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ORIGINAL ARTICLE

Feasibility of virtual reality-based balance rehabilitation in adults with spinocerebellar ataxia: a prospective observational study

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ABSTRACT

Objective: To test the effects of a virtual reality (VR) balance rehabilitation program in patients diagnosed with SCAs.

Materials and methods: A prospective observational study was carried out with a cohort of 28 patients diagnosed with SCAs, including eight females and 20 males, 15–70 years of age (mean, 41.5 ± 16.9 years). Patients were submitted to otorhinolaryngological assessment to exclude any kind of middle ear impairments that may hinder exam results, and vestibular evaluation to verify the existence of vestibular disorders, kind and site of the lesion. The Dizziness Handicap Inventory (DHI), Berg Balance Scale (BBS), and 36-item Short-form Health Survey (SF-36) questionnaires were applied before and after VR rehabilitation. The criterion for significance in before versus after VR training comparisons was $p < .05$.

Results: Regarding to baseline, the participants showed significant improvements posttraining in their DHI and BBS scores. These improvements were accompanied by improvements in perceived quality of life (QoL) as measured by the SF-36. There were significant improvements in balance and gait, fall frequency, and patients' self-confidence.

Conclusions: Showed consistent improvement postrehabilitation in their ability to play VR games (i.e. Soccer Heading, Tightrope, Table Tilt, and Ski Slalom). VR rehabilitation may be an effective SCA therapy. The breadth of improvements evidenced here should promote physical and psychological recovery, while fostering a better QoL.

KEYWORDS
Spinocerebellar ataxia; balance; quality of life; rehabilitation; virtual reality; balance exercises

Introduction

Spinocerebellar ataxias (SCAs) are a heterogeneous group of neurodegenerative diseases characterized by the presence of progressive cerebellar ataxia. The initial hallmark clinical manifestations of SCA are deterioration of balance and coordination, together with ocular disorders [1]. SCAs are classified based on how, or whether, the condition was inherited [2]. Most SCA cases are congenital, though SCA syndromes can develop secondary to central nervous system (CNS) trauma. Congenital SCA may be sporadic (underlying gene mutation not inherited) or, more commonly, inherited. Among the inherited forms of congenital SCA, autosomal recessive cerebellar ataxias (ARCAs; a.k.a. Friedreich's ataxia), autosomal dominant cerebellar/dominant spinocerebellar ataxias (DSCAs), X-linked hereditary ataxias, and mitochondrial ataxias have been identified.

An effective curative treatment for SCA has yet to be confirmed, and management remains supportive and symptomatic [3]. There are treatments that can be used to manage extra-cerebellar symptoms. Rehabilitation therapy may have beneficial effects on the motor symptoms of SCAs. For prospective parents hoping not to pass along their disease to their future children, preimplantation genetic diagnosis can be used to prevent hereditary ataxias, particularly DSCA forms. There are some promising pharmaceutical and cell therapies in development that may be tested in clinical trials in the coming years [3].

Patients suffering from SCAs are at high risk of fall injuries due to loss of balance. Bodily balance is highly dependent on the integrity of the peripheral and central vestibular system of the inner ear (i.e. semicircular canals and otolith organs, which detect head position vs. gravity and directional acceleration,

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of the vestibular nuclei in the vestibular area of the brainstem rhomboid fossa, vestibulo-oculomotor, vestibulocerebellar, vestibuloreticular, vestibulocortical, vestibulospinal pathways and their connections with the reticular formation (reflex mechanisms, including the autonomous ones), and other areas of the CNS, a component of the somatosensory system that specializes in proprioception (sensory receptors within tendons, muscles and joints), and vision. The brain integrates information from these sensory modalities, especially the former two, to achieve kinesthesia, that is, an ongoing sense of body movement. Dizziness and/or imbalance occur when normal kinesthetic function is compromised due to peripheral or central malfunction [4,5]. The CNS responds to vestibular stimulation by means of reflexes, including the vestibulo-ocular reflex (VOR), which stabilizes vision during head motion, and the vestibulospinal reflex (VSR), which generates a compensatory body motion to stabilize the head and body, and thus prevent falls [5]. The mechanism of learning, or re-learning, to maintain balance involves cerebellar plasticity, with the cerebellum being considered a critical region of vestibular reafference computation, that is, tracking of vestibular changes caused by one's own volitional movements [6].

The main goal of vestibular rehabilitation is to improve postural control and balance, and thereby to reduce the risk of falls, by means of specific, repetitive physical exercises across different settings. Neuroplasticity in the vestibular system may include habituation, adaptation, and replacement [5,7,8]. In habituation, the CNS becomes accustomed to abnormal stimulation, such that it can respond to it as if it were normal. In adaptation, the vestibular system learns to process inappropriate or incomplete information more effectively over time. In replacement, missing or abnormal body position- and balance-related information is compensated for with information from alternate origins [5,7,8].

SCA therapy exercises aim to improve vestibular-visual interactions during head motion, to expand static and dynamic postural stability under conditions of conflicting sensory information, and to improve the competence to carry out daily activities, with the ultimate goal of giving patients greater physical autonomy [8,9]. Compared to traditional therapy methods, virtual reality (VR) technology-based therapy has the distinct advantage of allowing the patient to encounter a wide range of stimuli with greater specificity that produce controlled sensory conflicts in a safer environment [9]. Vestibular rehabilitation by means of VR therapy enables patients to become immersed in an imaginary world, in which environmental perception is altered by artificial stimuli, thereby generating a sensory conflict that can act on the VOR.

Disrupted balance is a principal complaint of patients suffering from cerebellar dysfunction, particularly due to SCAs. Currently, there is a need for feasible alternative interventions that will facilitate the reestablishment of a functional neural circuitry that can compensate, at least to some degree, for SCA pathology of the CNS. Hence, the main objective of the present study was to investigate the effects of a VR-mediated balance rehabilitation program in patients with SCAs. We sought to obtain a broad understanding of the effects of VR training by considering results from multiple standard self-reporting instruments in addition to performance on VR games that rely on the use of fine motor skills as well as dynamic and static balance.

Materials and methods

Participants and study design

This study was approved by the Ethics Board Committee on Human Research (Brazil Platform; no. 832.502/2014). Participants signed Participant Free Informed Consent Forms.

A prospective, observational study was conducted with 28 patients (8 females and 20 males) who were referred by the Movement Disorders Unit, Department of Neurology, Clinical Hospital, for therapy treatment at the Otoneurology/Rehabilitation Department, at a large private University, with a diagnosis of SCA. The exclusion criteria were middle-ear disorders, comorbidity with any visual impairment or other abnormalities that prevented implementation of the VR protocol, inability to comprehend and respond to simple verbal commands, reliance on a gait-supporting device, and any prior rehabilitative therapy. The clinical and demographic data of the participants are summarized in Tables 1 and 2. Briefly, patients' ages ranged from 15 to 70 years old (mean, 41.6 ± 16.9 [standard deviation (SD)] years) and disease durations ranged from 2 to 40 years (mean 13.3 ± 12.4 [SD] years.

SCAs are highly diverse genotypically as well as phenotypically. The same genetic entities, etiologically, can present with varying signs, symptoms, and disease progression courses. The size of the trinucleotide repeat expansion (TNR) underlying an SCA is an important factor is disease course [4]. Thus, molecular genetics and clinical symptoms are used in

Table 1. Summary of patient (P) with DSCA ($N = 20$).

P	Age (years)/ Sex	SCA type	Disease duration (years)	Abnormal chromosomal locus	Gene affected[a]	Mutation type	SARA
1	47/M	SCA3	13	14q32.1	*ATXN3*	CAG	4
2	48/F	SCA3	16	14q32.1	*ATXN3*	CAG	10
3	43/M	SCA3	16	14q32.1	*ATXN3*	CAG	4.5
4	41/M	SCA3	12	14q32.1	*ATXN3*	CAG	10.5
5	53/M	SCA3	14	14q32.1	*ATXN3*	CAG	13
6	41/M	SCA2	14	12q24.1	*ATXN2*	CAG	28
7	36/M	SCA2	12	12q24.1	*ATXN2*	CAG	4.0
8	43/M	SCA4	13	16q24.qter	*SCA4*	PLEKHG4?	9.5
9	55/F	SCA10	14	22q13.3	*ATXN10*	ATTCT	7
10	46/M	SCA10	15	22q13.3	*ATXN10*	ATTCT	9
11	30/F	SCA10	11	22q13.3	*ATXN10*	ATTCT	7
12	70/M	SCA10	14	22q13.3	*ATXN10*	ATTCT	16
13	56/F	SCA10	14	22q13.3	*ATXN10*	ATTCT	14
14	28/M	Und.	2	–	–	–	7
15	27/M	Und.	10	–	–	–	16
16	34/M	Und.	17	–	–	–	4.5
17	32/M	Und.	9	–	–	–	9
18	62/M	Und.	10	–	–	–	7
19	37/F	Und.	11	–	–	–	16
20	48/F	Und.	10	–	–	–	8

[a]The proteins affected with *ATXN3*, *ATXN2*, and *AXN10* mutations were ataxin-3, ataxin-2, and ataxin-3, respectively.
SCA: spinocerebellar ataxia; Und: undetermined; M: male; F: female; SARA: scale for the assessment and rating of ataxia.

Table 2. Summary of patient (P) with ARCA ($N = 8$).

P	Age(years)/ Sex	Disease/duration (years)	SARA
21	43/M	25	20
22	41/M	10	3.5
23	30/F	18	8
24	24/M	8	4
25	29/M	13	14
26	15/M	3	13
27	63/F	40	7
28	44/M	10	3.5

M: male; F: female; SARA: scale for the assessment and rating of ataxia.

combination to assign SCA classification [4]. Diagnostic SCA typing was conducted, when possible, by genetic polymerase chain reaction testing [10]. The present cohort of 28 patients included 20 patients with DSCA and 8 patients with ARCA. The culprit gene was established in 13 of the 20 patients with DSCA, including 2 patients with type 2 SCA, 5 with type 3, 1 with type 4, and 5 with type 10 SCA. The remaining 7 patients did not have conclusive genetic studies at the time this report was prepared and are thus classified here as having non-specified DSCA.

All patients were submitted to otorhinolaryngological assessment in order to exclude any kind of middle-ear impairments that may hinder the exam result, anamnesis, and vestibular evaluation in order to verify the existence of vestibular disorders, kind and site of the lesion. The vestibular system analysis by digital vector electronystagmography (Neurograff Eletromedicina LTDA, São Paulo/São Paulo State, Brazil). Subsequently, the Dizziness Handicap Inventory (DHI) [11], Berg Balance Scale (BBS) [12], and 36-item Short-form Health Survey (SF-36) [13] were applied. The DHI, BBS, and SF-36 questionnaires were administered before rehabilitation (1st assessment, baseline) and after rehabilitation (2nd assessment, posttraining).

Procedures

Dizziness handicap inventory (DHI)

The DHI (adapted to the Brazilian population) is a questionnaire comprised of 25 questions, divided into physical (7 questions), emotional (9 questions), and functional (9 questions) domains. The physical domain of the DHI examines the relationship between dizziness experiences and eye, head, and body movements. The emotional domain assesses fear of going out or staying home alone, shame of clinical symptoms, concerns with the self-image, difficulty focusing, feelings of incapability, depression, and problems with family and social relationships. The functional domain detects impaired performance in professional, household, social, and leisure. Each item has three possible responses: 'affirmative' (4 points); 'sometimes' (2 points), and 'negative' (0 points). Hence, the maximum score for the DHI is 100 points wherein higher scores reflect a greater magnitude of dizziness.

Berg Balance Scale (BBS). The BBS assesses functional balance performance in 14 activities of daily life wherein the participant performs a series of timed body-balance control tasks. Each item has an ordinal 5-choice response scale ranging from 0 to 4 points, where 0 indicates the lowest level of balance function, and 4 the highest.

Sf-36

Intervention efficacy is often assessed by comparing pre- and postintervention SF-36 results, as was done here. The SF-36 is a 36-item questionnaire that assesses quality of life (QoL). It consists of eight components: functional capacity, physical aspects, pain, general health status, vitality, social aspects, emotional aspects, and mental health. Total SF-36 scores range from 0 to 100, with a higher score representing a better general health status.

Vestibular rehabilitation

For therapeutic body-balance rehabilitation, a Nintendo® Wii hand-held remote and Wii balance board were used, enabling monitoring of applied strength and balance changes via pressure sensors that are normally responsible for the machine-player interface. Before commencing with the rehabilitation program, patients received instructions about how to play the games, including the specific movements required. The following four balance games were played: Soccer Heading, Table Tilt, Tightrope Walk, and Ski Slalom. In the Soccer Heading game, the objective is to hit the ball with the avatar's head using antero-posterior and lateral-lateral weight transfer. In the Table Tilt game, the player is tasked with placing balls in holes on an unstable board using lateral-lateral and antero-posterior displacements. In the Tightrope Walk game, the player walks and jumps on a virtual tightrope by alternating his or her feet with a rapid knee flexion-extension movement. Finally, in the Ski Slalom game, the player skiis from side to side to deviate from the flag using lateral–lateral movement and pelvic flexion/extension. Successful performance in these games entails head motion, dynamic and static balance, motor coordination, circular movements of the pelvis, and weight transfer aimed at maintain balance and correcting for postural instability. All patients underwent twenty 50-min VR sessions, twice a week.

Statistical analysis

Data analyses were carried out by means of Spearman correlation tests and paired Student's *t* tests performed in Statistica 13.1 software. The significance level was 0.05 [5%] in all cases.

Results

The most reported otoneurological complaints in the anamnesis were: imbalance (85.7%), fall (28.5%), dizziness (17.8%), diplopia (10.7%), and tremor (7.1%). Vestibular screening detected abnormalities in 18/28 cases (64.3%), including 10 cases (35.7%) of peripheral vestibular disorders and 8 cases (28.6%) of central vestibular disorders. The screening results appeared to be normal in the remaining 10/28 cases (35.7%).

The DHI and BBS results before and after VR training are shown in Figure 1(A,B), respectively. As reported in detail in Table 3, we observed significant correlations between pretraining (baseline) Tightrope Walk game performance and both BBS score and the SF-36 functional capacity domain subscore, as well as between the Ski Slalom game and the SF-36 pain domain subscore. Our posttraining correlational analyses revealed significant correlations between posttraining Soccer Heading game performance and SF-36 functional capacity domain subscore. We also observed significant correlations between posttraining performance in both the Table Tilt and Tightrope Walk games and DHI score, BBS score, and SF-36 functional capacity domain subscore. Posttraining Ski Slalom game performance correlated with SF-36 mental health domain subscore.

Highly significant differences were observed between pre- and posttraining performance in all four VR games, namely, Soccer Heading, Tightrope Walk, Table Tilt, and Ski Slalom (Table 4). Comparing the results of the first assessments conducted before rehabilitation with those of the second assessments conducted after rehabilitation, we also observed significant improvements in several aspects of QoL and SCA symptoms (see Table 4 for all pre- versus posttraining comparison data).

Discussion

In the present study, we observed significant improvements in balance control, dizziness, and overall self-reported QoL following 20 daily Wii VR game sessions in a cohort of patients diagnosed with SCAs. Before the intervention, Tightrope Walk performance correlated with both the BBS score and SF-36 functional capacity subscore, and Ski Slalom performance correlated with SF-36 pain subscore. After the intervention, Soccer Heading performance correlated with SF-36 functional capacity subscore; Table Tilt performance and Tightrope Walk performance correlated with DHI score, BBS score, and SF-36 functional capacity subscore; and Ski Slalom performance correlated with SF-36 mental health subscore.

Interventions based on VR games are relatively novel for patients suffering from SCAs. Therapeutic benefits can be masked by the natural deterioration associated with the progression of SCAs.

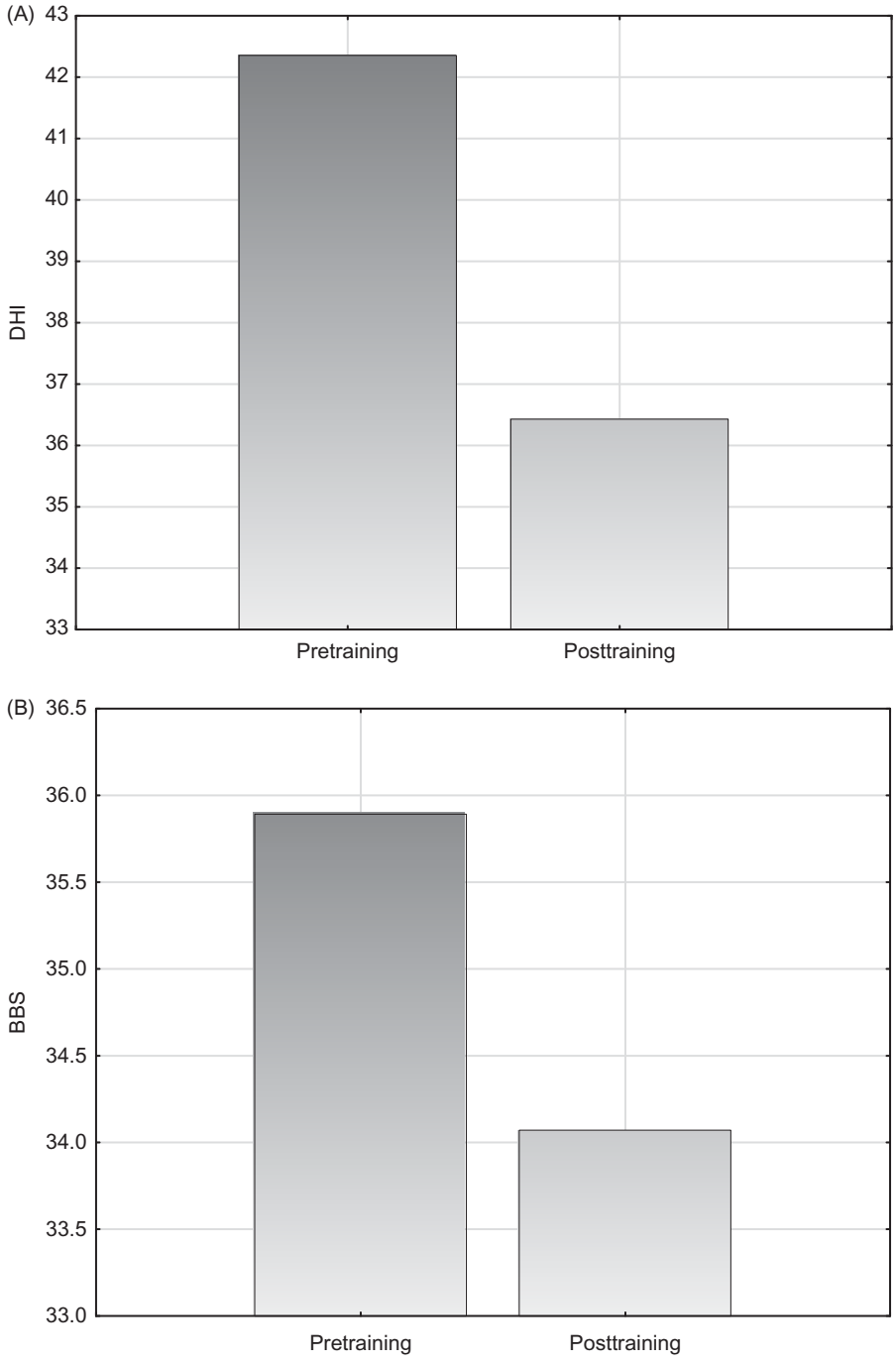

Figure 1. Training effects on dizziness and balance indices ($N = 28$). Pre- vs. post-VR training scores on the DHI (A) and BBS (B).

Notwithstanding, the few reports in literature addressing the efficacy of this kind of treatment for this population underscore the importance of elucidating treatment options for SCA [14]. Notably, in a study of 4 patients with DSCA, Zeigelboim and colleagues [7] observed improvements in BBS following training with Wii Fit VR games (Bird's-eye, Bull's eye, Big Top Juggling, and Hula Hoop); furthermore, fall risk was improved from high to low in most of the patients (3 of 4). With respect to QoL, one recent study [15] reported significant improvements in the general health status, vitality, and social aspects domains of the SF-36 after VR training in elderly patients with SCAs. Meanwhile, in the current study, we observed VR rehabilitation intervention benefits on the functional capacity, pain, and mental health domains of the SF-36.

The presently observed overall DHI score reduction from before to after the intervention indicates that the participants experienced an alleviation of the impairing effects of their dizziness. The presently observed amenability of dizziness problems to intervention is

Table 3. Clinical assessments and VR game performance ($N = 28$).

	SOCCER HEADING		TABLE TILT		TIGHTROPE		SKI SLALOM	
Assessment	R	*p*	R	*p*	R	*p*	R	*p*
1st assessment, pretraining baseline								
DHI	0.0005	.9978	0.1503	.4453	0.1310	.5065	0.0376	.8495
EEB	0.0677	.7322	0.3578	.0616	0.5771	**.0013**	0.0675	.7327
SF36 – FC	0.1661	.3983	0.3136	.1042	0.4749	**.0107**	0.0093	.9624
SF36 – FA	0.0389	.8441	0.0213	.9145	0.0012	.9953	0.0612	.7569
SF36 – P	0.2460	.2070	0.3961	.0369	0.0302	.8788	0.5262	**.0040**
SF36- GHS	0.3021	.1182	0.2370	.2247	0.3435	.0735	0.3613	.0589
SF36 – V	0.1600	.4159	0.1187	.5476	0.1912	.3298	0.0720	.7156
SF36 – SA	0.2057	.2937	0.0192	.9228	0.0648	.7434	0.1549	.4312
SF36 – EA	0.0624	.7526	0.0881	.6556	0.3362	.0803	0.0731	.7118
SF36 – MH	0.0302	.8788	0.2659	.1715	0.1409	.4745	0.2516	.1965
2nd assessment, posttraining								
DHI	0.3589	.0607	0.5112	**.0054**	0.4779	**.0101**	0.3706	.0522
EEB	0.0929	.6381	0.4268	**.0235**	0.4205	**.0259**	0.0542	.7843
SF36 – FC	0.5186	**.0047**	0.6429	**.0002**	0.5415	**.0029**	0.2625	.1772
SF36 – FA	0.0891	.6521	0.1691	.3895	0.0270	.8916	0.0555	.7793
SF36 – P	0.0192	.9226	0.0142	.9429	0.0265	.8936	0.3648	.0563
SF36- GHS	0.0153	.9386	0.1673	.3947	0.2065	.2917	0.1243	.5286
SF36 – V	0.0605	.7596	0.0328	.8683	0.1199	.5432	0.0162	.9346
SF36 – SA	0.2514	.1969	0.0061	.9756	0.1121	.5700	0.1105	.5756
SF36 – EA	0.0681	.7306	0.0186	.9252	0.0212	.9148	0.1876	.3390
SF36 – MH	0.1447	.4627	0.0085	.9656	0.0606	.7594	0.4220	**.0253**

R: Spearman Correlation test; DHI: Dizziness Handicap Inventory; BBS: Berg Balance Scale; SF 36: *Short Form*; FC: functional capacity; FA: physical aspects; P: pain; GHS: general health status; V: vitality; SA: social aspects; EA: emotional aspects; MH: mental health.
Significant *p* values are in bold.

Table 4. VR game performance ($N = 28$).

	Session 1		Session 20		
Game	Mean	SD	Median	SD	*p*
Soccer heading	27.3	21.8	58.7	64.0	**.0154***
Tightrope walk	12.5	8.5	24.0	13.3	**<.0001***
Table tilt	29.3	13.5	54.7	29.6	**<.0001***
Ski slalom	85.4	18.5	70.0	24.3	**.0178***

SD: standard deviation.
$p < .05$ was considered significant.
Significant *p* values are in bold.

consistent with the findings of a prior study of 22 patients with an assumed diagnosis of peripheral chronic vestibular disorder who showed improvements on their DHI total scores and QoL following six weeks of rehabilitation [16]. Moreover, our findings also corroborate the results of a prior study [17] in which a patient with peripheral vestibular dysfunction showed significant improvements in dizziness and balance control after participating in a VR rehabilitation program using the Wii system, similar to the present intervention, with the benefit maintained for 6 months. In another study, 3 patients suffering from encephalic trauma who underwent rehabilitation composed of 30 min of VR therapy followed by 50 min of swimming class daily for 21 days also experienced postintervention improvements in BBS score and DHI score [18]. Patients with traumatic brain injury have also responded positively to VR therapy in terms of improved balance and reduced fall risk as assessed by the BBS [19]. Likewise, a cohort of 70 patients with cerebellar infarction presenting with a gait imbalance and central vertigo also exhibited reduced fall risk, as indicated by BBS results, following VR therapy [20].

Rehabilitation with a VR interface simulates real-life situations, which is thought to stimulate neuroplasticity in the CNS through specific exercises for the eyes, head, and body that call for adaptations to compensate for impaired or absent sensory information [5]. Adaptive neural changes involving existing synapses and/or rewiring of neuronal circuity are thought to underlie functional improvements during rehabilitation [21]. Although we did not measure synaptic rewiring directly, we can infer that the robust behavioural improvements observed in balance functioning following VR rehabilitation involved neuroplastic changes in brain circuitry. Similar behavioural improvements have been observed by other authors [9,18,19], who have characterized VR games as involving mediolateral and anteroposterior areas in motor planning, facilitated by visual feedback [9,18,19]. The VR game Ski Slalom, in particular, was shown previously to improve postural control in neurologically intact subjects [22].

Rehabilitation protocols involving VR games have also been reported to be effective for improving performance on particular tasks in patients suffering with spastic hemiparesis following a traumatic brain injury or cerebrovascular accident [23], which can affect multiple regions, including the cerebellum, a brain

region that is critical for motor coordination and input-output integration underlying maintenance of balance [24]. Notably, Gordon et al. [25] observed outstanding recovery in gross motor function using VR games as a rehabilitative tool in a group of children with cerebral palsy. Additionally, in a study of 23 patients with Ménière's disease, Garcia and colleagues [26] observed improvements in DHI score and a dizziness visual analogue scale following VR rehabilitation training of postural control, stability, and muscle coordination with the BRU™ system.

In a 2013 reviewer of therapies used to treat patients with SCAs, Artigas and colleagues [27] described multiple therapeutic benefits, including balance and posture correction as well as improvements in limb motion and functionality. With respect to VR game-based therapy, they argued that the VR game-based approach is particularly effective at motivating patients to carry out the exercises. Relative to conventional rehabilitation methods, VR provides a more pleasant interface. Additionally, the inclusion of game elements with immediate performance feedback provides a motivational dimension that encourages patients to complete more repetitions [28].

In the current study, we can observe that the Wii Balance Board enables data collection regarding displacement of the centre of pressure. With practice, unimpaired users improve the magnitude of the centre of pressure displacement [22]. Wii Fit Plus games have also been shown to be useful for balance rehabilitation in elderly users [29]. These games promote saccadic, optokinetic stimuli, smooth pursuit ocular movement, and finer control of the centre of pressure, in addition to training joint response strategies via force platform feedback, which enables bodily balance improvement. Ultimately, the improvements observed can be attributed to neuroplasticity, in which the vestibular system habituated to the repeated exercises [28].

Our study has a noteworthy limitation. That is, we do not have posttreatment follow-up data to reveal whether the benefits of the VR training are maintained long term. Future studies should examine how shorter intervention times (following diagnosis) and different frequencies of training affect outcomes with the aims of optimizing therapy protocols and gaining a better understanding of how vestibular information is used in the control of bodily balance.

Conclusions

The incorporation of functional activities within rehabilitation treatment programs is essential for patient autonomy. VR rehabilitation is a low-cost, noninvasive treatment with no evident adverse secondary effects. Here, we observed improvement in SCA symptoms, particularly with respect to balance and gait, which reduces risk of falls and increases self-confidence, thus promoting physical and psychological recovery, while enabling greater independence during the performance of daily activities, and thus an improved QoL. Hence, the present results indicate that VR game-based interventions represent a promising approach to providing neurofunctional rehabilitative therapy to patients with SCAs.

Ethics approval and consent to participate

This study was approved by the Ethics Committee on Research Involving Human Subjects (registration number CEP n°. 832.502/2014) at Brazil Plataform. All examinations were performed after formal consent forms were obtained from all the participants.

Disclosure statement

The authors declare that there are no conflicts of interest.

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