

Improving neuropsychiatric symptoms following stroke using virtual reality

A case report

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Abstract

Rationale: Post-stroke cognitive impairment occurs frequently in patients with stroke, with a 20% to 80% prevalence. Anxiety is common after stroke, and is associated with a poorer quality of life. The use of standard relaxation techniques in treating anxiety in patients undergoing post-stroke rehabilitation have shown some positive effects, whereas virtual reality seems to have a role in the treatment of anxiety disorders, especially when associated to neurological damage.

Patients concerns: A 50-year-old woman, smokers, affected by hypertension and right ischemic stroke in the chronic phase (i.e., after 12 months by cerebrovascular event), came to our observation for a severe anxiety state and a mild cognitive deficit, mainly involving attention and visuo-executive processes, besides a mild left hemiparesis.

Diagnosis: Anxiety in a patient with ischemic stroke.

Interventions: Standard relaxation techniques alone in a common clinical setting or the same psychological approach in an immersive virtual environment (i.e., Computer Assisted Rehabilitation Environment – CAREN).

Outcomes: The patient's cognitive and psychological profile, with regard to attention processes, mood, anxiety, and coping strategies, were evaluated before and after the 2 different trainings. A significant improvement in the functional and behavioral outcomes were observed only at the end of the combined approach.

Lessons: The immersive virtual reality environment CAREN might be useful to improve cognitive and psychological status, with regard to anxiety symptoms, in post-stroke individuals.

Abbreviations: CAREN = Computer Assisted Rehabilitation ENvironment, *COPE-NVI* = Coping Orientation to the Problems Experienced-New Italian Version, DB = diaphragmatic breathing, FIM = functional independence measure, MoCA = Montreal Cognitive Assessment, VR = virtual reality.

Keywords: cognitive assessment, Neurorehabilitation, virtual reality

1. Introduction

Stroke is a neurological syndrome caused by a focal disruption in the cerebral blood flow due to occlusion (ischemic stroke) or rupture of a blood vessel (hemorrhagic stroke). Stroke is the leading cause of disability worldwide and the third cause of death in the western countries.^[1] Following stroke, especially in right hemisphere lesions, several psychological changes may arise,

being depression and anxiety the most common.^[2] The right hemisphere plays an important role in verbal communication, as it is mostly responsible for speech prosody and its emotional aspects.^[3] Moreover, previous studies indicate that post-stroke anxiety is also common and persistent,^[4,5] and this is attributable to a feeling of impotence and uncertainty about the future. Some personality factors, as coping strategies, can contribute to reduce or increase the anxiety's level. The prevalence of post-stroke cognitive dysfunctions varies from 23% to 55% within three months from the stroke onset, and declines to a percentage between 11% and 31% after 1 year.^[6,7] It has been found that after stroke most of the patients may have enduring difficulties in specific cognitive domains, such as attention process and concentration, memory abilities, spatial awareness, perception, praxis and executive functioning.^[8,9] Thus, a proper psychometric evaluation should be the mainstay of post-stroke patient's treatment. Limited evidences showed the relationship between cognition processes, emotions and anxiety. Anxiety disorders frequently coexist with depression, and may be more common in women and younger stroke survivors.^[10]

Patients with a 'probable anxiety disorder' at 3-months had a poorer quality of life at 1, 3, and 5-years post-stroke after adjusting for age, gender, and stroke severity. Moreover, anxiety symptoms persisted for up to 10 years.^[11]

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Relaxation techniques can be considered a useful tool, determining a positive emotional and psychological well-being.^[12,13] Among the different relaxation techniques, diaphragmatic breathing (DB), progressive muscle relaxation,^[12,13] and autogenic relaxing training^[14] are characterized by a significant positive association between physical and cognitive dimensions. The use of these techniques in treating anxiety in patients undergoing post-stroke rehabilitation have shown some positive effects.^[15]

In the last years, virtual reality (VR) and interactive video gaming are emerging as promising treatment approaches in stroke rehabilitation, both for cognitive rehabilitation and mood/anxiety disorder treatment.^[16] VR can provide exposure to nature for those living in isolated confined environments, and it has been demonstrated to reduce stress and improving mood.^[17] Virtual Reality Therapy with an Interactive Semi-Immersive Program (i.e., Bts-Nirvana System) can be considered a useful complementary treatment to potentiate functional recovery, with regard to attention, visual-spatial deficits, and motor function in patients affected by stroke.^[18] Moreover, relaxation and respiratory techniques in a semi-immersive virtual reality environment, using Bts-Nirvana, may be a promising tool in improving attention process, coping strategies, and anxiety in individuals with neurological disorders, including stroke.^[19]

Aim of this case study is to evaluate the effects of a combined rehabilitative approach, using conventional relaxation and respiratory techniques in a virtual immersive rehabilitative environment, that is, Computer Assisted Rehabilitation Environment (CAREN), in a patient with chronic stroke.

2. Case description

A 50-year-old woman, smokers, affected by hypertension and right ischemic stroke in the chronic phase (i.e., after 12 months by cerebrovascular event), came to our observation for a severe anxiety state and a mild cognitive deficit, mainly involving attention and visuo-executive processes, besides a mild left hemiparesis. To improve her cognitive and behavioral condition, she underwent 2 different rehabilitation trainings: the former including the use of standard relaxation techniques in a usual clinical setting (i.e., face to face with therapist, namely standard approach); the latter using the same psychological approach in a virtual environment (i.e., CAREN; namely combined approach). Each rehabilitation program was articulated in 3 sessions/weekly, for 2 months, each session lasting at least 45 minutes. The 2 training were separated by a 3-week interval. A blinded to treatment skilled neuropsychologist evaluated the patient's cognition and psychological status in 2 separate sessions: before and after the 2 different trainings, by using a proper psychometric battery including Montreal Cognitive Assessment (MoCA) Test, Attention Matrices Test, Hamilton Rating Scale for Anxiety, Hamilton Rating Scale for Depression, and Coping Orientation to the Problems Experienced-New Italian Version (COPE-NVI). These psychometric tools aimed at assessing the global cognition, attention processes and the presence of mood alterations, anxiety and coping strategies. The general functional status was evaluated by using the Functional Independence Measure (FIM). The main vital parameters (such as oxygen, blood pressure and heart rate) were also monitored as more objective markers of the treatment efficacy (see Table 1). Patient gave *written* informed consent for the diagnostic procedures, treatment, and publication of the case.

2.1. Conventional rehabilitative sessions

The standard relaxation technique consisted of diaphragmatic breathing, induced by the instructions of the therapist within a quiet and noiseless environment. DB is a breathing technique that uses the contraction of the diaphragm muscle to move air downward into the body, which increases diaphragm length and breathing efficiency and facilitates more efficient exhalation.^[20,21] During the first 5 minutes, the therapist invites the patient to assume a comfortable posture to facilitate muscular relaxation with well-supported back, legs slightly apart at the same width of shoulders, arms on the legs and loose jaw. In the next 25 minutes, she was guided to diaphragmatic breathing; then, she was invited to breathe without using the chest district but the abdominal one, prompting to hold a hand to stomach as self-monitoring function. In the final step, lasting 15 minutes, the patient underwent a paper and pencil cognitive task (i.e., attention process, spatial cognition and executive functioning) face to face with the therapist. At the end of the conventional cognitive training, we asked to talk about her physical and emotional feelings experienced during the treatment.

2.2. Virtual reality combined approach

The same amount of rehabilitative treatment (relaxation technique and diaphragmatic breathing, besides dual task motor-cognitive training) was provided by using an immersive virtual environment (Fig. 1). Indeed, the use of VR enables researchers to assess the subject's behavior and includes sensory inputs like visual, auditory, vestibular and tactile. Novel technologies, such as the CAREN, provide virtual simulations as a mean to improve physical and cognitive skills for individuals with different neurological and orthopedic disorders while promoting resilience and recovery. CAREN is a versatile, multisensory system for clinical analysis, rehabilitation, evaluation, and registration of the human balance system.^[22] In particular, the CAREN system, developed by MOTTEK Medical (Amsterdam, Netherlands), consists of a motion capture system and a base driven by hydraulic and mechanical actuators. The base where the user stands is retrofit with force plates and a treadmill, with up to 6 degrees-of-freedom.^[23] This allows the operator to generate physical, visual, and cognitive perturbations that require the user to make dynamic responses during their gait patterns. The CAREN system may also be equipped with varying degrees of VR immersion ranging from a flat video, dual-channel audio, theater in its "base" model to a 360°, surround sound dome enclosure in its "high end" version (the one we used was the Extended version with a 180° screen). Real-time motion tracking technology enables the CAREN system to follow patient movement's frame-by-frame for detailed kinematic and biomechanical analysis using up to 24 mounting locations.^[24] The device is unique in that it allows a patient's warrior to be immersed in a realistic clinical environment, while therapist and physicians collect kinematic and kinetic data in order to plan future rehabilitation regimens.^[25] For the training in the virtual environment, we used specific exercises, realized to stimulate motor, cognitive and behavioral domains, including visuo-spatial cognition, attention process (with one and dual task), executive functions, anxiety, ideo-motor praxis, visuo-motor coordination and balance. In particular, we have used 5 virtual scenarios (see image no.1). This combined approach was articulated in 2 specific programs to increase cognitive and behavioral abilities, besides a potentiation of balance (which however was out of the scope of our protocol). A single rehabilitative session included

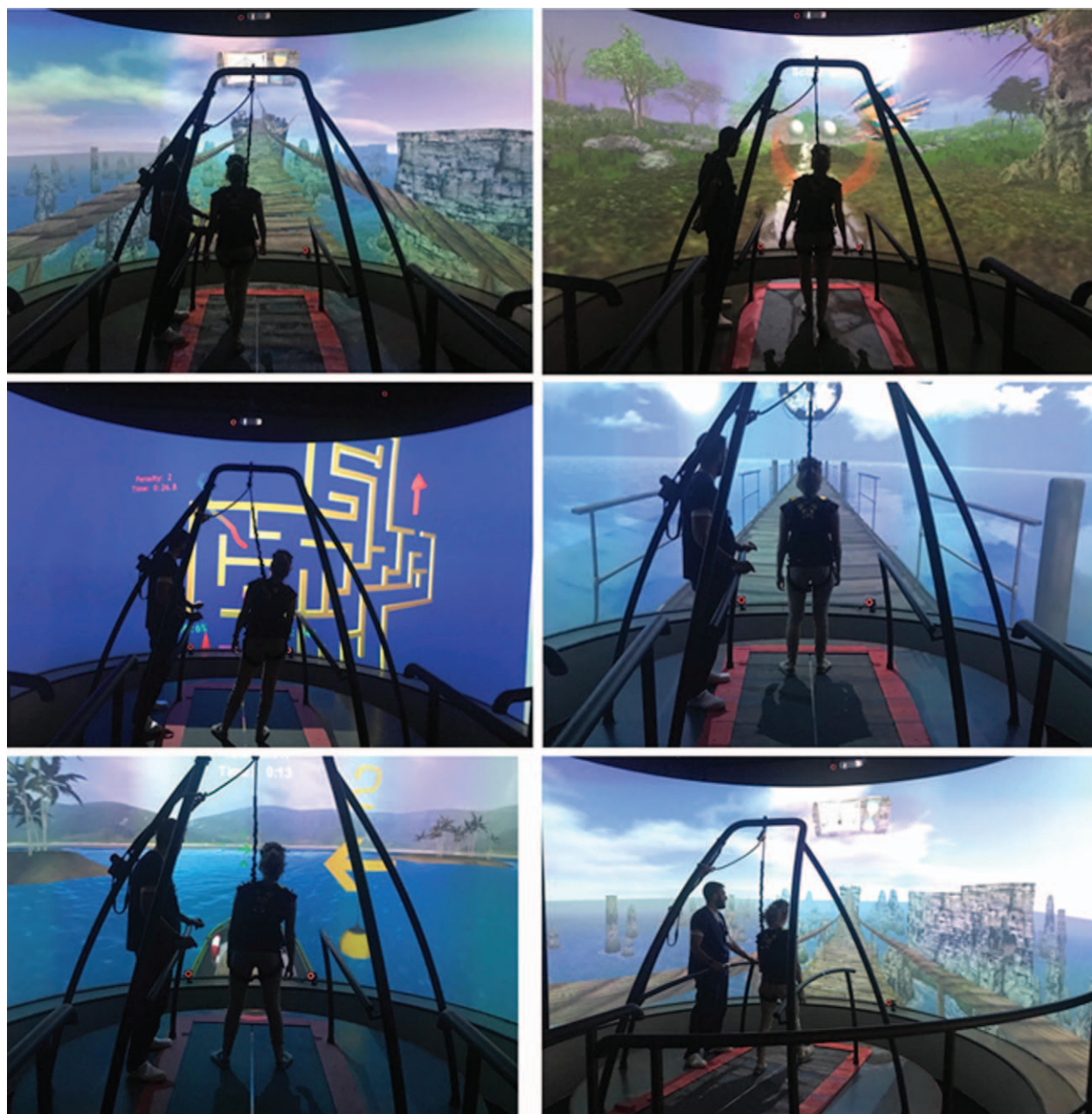


Figure 1. It shows the combined rehabilitative approach with the CAREN System. CAREN = Computer Assisted Rehabilitation ENvironment.

patient-tailored scenarios, lasted about 45 minutes, and was built to improve both cognition and anxiety by means of 2 different protocols. The first part of the training included:

1. *MM Boat*: that is, a marine environment with buoys to avoid, with the patient guiding the boat with his body shifting until the final goal, and
2. *Active Balance*, a labyrinth in which the patient drives a red ball, moving the load up to the finish line.

This training (lasting 15 minutes) was aimed at potentiating both balance, and attention and visuospatial abilities. The second part of the training consisted of

1. *a walk across the board*: This virtual scenario is task-oriented and describes a bridge surrounded by a marine setting; the

patient walks on the treadmill, self-adjusting the speed to achieve the objectives of the operator.

2. *Road encounters*, that is, a forest in which the patient walks or runs, with ascents or descents; the double task coincides to strike at the same time some distractor elements (often butterflies)
3. *Rope Bridge*: A suspension bridge along which the patient walks or runs; the double task consists in avoiding distracting elements (moving gulls).

By using a slow and self-selected gait speed, the patient was able also to perform breathing and relaxation techniques, when she walked in the virtual environments (at beginning without distractors). In fact, in this protocol (lasting about

Table 1

Comparison of behavioral, psychometric and functional measures at T0-T1-T2-T3; mean raw data with RCI (a statistic tool that is used to determine whether a change in an individual's score, for example, before and after some intervention, is statistically significant or not -based on how reliable the measure is-; if the RCI is >1.96, then the difference is statistically significant) are reported.

| Domain | Psychological and Cognitive status | | Conventional Techniques (RCI) | | CAREN System (RCI) | |
|---------------------|------------------------------------|-------------------------|-------------------------------|-----------|--------------------|-------------|
| | Psychometric Test | | T0 | T1 | T2 | T3 |
| Global Cognition | Sub-items | MOca Test | 19/30 | 22/30 | 22/30 | 26/30 (2.1) |
| | | Visuo-spatial/executive | 2/5 | 2/5 | 2/5 | 4/5 (2.3) |
| | | Naming | 3/3 | 3/3 | 3/3 | 3/3 |
| | | Selective Attention | 0/2 | 1/2 (1.9) | 1/2 | 2/2 (2.1) |
| | | Divide Attention | 0/1 | 0/1 | 0/1 | 1/1 (1.9) |
| | | Sustained Attention | 1/3 | 2/3 | 2/3 | 2/3 |
| | | Language | 2/2 | 2/2 | 2/2 | 2/2 |
| | | Abstraction | 1/2 | 2/2 | 2/2 | 2/2 |
| | | Delayed Recall | 4/5 | 4/5 | 4/5 | 4/5 |
| | | Orientation | 6/6 | 6/6 | 6/6 | 6/6 |
| Attention Process | AM Test | 33,50 | 35,50 | 36,50 | 59,50 (3.3) | |
| Anxiety | HRS-A | 20 | 18 | 18 | 15 (2.1) | |
| Depression symptoms | HRS-D | 16 | 16 | 16 | 13 (1.9) | |
| Coping Strategies | Cope-NIV | 80 | 90 | 85 | 105 (2.3) | |
| | Social support | 10 | 15 | 15 | 30 (2.1) | |
| | Avoidance strategies | 15 | 20 | 15 | 10 (3.1) | |
| | Positive attitude | 15 | 15 | 15 | 25 (2.9) | |
| | Problem Solving | 15 | 15 | 15 | 15 | |
| | Turning to religion | 25 | 25 | 25 | 25 | |
| Functional Status | FIM | 75 | 80 | 80 | 110 (3.3) | |

MOca Test (Montreal Cognitive Assessment); cut-off = ≤ 25 .

AM (Attentive Matrices Test); cut-off = ≤ 30 .

HRS-A (Hamilton Rating Scale for Anxiety); cut-off = ≥ 8 .

HRS-D (Hamilton Rating Scale for Depression) cut-off = ≥ 8 .

Cope-NIV (Coping Orientation to Problems Experienced - New Italian Version); Range from 72 to 228.

FIM (Functional Independent Measure); cut-off = 0–126.

30 minutes), dual task training lasted only 10 minutes, whereas 20 minutes were entirely dedicated to anxiety treatment.

3. Results

At the end of the conventional training, using standard relaxation techniques (T0-T1), including DB, the patient presented a mild improvement in the selective attention and mood with a reduction of crying episodes and negative thoughts. Nonetheless, only at the end of the training in the immersive virtual environment, that is, “CAREN System”, we have observed a significant improvement in cognitive and behavioral functioning. In fact, by comparing the psychometric measures, at the end of the combined approach, (i.e., the use of standard techniques in a total immersive virtual environment), the patient gained a considerable improvement in attention processes, visuo-spatial abilities and executive functioning. Moreover, we have observed a better stabilization of the cardiac frequency, blood pressure and oximetry parameters with a relevant reduction of anxiety symptoms (from T2: HRS-A: 18; to T3: HRS-A = 15). Finally, we noted an optimization of the coping strategies, with regard to social support and positive attitude with an important decrease of the avoidance strategies (see Table 1). Moreover, at 6-month follow-up the improvement persisted, and we did not planned any other training.

4. Discussion

The most common neuropsychiatric outcomes of stroke are depression, anxiety, fatigue, and apathy, which each occur in at

least 30% of patients and have substantial overlap of prevalence and symptoms. Emotional lability, personality changes, and psychosis, are less common but equally distressing symptoms that are also challenging to manage.^[26] Anxiety is a psychic state of an individual, predominantly conscious, characterized by a feeling of intense worry or fear, often unfounded. Hoehn-Saric et al define anxiety like a biological warning system that prepares us for action.^[27] Anxiety is characterized by a set of biochemical changes in the body, autobiographical memory, the patient's history and the social situation during acute stress. In the onset of anxiety, the thalamus plays a major role as it receives sensory inputs and projects them into areas of associative cortex including the *locus coeruleus*, the amygdala, and the orbito-frontal cortex. The onset of anxiogenic stimuli causes a change in noradrenergic, serotonergic, and dopaminergic systems and an inhibition of GABA effects.^[28] Some studies have shown that DB has a relaxing and stabilizing effect on the autonomic nervous system,^[29,30] enhances levels of carbon dioxide in the blood, strengthens nerve activity parasympathetic,^[30,31] increases body temperature and stabilizes heartbeat and blood pressure.^[32,34] To this end, a normalization of blood pressure and oximetry parameters was noted at the end of the combined approach in our patient. Although the DB is considered one of the privileged and useful techniques for stress and anxiety reduction,^[29,34,35] there are no studies in the literature that demonstrate its effectiveness in patients with stroke and neuropsychiatric symptoms. Instead, for the treatment of anxiety in stroke patients, various researches claim that autogenous training may lead to good results.^[14,15] During the last decade, a number of studies have been conducted in order to examine whether and to what extent VR might be an

alternative form of therapy for the treatment of anxiety disorders. VR, a tool of human–computer interaction that allows researchers and clinicians to immerse people in virtual worlds, is gaining considerable traction in the research, education, and treatment fields. VR has been used successfully to treat anxiety disorders, such as fear of flying and post-traumatic stress disorder, as an aid in stroke rehabilitation, and as a behavior modification aid in the treatment of attention deficit disorder.^[36] Moreover, Calabrò et al showed that robot-assisted movement training with virtual avatar may improve not only motor function (including gait, balance and muscle force), but also mood, cognition, and coping strategies.^[37] In fact, augmented feedback during robot-assisted gait appears to be a promising way of facilitating gait and physical function, but also of improving psychological and cognitive status, particularly in executive process.^[37–39]

To the best of our knowledge, this is the first time that CAREN has been used as a tool to improve anxiety in a patient with a chronic stroke. Indeed, only another case reporting a 45-year-old woman suffering from anxiety disorders and treated by means of CAREN has been reported. In particular, the authors (2016) showed that VR exposure therapy was able to improve her anxiety disorder with the subsequent gradual adaptation of the patient to the stressful situation, as per the gradual decrease in the levels of salivary cortisol. In line with these findings, we may argue that the training with CAREN system can be promising also in the treatment of neuropsychiatric symptoms, including anxiety. Differently from Krysta, we have used a combined approach to treat generalized anxiety due to ischemic stroke. In fact, in our case, the virtual scenarios served as a good mean to potentiate relaxation techniques, besides improving cognitive function thanks to the complex dual-task training. Indeed, as compared to traditional treatment, after VR the patient gained better results in terms of functional outcomes (i.e., in both behavioral and cognitive status) and compliance to the training. The efficacy of VR in boosting the relaxation training has been investigated.^[40] The authors showed that the use of combined relaxation strategies in specific virtual environment (i.e., natural scene, namely Relaxation Island; European Project EMMA – IST-2001-39192) characterized by a high level of presence, might be a promising rehabilitative approach.^[40–42] Indeed, VR natural scenes may provide relaxation both objectively and subjectively, and scene preference had a significant effect on mood and perception of scene quality.^[17] This is the reason why we used 3 different natural scenarios to perform DB. According to Isaacson et al,^[43] another important finding of our paper is the attempt to show how novel technologies, such as the CAREN, may improve cognitive rehabilitation. In fact, beyond the important role of dual task training in the VR environment, patient's cognitive status may have improved also thanks to the relaxation techniques, given that mood and anxiety may affect cognition. Finally, our patient showed, after the combined rehabilitative approach, a reduction of avoidance strategies, improving a positive attitude to problem solving. To this end, previous studies showed that adaptive coping strategies could facilitate better functional outcomes, given that coping has been put in relation with executive functions.^[44]

Although the training with CAREN is feasible and promising, patients with severe sensory-motor and cognitive deficits, those affected by severe medical illness potentially affecting the training, as well as those with active epilepsy (with regard to the photosensitive forms) should be excluded from the treatment with the device.

Moreover, cybersickness (a syndrome occurring during and/or after the VR training, characterized by blurred vision, headaches, vertigo, imbalance and nausea and due to conflicts between 3 sensory systems, i.e., visual, vestibular, and proprioceptive when the “body” is immersed in the virtual environment) should be taken into consideration when using the VR device.

We are aware that findings from a single case report have many limitations, including epidemiological bias, impossibility of causal inference and generalization and over-interpretation. Thus, our results should be confirmed by well-designed clinical studies, also evaluating the cost-effectiveness analysis.

5. Conclusion

Relaxation and respiratory techniques in a total immersive virtual reality environment, using the novel device CAREN, may be an advanced system in potentiating attention process, coping strategies and reducing anxiety. Further studies are needed to clarify the role of VR in improving neuropsychiatric symptoms, including anxiety, in the post-stroke patients.

Author contributions

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Writing – original draft: Rosaria De Luca, Rocco Salvatore Calabrò.

Writing – review & editing: Rocco Salvatore Calabrò.

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