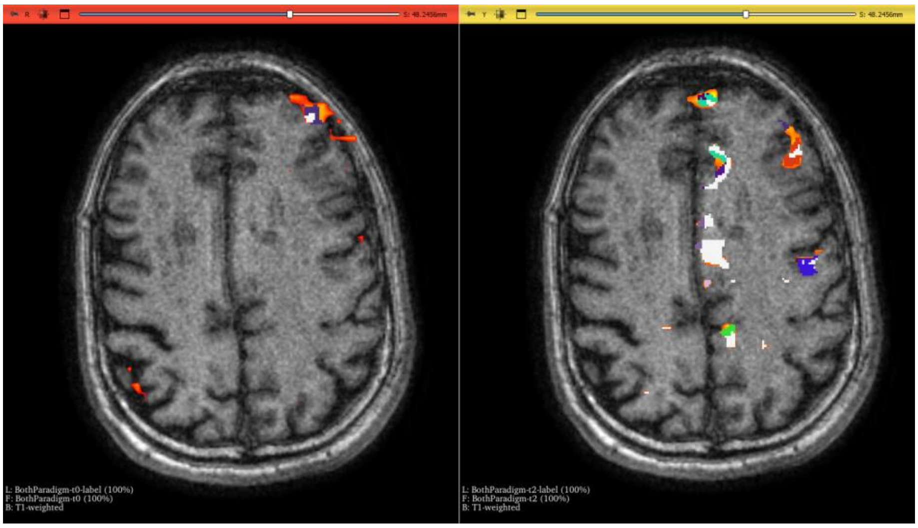


Figure 10. Left arm paradigm (Right hemisphere): T0 vs T2. a). Results of processing t-MRI. b). Statistics for right hemisphere regions with left paradigm.

a)



Bilateral paradigm, T0 Bilateral paradigm, T2

b)

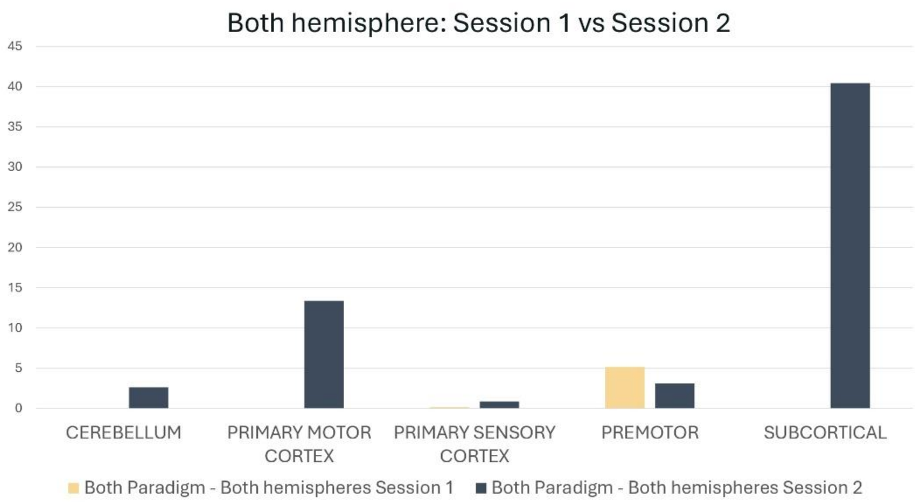


Figure 11. Bilateral paradigm: T0 vs T2. a). Results of processing t-fMRI. b). Statistics for brain regions with bilateral paradigm.

Table 4. Statistical analysis of paradigms for upper limb sessions

Problem	Hypothesis	Results
Paradigm corresponding to the left upper limb	H_0: There is no significant difference between both sessions. H_1: There is a significant difference between both sessions.	p-value: 0.0644
Paradigm corresponding to the right upper limb	H_0: There is no significant difference between both sessions. H_1: There is a significant difference between both sessions.	p-value: 0.3125
Paradigm corresponding to both upper limbs	H_0: There is no significant difference between both sessions. H_1: There is a significant difference between both sessions.	p-value: 0.0016

3.3. RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING RESULTS

3.3.1 ROI-to-ROI analysis

Figures 12 and 13 show the ROI-to-ROI connectivity matrices for the patient at T0 and T2, respectively. At T0, the matrix exhibited a heterogeneous and asymmetric pattern, with reduced interhemispheric connectivity between homologous areas and limited integration of associative regions (e.g., central opercular cortex and parietal operculum, cool colours).

Figure 12. Connectivity matrix of the patient prior to therapy, T0.

At T2, a more organized pattern was observed, with an increase in positive connectivity between Precentral Gyrus, Postcentral Gyrus, and Supplementary Motor Cortex of both hemispheres, and enhanced interhemispheric connectivity between homologous areas.

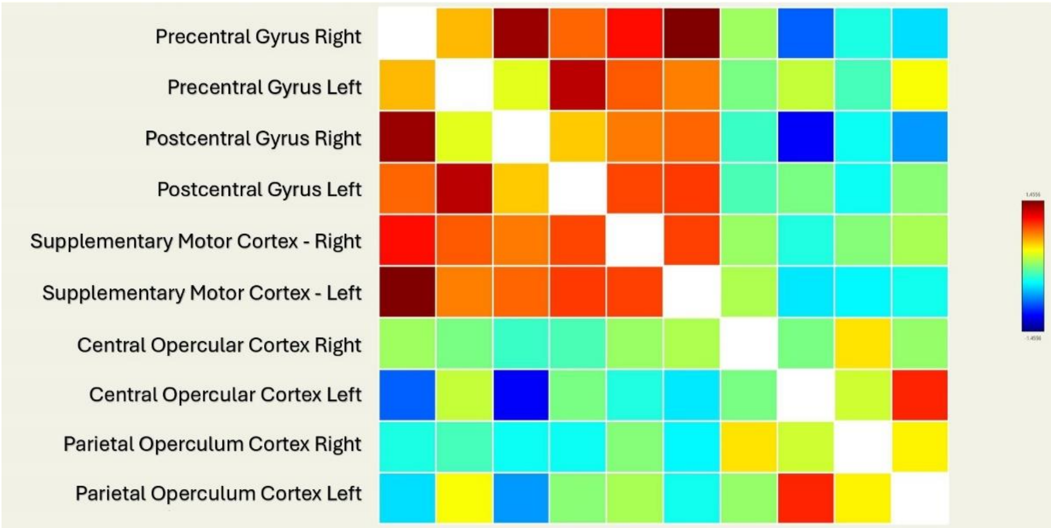


Figure 13. Connectivity matrix of the patient after therapy, T2

3.3.2 Connectivity Maps

The three-dimensional segmentation of the average connectivity map for the control group, using the right Precentral Gyrus as a seed, revealed the characteristic bilateral pattern of the somatomotor network (Figure 14). This pattern was taken as a normotypical reference to contrast with the patient's individual results before and after therapy.

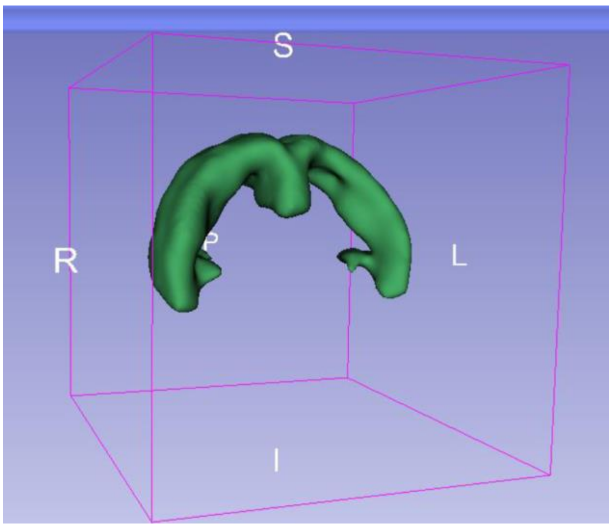


Figure 14. Three-dimensional segmentation of the average connectivity map corresponding to the control group.

The superimposition of this normative segment with the patient's T0 map (Figure 15) showed a fragmented segmentation, loss of symmetry, and multiple small, disconnected islands predominantly in central and right lateral regions.

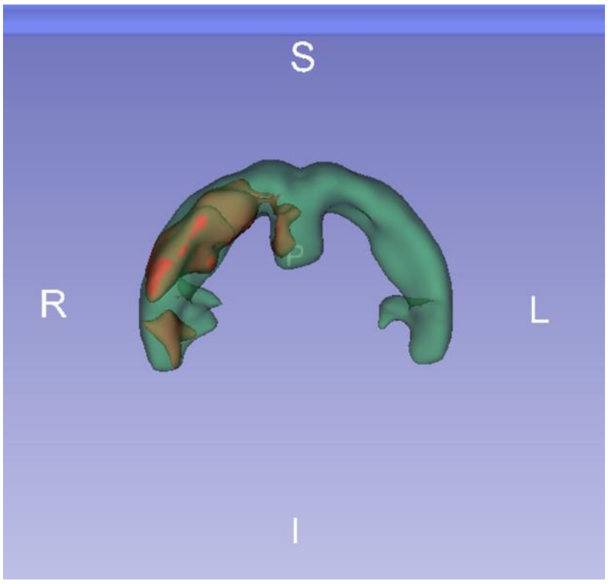


Figure 15. Overlay of the three-dimensional segments of the average connectivity map of the controls (green) and the patient's map in the T0 condition (red).

The post-therapy (T2) superimposition (Figure 16) displayed a more defined bilateral organization, reduced scattered areas, and a closer approximation to the normative topography.

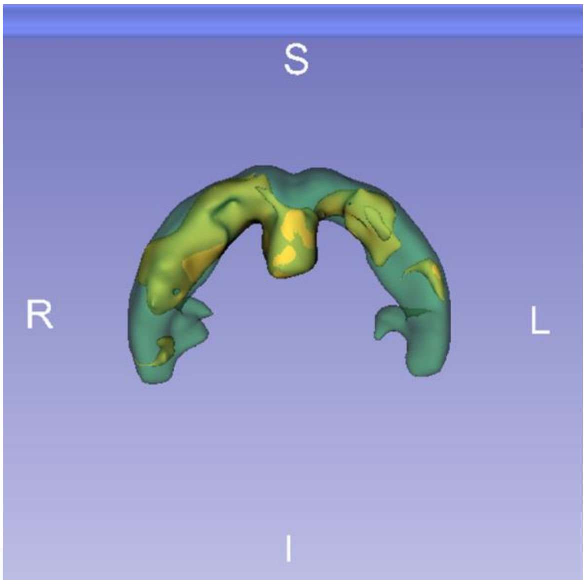


Figure 16. Overlay of the three-dimensional segments of the average connectivity map of the controls (green) and the map of the patient in the post-therapy condition (yellow).

4. Discussion

4.1 DISCUSSION OF CLINICAL AND SERIOUS VIDEO GAME PERFORMANCE RESULTS

The evolution observed in the FMA and SVG performance metrics demonstrates a functional improvement of the affected upper limb. The consistent increase in total FMA score and enhanced accuracy in interactive tasks suggest recovery of motor control, particularly in proximal segments (shoulder and elbow), which were the therapeutic focus.

The presence of an initial adaptation phase (sessions 1–4), followed by consolidation and convergence toward contralateral performance in later sessions, aligns with motor learning and skill transfer processes. The sustained improvement at higher complexity levels (levels 3* and 3**) indicates that the progressive load of the SVG was adequate and that the patient successfully transferred sensorimotor gains to tasks with higher cognitive-motor demand.

4.2 DISCUSSION OF TASK FUNCTIONAL MAGNETIC RESONANCE IMAGING RESULTS

Only the bilateral paradigm reached statistical significance ($p = 0.0016$), indicating that intervention-induced changes manifest most consistently during tasks requiring interhemispheric coordination. Unilateral paradigms did not show statistically significant differences, which may stem from the limited sample size (single case), intrinsic variability of post-lesion unilateral activation, or a functional reorganization favoring bilateral networks rather than isolated unilateral reactivation.

Segmented images corroborate spatial redistribution of activation between T0 and T2 and support the idea that functional recovery in this case is associated with coordinated bilateral processes.

4.3 DISCUSSION OF RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING RESULTS

The shift from an asymmetric and fragmented connectivity matrix at T0 to a more organized and symmetric configuration at T2 reflects functional reorganization within the somatomotor network. Enhanced connectivity among the Precentral Gyrus, Postcentral Gyrus, and Supplementary Motor Cortex, along with increased interhemispheric coherence, suggests the activation of neuroplastic mechanisms associated with motor recovery.

Nevertheless, residual weaknesses in connectivity—particularly in associative areas such as the opercular cortices—indicate that reintegration of these regions remains incomplete. These findings imply that while the intervention facilitated substantial network-level reorganization, certain higher-order motor areas may require extended or targeted rehabilitation to achieve full functional connectivity restoration.

4.4 MULTIMODAL INTEGRATIVE DISCUSSION

A synthesis of behavioural outcomes (FMA scores and SVG performance), t-fMRI activation patterns, and rs-fMRI connectivity provides a coherent and multidimensional representation of functional recovery. Clinically, the patient demonstrated sustained improvements in motor control and task performance. The significant change observed in the bilateral t-fMRI paradigm, accompanied by a redistribution of activation, supports the involvement of re-engaged bilateral circuits in recovery. Furthermore, rs-fMRI revealed enhanced intra- and interhemispheric connectivity within the motor system, approximating normative patterns and reinforcing the presence of functional reorganization.

Collectively, these multimodal findings suggest that the SVG-mediated intervention elicited both measurable clinical improvements and neural adaptations. The convergence of behavioural gains with imaging evidence underscores the value of combined assessment strategies for monitoring recovery and understanding the neurophysiological basis of rehabilitation outcomes.

5. Conclusions

This case report provides preliminary evidence that the integration of a serious video game within a motor neurorehabilitation protocol may promote measurable clinical improvements—reflected in the FMA score increase—and progressive enhancement of in-game performance. Functional MRI findings revealed patterns of neural reorganization and increased interhemispheric connectivity, suggesting the activation of neuroplastic mechanisms potentially associated with the intervention.

The multimodal assessment—combining clinical, behavioural, and neuroimaging metrics—proved feasible and informative for evaluating therapeutic effects from a comprehensive perspective. These results highlight the potential value of virtual reality–based strategies as complementary tools to conventional rehabilitation methods and underline the importance of further research to validate and systematise their clinical application in larger cohorts.

Although the findings indicate a clear trend of improvement, they must be interpreted with caution. As this investigation concerns a single case, generalization is limited, and statistical analyses are constrained by the small number of observations and the methodological boundaries of single-subject t-fMRI and rs-fMRI studies. Future implementations involving expanded samples and longitudinal follow-up will be essential to confirm the reproducibility of these findings and to strengthen understanding of the neuroplastic mechanisms underlying motor recovery.

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6. Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

7. Funding Statement:

None.

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