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m- and e-Health applications in diagnosis and rehabilitation of balance disorders- Εφαρμογές m- και e-health για τη διάγνωση και αποκατάσταση διαταραχών ισορροπίας

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Dedicated to…

My father for his constant guidance and inspiration

My mother for her silent patience

My aunt Kaiti, without whom I would have probably not been a doctor

Dr Kikidis and Professor Bibas, who stood by my side during this whole journey

In memoriam of my Professor Theodoros Papadas,

Without whom I would never have loved ENT surgery.

Abstract

Background: Balance is a primary human sense which requires multisensory integration from the vestibular, the visual and the proprioceptive systems and involvement of the cerebellum and several other neural circuits. Additionally, a number of reflexes, such as the vestibulo-ocular and the vestibulospinal reflexes, along with many other higher cerebral functions are engaged. Under certain circumstances, a peripheral or central lesion can occur to the system leading to instability and vertigo symptomatology. Since the 1940s, when Cooksey and Cawthorne began to investigate rehabilitation following such lesions, many things have changed in the field of balance rehabilitation and during the last decades modern technologies have been incorporated in this effort. Nowadays, a great amount of mHealth, eHealth and Virtual Reality applications have been developed aiming to contribute in diagnosis or/and rehabilitation of patients with vestibular disorders.

Methods: The electronic database MEDLINE was searched for relevant studies from January 1, 2015 up to April 15, 2021. The papers included in this review were determined according to certain inclusion and exclusion criteria.

Results: A total number of 187 studies occurred after the initial search strategy, out of which 43 were considered eligible and included in this review. They were subdivided into 5 major categories and further discussed.

Discussion: Gaming consoles, such as the Nintendo Wii, Nintendo Wii Fit and Sony PlayStation 2 EyeToy and Internet-based applications have been implemented during the last years to assist in the diagnosis and rehabilitation of patients with balance disorders. As novel technologies emerge and smartphones become an essential part of our everyday lives, vestibular diagnosis and rehabilitation will rely more and more on head-mounted display, mobile phone and sophisticated platform applications.

Περίληψη

Υπόβαθρο: Η ισορροπία είναι μια αρχέγονη ανθρώπινη αίσθηση που απαιτεί πολυαισθητηριακή ολοκλήρωση από το αιθουσαίο, το οπτικό και το ιδιοδεκτικό σύστημα και συμμετοχή της παρεγκεφαλίδας και αρκετών άλλων νευρωνικών κυκλωμάτων. Επιπλέον, εμπλέκονται ένας αριθμός αντανακλαστικών, όπως το αιθουσοοφθαλμικό και το αιθουσονωτιαίο αντανακλαστικό, μαζί με πολλές άλλες ανώτερες εγκεφαλικές λειτουργίες. Υπό συγκεκριμένες συνθήκες, μια περιφερική ή κεντρική βλάβη μπορεί να συμβεί στο σύστημα οδηγώντας σε αστάθεια και συμπτωματολογία ιλίγγου. Από τη 1940, όταν οι Cooksey και Cawthorne ξεκίνησαν να διερευνούν την αποκατάσταση μετά από τέτοιες βλάβες, πολλά πράγματα έχουν αλλάξει στο πεδίο της αποκατάστασης ισορροπίας και κατά τις τελευταίες δεκαετίες οι νέες τεχνολογίες έχουν ενσωματωθεί σε αυτή την προσπάθεια. Σήμερα, ένας μεγάλος αριθμός από εφαρμογές mHealth, eHealth και εικονικής πραγματικότητας έχον αναπτυχθεί με σκοπό να συνεισφέρουν στη διάγνωση ή/και αποκατάσταση ασθενών με αιθουσαίες διαταραχές.

Μεθοδολογία: Η ηλεκτρονική βάση δεδομένων MEDLINE διερευνήθηκε για σχετικές εργασίες από την 1η Ιανουαρίου 2015 έως την 15η Απριλίου 2021. Οι συμπεριληφθείσες στην ανασκόπηση εργασίες καθορίστηκαν βάσει συγκεκριμένων κριτηρίων ένταξης και αποκλεισμού.

Αποτελέσματα: Ένας συνολικός αριθμός από 187 εργασίες προέκυψε μετά την αρχική στρατηγική αναζήτησης, από τις οποίες 43 κρίθηκαν επιλέξιμες και συμπεριλήφθηκαν σε αυτή την ανασκόπηση. Χωρίστηκαν σε 5 μείζονες κατηγορίες και συζητήθηκαν περαιτέρω.

Συζήτηση: Οι κονσόλες παιχνιδιών, όπως το Nintendo Wii, το Nintendo Wii Fit και το Sony PlayStation 2 EyeToy, και οι εφαρμογές Internet έχουν χρησιμοποιηθεί τα τελευταία χρόνια για να συνδράμουν στη διάγνωση και αποκατάσταση ασθενών με διαταραχές ισορροπίας. Καθώς αναδύονται νέες τεχνολογίες και τα smartphones γίνονται βασικό μέρος της καθημερινότητας μας, η αιθουσαία διάγνωση και αποκατάσταση θα βασίζονται όλο και περισσότερο σε εφαρμογές για γυαλιά εικονικής πραγματικότητας, για smartphones και για εξελιγμένες πλατφόρμες.

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Introduction

1.1 Basic anatomy and function of the Vestibular System

Balance, although it is not included among the five senses, is one of the primary human properties older evolutionarily than hearing and sight and probably older than taste and smell (1). It is mediated via the vestibular system, which is a complex sensory system comprising of the peripheral and the central vestibular system.

The peripheral system comprises bilaterally of the posterior labyrinth of the inner ear– consisting of the saccule, the utricle and the three semicircular canals – and the vestibular nerve. The latter has two portions, the superior and the inferior vestibular nerves, which fuse to form the vestibular nerve, which then pairs with the cochlear nerve to form the vestibulocochlear (or eighth cranial) nerve (2).

The vestibulocochlear nerve enters the brainstem at the level of the cerebellopontine angle. There are four vestibular nuclei related to each of the two vestibulocochlear nerves. Ascending neural pathways lead to higher level cortical domains (2). Overall, the vestibular system is a multisensory and multimodal system, which is closely attached to the cerebellum, the brainstem, the visual and the proprioceptive systems and has been traditionally linked to balance and gaze control (2), (3).

A great variety of processes, on top of the aforementioned ones, are mediated by the vestibular system. Several cognitive functions are involved. Such are spatial perception and orientation (4), body parts identification (5), spatial memory (6), attention (7). Additionally, the vestibular system is believed to be linked to anxiety disorders and depression (8).

1.2 Natural history of vestibular disorders

An acute unilateral vestibular lesion is followed by unequal neural discharges arising from the two peripheral vestibular nuclei complexes towards the central vestibular system. This imbalance initially occurs during both static and dynamic conditions. Static disequilibrium refers to impaired tonic inputs between the bilateral vestibular nuclei when the head is fixed, and thus solely under the force of gravity. On the other side, dynamic disequilibrium refers to uneven neural discharges between the bilateral nuclei when the head is in motion and subject to linear and angular accelerations (9), (10).

The aforementioned changes in neural depolarization of the afferent vestibular fibers, also known as unilateral vestibular deafferentation, lead to a wide range of symptoms (11). The static syndrome comprises of the oculomotor, the postural and the perceptual syndromes. The first one involves skew deviation, spontaneous horizonto-rotatory nystagmus and ocular cyclotorsion, while the second one includes instability of the head and body, most notably when the patient rotates towards the side of the lesion. The patient is also prone to incline and even fall towards that side. The perceptual syndrome includes vertigo, usually described as a spinning sensation, alteration in the subjective visual vertical and autonomic syndromes (e.g. nausea, vomiting, bradycardia, pallor) (10), (12).

Following the initial event, the function of the injured vestibular apparatus can return to normal. In case that the lesion remains, neuroplasticity in the affected vestibular nuclei group takes over. More specifically, it appears that restoration of function occurs to some extent, leading to recovery of the spontaneous tonic input rate of the impaired vestibular nuclei complex. Consequently, symptoms of static imbalance improve. The duration of this symptomatology is usually relatively short, and its resolution is characterized as Vestibular Compensation, which occurs within a few weeks or months (11), (13).

On the contrary, vestibular compensation commonly does not include recovery in deficits of the dynamic equilibrium. These remain and include instability in complex environments and affected vestibulo-ocular reflex parameters, such as reduced gains, phase shifts and time constants towards the side of the lesion. When the Head Impulse Test (Halmagyi test) is performed, the normal vestibulo-ocular reflex is affected and sometimes replaced by a delayed compensatory saccade. This overt saccade can be covered by behavioral and sensory mechanisms. In that case, covert saccades can be discovered in the Video Head Impulse Test (VHIT) (12).

Overall, the clinical manifestation of dynamic instability usually ameliorates as a result of substitution by non-vestibular gaze and equilibrium mechanisms, but certain symptoms can potentially remain (11).

1.3 Vestibular rehabilitation

Vestibular hypofunction, resulting from unilateral or bilateral vestibular impairment, constitutes a severe factor of morbidity in patients suffering, since it is related to chronic disability and increased risk of falls. The individuals estimated to suffer from vestibular hypofunction are estimated from 53 to 95 million adults in the USA and in Europe (14). Falls, on the other hand, constitute a significant social, economic and health problem of modern societies. Apart from these, falls and injuries commonly lead older patients to long-term care facilities, in which a greater fall risk exists compared to general population (15). In regards to financial burden, the cost for non-fatal injuries reaches 50 billion dollars annually, while the cost for fatal injuries reaches 750 million dollars (16). That way, it is imperative that a proper diagnosis should be followed by an appropriate treatment program. During the acute phase, a pharmacological approach is usually followed. Following the acute stage of the disorder, however, patients usually follow special rehabilitation programs, known as vestibular rehabilitation.

Vestibular, or balance, rehabilitation applies to an extended spectrum of diseases, the most important of which, are vestibular disorders. It also applies, however, to other disorders responsible for dizziness, instability and vertigo. It refers to different sets of exercises, the goal of which is postural compensation. This training can be individualized and requires the use of certain diagnostic tools to help determine the patient’s deficits and needs, e.g. identification of the status of the different sensory modalities involved in postural control and of factors which can potentially facilitate rehabilitation (17).

Cooksey and Cawthorne in the 1940s were the pioneers in conceiving and describing exercises for the head, the eyes and the body. Apart from the aforementioned, they also referred to mental exercises and occupational therapy. At first, this exercise program was intended for soldiers with brain injuries, but was soon applied to patients who were operated for Meniere’s disease too. It was believed to expedite balance rehabilitation following pathology of the peripheral vestibular system in these patients. (1), (18), (19) These exercises have been modified and are still in use in our days, known as the Cawthorne- Cooksey exercises.

The next major event in the history of vestibular rehabilitation happened on 1980, when Brandt and Daroff described a new exercise, in which patients with Benign Paroxysmal Positional Vertigo (BPPV) repeated certain precipitating head movements. According to their publication, a vast majority of patients showed complete symptom alleviation within 3 to 14 days (20).

Subsequently, it was Epley in 1992, who, like Brandt and Daroff, was based on Schucknecht's canalith theory and proposed the Canalith Repositioning Procedure. Specifically, Epley suggested a 5-position sequence of the head, during which, he believed that free otoliths were led from the posterior semicircular canal back to the utricle. (21) The Canalith Repositioning Procedure or Epley maneuver constitutes a paramount in vestibular rehabilitation history and was succeeded by several new maneuvers and modifications for treatment of the BPPV of all semicircular canals.

Nowadays, vestibular rehabilitation is subdivided into 2 categories. Physiotherapy for peripheral vestibular hypofunction includes exercise-based treatment protocols aimed 1.to enhance the vestibulo-ocular reflex, which is responsible for gaze fixation, 2.to alleviate vertigo symptoms, 3.to improve postural balance, and 4.to facilitate everyday life activities. Canalith repositioning maneuvers for BPPV include certain position cycles of the head and body (9).

Peripheral vestibular disorders are usually benign and self-limiting. They are subject to spontaneous remission due to different compensatory stages occurring in the central nervous system following a lesion of the vestibular apparatus. Balance rehabilitation therapy intends to act on several of these stages, so that the aforementioned four goals are achieved (22).

Since vestibular compensation is a usually met term through our study, it would be useful to firstly delineate certain definitions. By 'vestibular compensation', we either describe an improvement in unilateral vestibular hypofunction or vestibular substitution following a vestibular syndrome. 'Well compensated' refers to a complete regaining of function, whereas 'poorly compensated' to a partial procedure. As far as 'decompensation' is concerned, it is used to characterize a relapse of the vestibular syndrome. Finally, a unilateral vestibular lesion with persisting symptomatology is described as 'uncompensated' (9).

1.4 Physiology of vestibular rehabilitation

The innate vestibular compensation, along with exercises for vestibular rehabilitation rely significantly on the neuroplastic capacities of the individual's central nervous system. Notably, vestibular rehabilitation revolves around the following principles: restoration, adaptation and habituation.

Restoration describes the procedure of recovery of the neural activity that existed before the vestibular injury. It has been shown that the VOR gain is restored in some individuals recovering from vestibular neuritis, which poses an indication for restoration of the preexisting activity in the damaged vestibular nuclei complex. It is believed that a recovery of hair cells in the vestibular apparatus or of afferent neurons in the eighth cranial nerve occurs. (23)

Next, adaptation comprises of sensory substitution and behavioral substitution. Sensory substitution relies on the principle of multimodal integration, namely the dependence of the central vestibular system on vestibular, somatosensory and visual stimuli. Our central nervous system looks capable to reweight among these different sources of sensory information, when one modality does not suffice, leading to compensation. For example, when the vestibulo-ocular reflex is absent, it is usually replaced by other ocular motor control systems, such as by saccades observed in the Head Impulse Test. The next step in neural adaptation is based on learning-dependent functional rearrangement of the vestibular pathways. This process is defined as behavioral substitution (23).

Finally, unilateral vestibular hypofunction establishes a gap between the afferent stimuli from the two posterior labyrinths. This difference is compensated by habituation and relies on repetition of the triggering stimuli (23).

1.5 Indications for vestibular rehabilitation

As already mentioned, balance rehabilitation aims either to facilitate vestibular compensation through physiotherapy exercises in cases of unilateral and bilateral peripheral vestibular damage, or to reposition canalith back into the vestibule using specific maneuvers in cases of BPPV. In general, vestibular dysfunction is met in 1 out of 3 people over 40 years of age (24). BPPV, which can be idiopathic or secondary to head trauma, vestibular neuritis etc, is met in all age groups but more commonly in individuals of 50 to 70 years old. BPPV appears with an incidence of 11-64/100.000/year (25).

Vestibular schwannoma, vestibular neuritis, Ménière's disease, iatrogenic injury of the peripheral vestibular system (e.g. labyrinthectomy, vestibular neurectomy, therapeutic trans-tympanic injection of Gentamicin), herpes zoster oticus, labyrinthitis are commonly met causes of unilateral vestibular hypofunction. Bilateral vestibular loss causes include drug-induced ototocixity (e.g. systemic administration of gentamicin), bilateral vestibular neuritis, congenital or age-related vestibular degeneration (26).

Balance rehabilitation programs can be applied to individuals who suffer from both peripheral and central vestibular damage. It can also be conducted on patients with a sole central lesion, but in these last cases the prognosis is considered worse than in patients with an exclusive peripheral lesion (9).

It is clear that vestibular rehabilitation has traditionally been linked to vestibular loss. Nowadays, however, vestibular rehabilitation applies not only to disorders of the vestibular system, but also to several other diseases of the nervous system, which affect gait and postural control. For example, relative indications for vestibular rehabilitation include head injuries, which usually involve both central and peripheral vestibular loss, psychogenic vertigo, dizziness in the elderly and vertigo of unknown origin. Physiotherapy in these conditions can be applied as monotherapy or in combination with other treatments (9).

In a stroke of ischemic or hemorrhagic origin, blood flow of the central nervous system is impaired, leading to cell death and parenchymal necrosis. Consequently, the different neurological systems involved in balance control are usually harmed. As a result, strokes are considered as a major cause of incapacity in adults, affecting walking and mobility in general (27), and also constitute an important factor of reduced quality of life (28). Vestibular rehabilitation has been studied in post-stroke patients and appears to ameliorate physical, emotional and perceptual features of vestibular symptomatology. Continuing training following a vestibular rehabilitation program may be of importance (29).

Parkinson's disease, a common mobility disorder is attributed pathologically to neuronal degeneration in the substantia nigra and other brain regions and to the presence of Lewy bodies. Its prevalence augments significantly after 65 years old of age and it presents with resting tremor, bradykinesia and impaired balance control (30). According to a growing body of evidence, vestibular rehabilitation appears favorable to several balance-related outcome measures (31), (32).

Spinal cord injury disrupts efferent and afferent neural pathways, thus leading to impairment of both sensory and motor pathways. As a consequence, motor functions, including gait and postural control are harmed. Repetitive mobility exercises included in vestibular training are considered to facilitate partial or complete recovery of several of these functions (33).

Cerebral palsy refers to a group of heterogeneous cerebral disorders, which present early in childhood and are not progressive in nature. With a prevalence of 2,11/1000 live-born children, cerebral palsy is enlisted among the most common causes of juvenile disability of mobility (34). Since equilibrium is severely impaired, vestibular rehabilitation constitutes a treatment goal in this patient category (35).

1.6 Categories of Vestibular Rehabilitation exercises

Vestibular rehabilitation has surpassed the stage of a standard set of exercises, as was initially proposed by Cooksey and Cawthorne. Nowadays, it refers to a holistic therapy, which must always be preceded by several diagnostic tools to help assess the patient's actual deficits and needs. As a general rule, the sooner vestibular rehabilitation is initiated, following a vestibular lesion, the better for the patient is. Exercises for gaze stability should be repeated 5 times a day with a total duration of 20-40 minutes per day, combined with 20 minutes of gait and stability training, in a daily basis. Vestibular rehabilitation programs usually endure for 4-8 weeks.

First of all, enhancement of gaze stability is a fundamental principle of vestibular rehabilitation therapy, which is attained by vestibular adaptation. The main concept involved in this, is that retinal slip, achieved by moving the head horizontally (yaw plane) or vertically (pitch plane) while the gaze remains fixed on a certain point, leads to error signals in the visual stimuli, provoking an increase in the gain of the impaired VOR. Optokinetic eye movements induced by e.g. an optokinetic drum constitute an alternative of these exercises for VOR gain increase. In cases of severe unilateral or bilateral vestibular lesion, the VOR cannot be efficiently amplified and thus central processes, such as saccades and smooth-pursuit eye movements undertake. Certain exercises can enhance this procedure (9).

In addition, postural balance needs to be enhanced and to do so, patients need to augment their dependency on the somatosensory and visual systems, through restoration exercises, along with their remaining vestibular responses, through vestibular adaptation. Since patients with vestibular loss can become dependent on visual or somatosensory cues, it is of importance that physiotherapists and clinicians use a tool, like the Clinical Test for Sensory Interaction in Balance to evaluate the contribution of the different sensory modalities on balance control (9).

Specifically, individuals with unilateral hypofunction commonly develop dependency on somatosensory stimuli during the acute phase and on visual stimuli during the chronic phase. The opposite occurs in people with bilateral lesions. Visual dependency can be perturb patients' equilibrium, because it is possible that they orient their body in accordance to visual stimuli, leading to imbalance and falls. This phenomenon also creates an illusion of self-motion. Vestibular rehabilitation in this patients' category includes exercises in environments with disrupted visual cues, e.g. use of optokinetic stimuli. Respectively, somatosensory reliance should be faced with exercises with reduced somatosensory input, e.g. standing on foam cushions (9).

Finally, there are exercises aiming towards the recovery of the normal ankle, hip and step strategies, when possible in individuals with vestibular loss. When this is not possible, exercises for new postural strategies identification should be implemented. Exercises aiming to alleviate vertigo perception should be applied, too. This training is based on habituation of the remaining vestibular function to rapid motion (9).

Patients who are unable to retain their previous daily routine for 6 months or more are considered disabled. Vestibular rehabilitation therapy is considered successful when the patient is able to improve his everyday activities, and even recover the functionality he had before the vestibular lesion. That way, it is imperative that we aid these patients to return to work and recover their previous status quo. This procedure can be realized by combining the vestibular rehabilitation exercises with normal activities and games (9).

1.7 Modern technologies and vestibular rehabilitation

As already mentioned, vestibular rehabilitation addresses to many peripheral and central mobility and balance disorders. Conventional rehabilitation has been implemented as a major treatment option in patients with peripheral vestibular lesions, stroke, Parkinson's disease, spinal cord injury, cerebral palsy and more. During the last years, however, new technologies have had a major impact on balance rehabilitation. The efficacy of these technologies has been already tested in health care in situations like simulation training for surgeons (36), treatment for psychiatric disorders (37), (38), smartphone-based management of diabetes (39), and interactive mobile encyclopedias for learning (40).

Much of the vocabulary associated with modern technologies is in everyday use. Since the scope of the current thesis relates with m- and e-Health applications in diagnosis and rehabilitation of balance disorders, a disclosure of relevant definitions is considered vital before proceeding to the main body of this review.

E-Health, according to Eysenbach, is an emerging area in informatics of medicine, public healthcare and business, related to information and functions applicable through the Internet and modern technologies. Apart from this technical view, e-Health encompasses a manner of thinking and an aspect for a networked, catholic perspective that uses communications and information to ameliorate medical care from a local to a global level (41).

M-health or mobile health is a newer term in relation to e-Health and forms part of the second. According to the WHO, it is defined as healthcare practice delivered through mobile devices, like mobile phones (42). Nowadays, mobile applications are m-Health's main expression.

As far as Virtual Reality is concerned, there is interestingly a definition concerning virtual reality in vestibular rehabilitation. Specifically, it is about computer software and hardware which enables users to interact employing their own body with a simulation of a realistic or imaginary virtual world (43).

Methods

A scoping review of the literature was conducted with the aim to present a thorough understanding of the current views concerning the implementation of virtual reality, e-Health and m-Health in vestibular diagnosis and treatment. Specifically, a series of articles published between January 1, 2015 and April 15, 2021, were evaluated and presented.

Search of the literature was materialized in MEDLINE. The keywords utilized were: mHealth, eHealth, mobile applications, game, virtual reality, gamification, smartphone, iPhone, vestibular rehabilitation, balance rehabilitation, peripheral vestibular loss, dizziness, vertigo, Benign Paroxysmal Positional Vertigo.

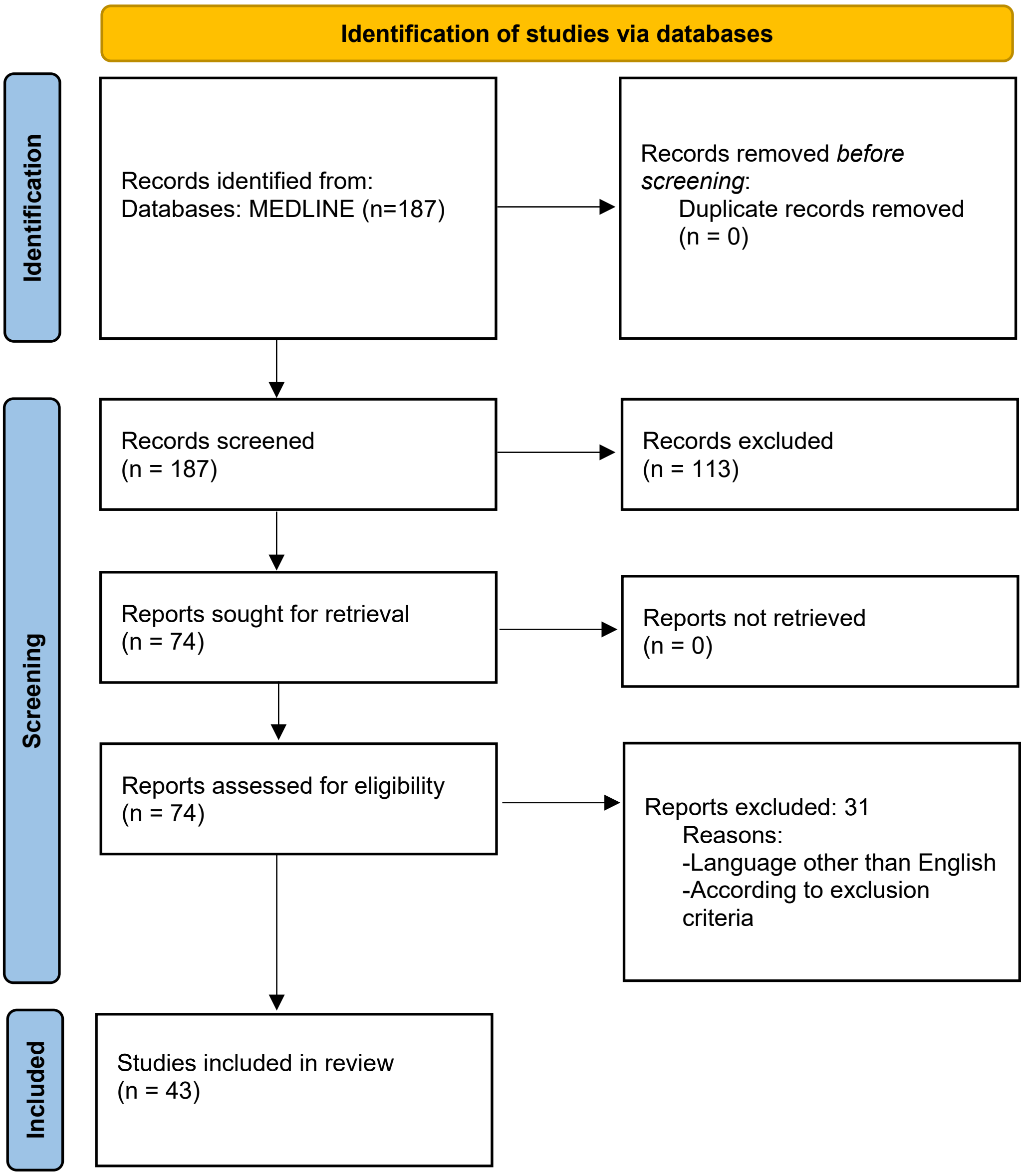
The search strategy used in MEDLINE was: ((((((((((mHealth) OR (eHealth)) OR ("mobile application")) OR ("mobile applications"[MeSH Terms])) OR (game)) OR ("virtual reality")) OR ("virtual reality"[MeSH Terms])) OR (gamification)) OR (iphone)) OR (smartphone)) AND (((((((("vestibular rehabilitation") OR ("balance rehabilitation")) OR ("peripheral vestibular loss")) OR (dizziness)) OR (dizziness[MeSH Terms])) OR (vertigo[MeSH Terms])) OR (vertigo)) OR ("Benign Paroxysmal Positional Vertigo")) OR ("Benign Paroxysmal Positional Vertigo"[MeSH Terms])).

Studies with the following criteria were included in the review: 1. Studies with healthy subjects or with patients suffering from central or peripheral vestibular disorders, 2.Studies with participants of all ages, 3.Studies which exhibit mHealth, eHealth and virtual reality applications used as diagnostic or intervention tools, 4.Studies with health technologies intended for clinicians' and/or patients' use, 5.No specific outcome measures were investigated, as long as a mHealth/eHealth/Virtual Reality technology was involved, 6.Studies the whole text of which was available, 7.Studies in English.

The following exclusion criteria were implemented: 1.All articles that did not meet an inclusion criterion or more were excluded, 2.Studies with patients suffering from musculoskeletal or peripheral neural disorders, 3.Articles that exhibit mHealth, eHealth or Virtual Reality applications as a supporting tool and not as a main intervention.

Following an initial search of the relevant literature, the different modern technology applications were divided in five major categories, as shown in the results. This categorization will be further discussed in the Discussion section.

Results



Identification of studies via databases
Identification
Screening
Included
Records identified from:
Databases: MEDLINE (n=187)
Records removed *before screening*:
Duplicate records removed
(n = 0)
Records screened
(n = 187)
Records excluded
(n = 113)
Reports sought for retrieval
(n = 74)
Reports not retrieved
(n = 0)
Reports assessed for eligibility
(n = 74)
Reports excluded: 31
Reasons:
-Language other than English
-According to exclusion criteria
Studies included in review
(n = 43)

Mobile applications (mHealth)

Study	Study design	Technology used	Applies to	Sample	Outcome measures	Results
Organ et al., 2015 (44)	Prospective, randomized, blinded, placebo-controlled study	iPhone application DizzyFIX	Medical students and health-care professionals	41 third-year medical students randomly divided into a test group (n=20) and a placebo group (n=21)	Epley maneuver performance	Statistically significant better particle repositioning maneuver performance (p<0,0001) in the test group (9,65/11) compared to the placebo group (4,67/11)
Dlugaiczyk et al., 2018 (45)	Single-center, two-arm, prospective, randomized, controlled study	Simulation-based medical education/ Smartphone application	Medical students and health-care professionals	113 medical students randomly divided into a study group (n=46) and a control group (n=67)	Correct arrangement of the steps of the Epley maneuver and satisfaction of students with the course	Significantly better teaching quality (p<0.0001) and higher Epley maneuver completion (p=0,006) in the study group
Brodsky et al., 2015 (46)	Cross-sectional study	iPhone application Visual Vertical-Smartphone-based SVV (ip-SVV)	Patients	31 patients with dizziness and 8 non-otologic control patients (7-18 y.o.)	Mean ip-SVV score for certain conditions causing dizziness	Statistically significant elevation in the ip-SVV score in the patients with peripheral vestibular loss (2,77±1,45) compared to the rest of groups (p<0,01). ip-SVV score has a negative predictive value of 94,1%, positive predictive value of 80%, sensitivity of 66,7%, specificity of 97% in diagnosis of peripheral vestibular loss in younger patients
Shah et al., 2019 (47)	Feasibility study	iPhone application TigerText-smartphone-based HIPAA-compliant encrypted data-sharing platform	Clinicians	30 patients with dizziness (>18 y.o.)	Telemedical diagnosis of BPPV with ocular movement recording after DHT.	Telemedical diagnosis of BPPV has a sensitivity of 92,86%, specificity of 100% and negative predictive value of 97.87%
De Joode et al., 2020 (48)	Usability study	iOS/ Android mobile application DizzyQuest	Patients with vestibular disorders	57 patients with different vestibular disorders (>18 y.o.)	Comparison of the use of two different 'vertigo reporting' questionnaires of the DizzyQuest app	Evening questionnaire was used 446 times with at least 749 episodes of vertigo reported, whereas the attack questionnaire was completed 192 times

BPPV: Benign Paroxysmal Positional Vertigo; DHT: Dix-Hallpike test; SVV: Subjective Visual Vertical; y.o.: years old

Organ et al. evaluated DizzyFIX, an iPhone application, which aims to assist clinicians in a more correct application of the Epley maneuver. The DizzyFIX makes use of the cell phone's integrated orientation sensors. The device is positioned against an individual's head, presenting immediate feedback concerning the phone's and thus the head's position and orientation. The 41 students were divided into a test group of 20, which utilized the application and a placebo group of 21 which made use of a non-functional application, working as placebo to the observer who scored their Epley maneuver performances. It was found that the test group had significantly better particle repositioning maneuver performance (9,65/11) than the placebo group (4,67/11) (p<0,0001) and that it completed the maneuver faster (p<0,0001). The authors however, emphasize that better Epley maneuver performance does not mean necessarily a higher treatment success (44).

Dlugaiczyk et al divided 113 medical students registered for the Otorhinolaryngology class into two instructional groups, in a prospective, randomized, controlled study. Participants of the control group (n=67) applied the Dix-Hallpike and the Epley maneuvers on each other, while students in the study group (n=46) applied the maneuvers both on each other and on a virtual patient in the aVOR application. The study's goal was to assess students' evaluation of the course and competence in realization of the Epley maneuver with the use of the aVOR application on a tablet computer (iPad). The teaching media quality was significantly higher in the study group (p < 0.0001), while a statistical significance was found in the students' percentage who completed successfully the Epley maneuver in the aVOR group (56,3%) opposite to the control group (25,9%) (p=0,006). They concluded that the application could be used in ORL teaching (45).

Brodsky et al. utilized the application "Visual Vertical" on an iPhone 5 and asked the patients to align a red line provided by the application with their perception of true vertical. Subsequently, the deviation of the perceived from the true vertical in degrees is assessed by the application. Of the pediatric patients, 6 had peripheral vestibular loss, 6 BPPV, 11 central vertigo, 8 non-vestibular dizziness, while 8 were control patients. The mean ip-SVV score in the first group (2,77±1,45) was significantly higher than in the rest of groups (p<0,01). Overall, the ip-SVV can be used as a screening tool for peripheral vestibular lesions in children with dizziness, with a cut-off score of >2,138, negative predictive value of 94,1%, positive predictive value of 80%, sensitivity of 66,7%, specificity of 97%, If patients with over 1 month of dizziness are excluded, sensitivity and specificity ascend to 75% and 100% respectively (46)

Shah et al used the application TigerText on an iPhone 5 to assess the feasibility of diagnosing BPPV through remote evaluation of ocular movement videos by 2 neuro-otologists. These videos were recorded by a resident physician. The patients had been examined before by a neuro-otologist in person and had undergone certain vestibular tests. After comparing the results from in person and remote examination, a sensitivity of 92,86%, a specificity of 100% and a negative predictive value of 97.87% for diagnosing BPPV was calculated (47).

De Joode et al. evaluated the DizzyQuest application for smartphones, which provides the users with standardized questionnaires based on their vestibular symptomatology during the day. They recruited 57 adult patients with different vestibular disorders, who undertook the completion of two different questionnaires: an evening questionnaire that offers time sampling of vertigo attacks during the day and an attack questionnaire that offers event sampling of individual episodes of vertigo. The authors evaluated the nature and number of the attacks between the 2 questionnaires. They concluded that the evening questionnaire was used 446 times with at least 749 episodes of vertigo reported, whereas the attack questionnaire was completed 192 times. Thus, a low recall bias with a reliable record of the nature of attacks is observed in the attack questionnaire, but is accompanied by under-sampling. The opposite applies to the evening questionnaire (48).

Internet-based applications

Study	Study design	Technology used	Applies to	Sample	Outcome measures	Results
Van Vugt et al., 2019 (49)	Pragmatic, three group, parallel arm, individually randomised controlled trial. 59 general practices in the Netherlands	Internet-based vestibular rehabilitation	Patients with a chronic vestibular lesion	322 patients with a chronic vestibular lesion (>50 y.o.). 98 received stand-alone internet-based rehabilitation, 104 combined internet-based and conventional physiotherapy and 120 usual GP care	Primary o.m.: Vestibular symptoms assessment by VSS-SF at 6 months Secondary o.m.: DHI, subjective improvement in vestibular symptoms, PHQ, GAD-7 subscale, PHQ-9 subscale	The first group reported a mean difference of -4,1 points (95% confidence interval −5,8 to −2,5) and the second one a mean difference of −3,5 points, (95% confidence interval −5,1 to −1,9) compared to the usual GP group after 6 months in the VSS-SF. A reduction in dizziness-related disability and anxiety and a subjective amelioration in vestibular symptoms were reported.
Geraghty et al., 2017 (50)	Single-center, single-blind randomized controlled trial	Balance Retraining: an Internet-based vestibular training tool	Older persons with chronic dizziness	Intervention group: 160 patients with chronic dizziness (mean age: 67,3 y.o.). Control group: 136 patients with chronic dizziness (mean age: 67,5 y.o.).	VSS-SF, autonomic and vertigo symptom subscales of the VSS-SF, DHI, HADS	The intervention group reported a significant symptom amelioration on the VSS-SF at 3 ($p<0,001$) and 6 months ($p=0,02$) and a significantly diminished dizziness-associated disability at 3 ($p<0,001$) and 6 months ($p=0,01$).

DHI: dizziness handicap inventory; GAD-7: General Anxiety Disorder-7; HADS: Hospital Anxiety and Depression Scale; o.m.: outcome measure; PHQ: patient health questionnaire; VSS-SF: Vertigo symptom scale– short form ; y.o.: years old

Van Vugt et al. compared the safety and clinical effectiveness of internet-based rehabilitation with combined internet and conventional rehabilitation and with usual GP care. Patients in the first two groups presented diminished VSS-SF scores after 6 months, compared to patients in the usual GP care group. Specifically, the first group reported a mean difference of -4,1 points (95% confidence interval −5,8 to −2,5) and the second one a mean difference of −3,5 points, (95% confidence interval −5,1 to −1,9). Concerning secondary outcomes, a reduction in dizziness related disability and anxiety, along with a subjective amelioration in vestibular symptoms were reported. The authors concluded that the first two intervention strategies are safe and clinically effective in this group of patients (49).

Geraghty et al evaluated Balance Retraining, an internet-based vestibular rehabilitation tool in 296 patients with dizziness. The Internet-based vestibular rehabilitation group received the aforementioned rehabilitation, while the control group received usual care. As a result, the intervention group reported significantly less dizziness symptoms on the VSS-SF at 3 ($p<0,001$) and 6 months ($p=0,02$) and significantly diminished dizziness-associated disability at 3 ($p<0,001$) and 6 months ($p=0,01$). Thus, the Internet application has significantly better results in comparison with conventional treatment (50).

Sensors system technology

Study	Study design	Technology used	Applies to	Sample	Outcome measures	Results
Hall et al., 2016 (51)	Feasibility study	Wii Fit	Community-dwelling older women	16 community-dwelling older women	History of falls, composite physical function, 30-s chair stand, gait speed, TUG, DGI, posturographic parameters	Statistically significant correlations between various balance assessment tools and the Ski Slalom game. This did not apply to the Table Tilt game scores
Karasu et al., 2018 (52)	Single-blind randomized-controlled trial	Use of 6 balance games on the Nintendo Wii Fit and Wii Balance Board	Patients with a history of stroke during the last 1 year.	23 stroke patients randomly divided into an experimental group (n=12) and into a control group (n=11)	Primary o.m.: BBS, FRT, PASS, TUG, SBI. Secondary o.m.: postural sway, Functional Independence Measure Transfer and Ambulation Scores.	Significantly better results were found in the Berg Balance Scale, Functional Reach Test and several other outcome measures (p<0,001) when comparing the experimental to the control group
Alves et al., 2019 (53)	Case report	VR Xbox Kinect games	Children with visual vertigo symptoms	A 9 y.o. girl with headache, dizziness and motion sickness	Nystagmus, HIT, smooth pursuit, saccades, ocular vergence, HST, visual acuity, SVV, mCTSIB, FRT, PVSQ, DHI-PC, VVAS	Reduced visual vertigo symptoms, less headaches, visual vertigo analog scale rating ameliorated, DHI-PC score declined from 22 to 12 and pediatric vestibular symptom questionnaire rating improved from 0,7 to 0,1
Noveletto et al., 2018 (54)	Quasi-experimental study	Novel serious game 'myBalance' with inertial sensors for balance assessment and treatment	Hemiparetic stroke patients	Experimental group: 6 hemiparetic stroke patients (mean age: 54,5 y.o.). Reference group: 12 healthy subjects (mean age: 56,1 y.o.)	BBS, TUG, QFG, NHP, COP	Amelioration in the experimental group in the BBS (12,1±7,8% with a large ES=0,9), the TUG test (15,1±7,4%, with a small ES=0,4), the QFG strength assessment (paretic side: 21,3±11,2% with a medium ES=0,6. Non-paretic side: 32,3±19,2% with a large

						ES=1,5), the NHP (51,4±27,6% with a medium ES=0.6) and the oscillation level difference (p=0,001) compared to the control group
Severiano et al., 2018 (55)	Prospective observational cohort study	Nintendo Wii-Remote and Wii Balance Board	Patients with Parkinson’s disease	16 patients with Parkinson’s disease (mean age: 57.5 y.o.)	DHI, BBS, SF-36, SRT	Significantly improved DHI, BBS, SRT, SF-36 Quest. scores especially in the Ski Slalom game (p<0,05)
Albiol-Pérez et al., 2017 (56)	Observational cohort study	‘ABAR’ (Active Balance Rehabilitation) system comprising of a Nintendo Wii Balance Board connected to a large TV screen	Patients with Parkinson’s disease, multiple sclerosis, stroke	10 patients with Parkinson’s disease (mean age: 79,6 y.o.)	Center of pressure, suitability of system	Statistically non-significant, with a trend to amelioration, balance control improvement in all positions. Excellent scores in enjoyment, helpfulness, success and clarity
Hsu et al., 2016 (57)	Single-blind randomized controlled study	3D VR interactive rehabilitation system with Nintendo Wii Fit	Patients with Meniere’s disease	Study group: 36 patients with Meniere’s disease (mean age: 69 y.o.). Control group: 34 patients with Meniere’s disease (mean age: 66,5 y.o.)	COP, maximum ML and AP trajectory excursion, mean ML and AP trajectory excursion, statokinesigram	Statistically significant improvement in coordination and extension exercises in the study group. Statistically significant amelioration in ML trajectory excursion and COP oscillation in patients with shorter disease. Significant improvement in statokinesigram and max AP trajectory excursion in patients with mild symptoms
Swanenburg et al., 2020 (58)	A-B study design	4 exergames on the exercise system Senso	Patients with a chronic peripheral unilateral vestibulopathy	12 patients with chronic peripheral vestibulopathies (mean age: 65 y.o.)	DVA, VOR gain, COSA, FGA, ETGUG, DHI	Significant improvement in COSA (p=0,006), FGA (p < 0,001), ETGUG (p < 0,001)

Pedreira da Fonseca et al., 2017 (59)	Randomized, blinded clinical trial	VR games on Nintendo Wii	Hemiparetic patients after a stroke	Experimental group: 14 patients (mean age: 53,8 y.o.). Control group: 13 patients (mean age: 50,9 y.o.)	DGI, number of falls	Statistically significant differences in DGI in the control group (p=0,047) and in reduction of falls in the intervention group (p=0,049). No difference in intergroup analysis
Wada et al., 2016 (60)	Observational cohort study	Virtual snowboard exercise system	Patients with dizziness	42 healthy subjects (mean age: 21,9 y.o.)	Subjective slalom run performance, head linear accelerations	Significant increase in standard deviations of inter-aural head linear accelerations in the exercise with the highest time lag, with significant decrease in the exercise with no time lag. Statistically significant decrease in the subjective slalom run performance in the trial with the highest time lag and a significant increase in the following trial with no time lag. No motion sickness symptoms reported
Kumar et al., 2018 (61)	Usability study	Virtual CoMBat platform augmented with a Wii Balance Board and a Kinect sensor	Poststroke hemiplegic patients	12 hemiplegic stroke patients	COM trajectory in different directions and NEP (in ankle strategy), System Usability-related Questionnaire	Patients' performance improvement in tasks of two difficulty levels. Patient ability to understand and willingness to use again the system
Held et al., 2020 (62)	Case report	ARISE (AR for gait Impairments after StrokE): Sensor-based motion capture system (Xsens MVN) and mobile AR	Patients after stroke	1 patient (74 y.o.) with a stroke	Gait performance in AR and normal conditions, SUS, Virtual Reality Symptom Questionnaire, interview	Patient's kinematics improved with the system. System ranked as excellent according to the patient

		technology (HoloLens 2 smart glasses)				
Andreikanich et al., 2019 (63)	Exploratory study	Non-immersive VR therapeutic games with the ‘Kinect v2’ tracking device: a novel car racing game and the game ‘Tanks’	Patients with SCI or stroke	9 healthy students tested the car racing game and 6 males with SCI (38-66 y.o.) tested ‘Tanks’	Ease of use and learn of therapeutic games	Healthy participants enjoyed the car racing game, but car difficult to steer. Tanks game was reported as enjoyable and useful in rehabilitation according to patients with SCI
Sengupta et al., 2020 (64)	Comparative, prospective matched pre–post trial	‘Rhetoric’: a semi-immersive VR technology used in neurological rehabilitation and ‘Microsoft Kinect’ tracking system	Patients with SCI	Experimental group: 21 individuals with SCI (mean age: 28 y.o.). Control group: 12 patients with SCI (mean age: 30,5 y.o.)	BBS, POMA-B, FRS, AIS	No statistical significance was found in the BBS (p=0,396), FRS (p=0,294), POMA-B (p=0,238) between the 2 groups
Meyns et al., 2017 (65)	Monocentric, two-group, pre-test–post-test feasibility trial	3 exergames played with a Wii Balance Board	Children with cerebral palsy	11 children (5-18 y.o.) with spastic cerebral palsy after lower limb operation. Intervention group: 4 participants. Control group: 7 participants	TCMS, VAS for participants’ amusement	Both groups improved in sitting balance with better results in the intervention group. Exergames did not report as more amusing than conventional training
Rosiak et al., 2018 (66)	Prospective non-randomized controlled group study	Hybrid (motion trackers and force plate platform) VR therapy unit	Patients with peripheral vestibular dysfunction	Intervention group: 25 patients (mean age: 46,48 y.o.). Control group: 25 patients (mean age: 45,2 y.o.)	Posturographic parameters (COP total length and total surface), VSS-SF	Statistically significant differences were found in posturographic parameters, and in postural sway, in both groups, with no inter-group difference
Ayed et al., 2018 (67)	Case study	3 games applied on a personal computer with a Microsoft Xbox Kinect sensor	Patients in need of vestibular rehabilitation	2 individuals over 55 y.o. in an elderly house	Tinetti balance test, recruitment, adherence, safety	Improved Tinetti test scores with low recruitment, high adherence, high amusement and no adverse effects

AIS: American Spinal Injury Association Impairment Scale; AP: anteroposterior; AR: Augmented Reality; BBS: Berg Balance Scale; CoMBaT: Center-of-Mass-assisted balance task; COM: Center of Mass; COP: Center of Pressure; COSA: cumulative overt saccade amplitude; DGI: dynamic gait index; DHI: dizziness handicap inventory; DHI-PC: Dizziness Handicap Inventory— pediatric caregivers version; DVA: Dynamic visual acuity; ETGUG: Extended Timed Get-Up-and-Go; FGA: Functional Gait Assessment; FRS: Functional Reach Score ; FRT: Functional Reach Test; HST: Head Shake Test; IMI: Intrinsic Motivation Inventory; mCTSIB: Modified Clinical Test of Sensory Interaction on Balance; ML: mediolateral; NEP: Normalized Equivalent Performance; NHP: Nottingham Health Profile; o.m.: outcome measure; PASS: Postural Assessment Scale for Stroke Patients; POMA-B: Balance component of the Tinetti Performance-Oriented Mobility Assessment; PVSQ: pediatric vestibular symptom questionnaire; QFG: quadriceps femoris group; RAGT: Robot-assisted gait training; SBI: Static Balance Index; ; SCI: Spinal Cord Injury; SF-36: 36-Item Short-Form Health Survey; SRT: Sitting-Rising Test; SUS: System Usability Scale; TCMS: Trunk Control Measurement Scale; TUG: Timed Up and Go test; VAS: Visual Analog Scale; VOR: vestibule-ocular reflex; VR: Virtual Reality; VSS-SF: Vertigo symptom scale–short form; VVAS, visual vertigo analog scale; y.o.: years old

Hall et al aimed to test the Wii Fit platform as a means for balance assessment in a group of 16 community-dwelling older women. It was found feasible for this population to use Wii Fit as a balance assessment tool and a strong correlation was found between the scores from the Ski Slalom game with certain stability and mobility outcome measures. This did not apply to the Table Tilt game scores (51).

Karasu et al recruited 23 stroke patients who were able to take part in a balance rehabilitation program. The patients were randomly divided into an experimental group (n=12), who received Wii Fit-based and conventional rehabilitation and into a control group (n=11), who received solely a conventional rehabilitation program. Statistically significant results were found in the Berg Balance Scale, Functional Reach Test and several other outcome measures and the better results were reported in the experimental group compared to the control group. The authors suggest that such an eHealth system could constitute a supplemental treatment solution in the aforementioned population (52).

Alves et al applied a conventional rehabilitation program in the clinic and at home combined with Xbox Kinect games on a 9-years-old girl with headaches, dizziness and visual vertigo symptoms. The girl's condition improved with reduced visual vertigo symptoms, less headaches. Her visual vertigo analog scale rating ameliorated, her DHI-PC score declined from 22 to 12 and her pediatric vestibular symptom questionnaire rating improved from 0,7 to 0,1. According to the authors, VR games can complement vestibular rehabilitation programs in children with visual vertigo symptoms (53).

Noveletto et al developed 'myBalance', a novel serious game used to assess and treat balance disorders and studied it on an experimental group of 6 hemiparetic stroke patients and a control group of 12 healthy subjects. Two modes were used for balance impairment evaluation, Basic and Sequential Dynamic Stabilometry, and two modes for balance training, Sequential and Random Dynamic Stabilometry. The 6-patient group showed an amelioration in all outcome measures following intervention: the BBS (12,1±7,8% with a large ES=0,9), the TUG test (15,1±7,4%, with a small ES=0,4), the QFG strength assessment (paretic side: 21,3±11,2% with a medium ES=0,6. Non-paretic side: 32,3±19,2% with a large ES=1,5), the NHP (51,4±27,6% with a medium ES=0.6). Additionally, the difference in the oscillation level between the two groups was statistically significant in the Basic Dynamic Stabilometry assessment (p=0,001), while there was no statistical difference in the center of pressure displacement between the two groups after training (p=0,109). However, it was better in the experimental group. The study demonstrated the feasibility of postural evaluation and rehabilitation in stroke patients with the use of a serious game (54).

Severiano et al implemented four games on the Wii platform- Soccer Heading, Ski Slalom, Tightrope Walk and Table Tilt- and incorporated several balance training strategies, such as head movement, saccadic ocular movements, optokinetic stimulation etc. Twenty sessions of training were conducted in 16 patients with Parkinson's disease. The patients presented improved Dizziness Handicap Inventory and Berg Balance Scale scores after training, especially in the Ski Slalom game (p<0,05). A statistically significant amelioration was also reported in the Sitting-Rising Test and in the SF-36 questionnaire. In the latter outcome measure, a significant change was reported for the Ski Slalom and Tightrope Walk games (p<0,05). These two games showed the best results in these patients (55).

Albiol-Pérez et al investigated possible spatial postural control changes on 10 patients with Parkinson's disease following fifteen sessions with the 'ABAR' system. This is a VR platform with different virtual environments, which allows and records body weight transferences. They studied the center of pressure in the center, the right and the left sitting positions and did not find any significant changes in balance control in the aforementioned positions. Additionally, the center of pressure was improved in all positions. The 'ABAR' system received excellent scores in enjoyment, helpfulness, success and clarity. The authors conclude that balance control appears to be preserved or even ameliorated with use of the system and believe that this fact is mainly attributed to cognitive processing (56).

Hsu et al evaluated a 3D VR interactive system comprising of an assessment and a rehabilitation component on individuals with Meniere's disease. The rehabilitation component comprises of exercises for head, eye, extension and coordination. A study group of 36 patients received a 3D VR training, while a control group of 34 patients performed Cawthorne–Cooksey exercises at home for 4 weeks. Statistically significant results occurred in extension and coordination exercises. Individuals with a shorter duration of symptoms had a statistically significant amelioration in mediolateral trajectory excursion and in the center of gravity oscillation compared to individuals with longer disease duration. Finally, patients with a mild functional disorder due to Meniere's disease significantly improved in the statokinesigram and the maximum anteroposterior trajectory excursion, while no significant results were seen in patients performing the conventional exercises (57).

Swanenburg et al conducted a study to evaluate vestibular rehabilitation with the use of 4 exergames in people with one-sided chronic peripheral vestibular loss. These games are based on the patients' performance of head movements and physical tasks in a VR environment. Eight sessions of exergaming were realized. Statistically significant changes occurred in the cumulative overt saccade amplitude ($p=0,006$), the FGA ($p < 0,001$) and the Extended Timed Get-Up-and-Go ($p < 0,001$). On the other side, no statistically significant improvements were found in the dynamic visual acuity, the ipsilateral VOR gain, the DHI. According to the authors, this is the first trial to highlight improved cumulative overt saccade amplitudes in this population following active video games rehabilitation (58).

Pedreira da Fonseca et al evaluated the combination of VR games on Nintendo Wii with conventional physiotherapy in post-stroke patients. Thus, an intervention group received the combined treatment, while a control group only received conventional rehabilitation. Twenty treatment sessions were offered in every group. Eventually, both groups were improved in terms of dynamic balance and occurrence of falls and no difference was found in intergroup analysis. Nevertheless, statistically significant differences were only observed in gait stability in the control group ($p=0,047$) and in reduction of falls in the intervention group ($p=0,049$) (59).

Wada et al aimed to study the effect of VR-induced visual-vestibular conflict on dynamic balance. They implemented a virtual snowboard exercise system which produced time lags between visual scenery and body motion and 42 young healthy participants took part in the study. Snowboard exercises with increasing time lags were used and standard deviations of inter-aural head linear accelerations significantly increased in the exercise with the highest time lag, while significantly decreased in the following exercise with no time lag. Additionally, a statistically significant decrease was found in the subjective slalom run performance in the trial with the highest time lag and a significant increase in the following trial with no time lag. The participants reported no motion sickness symptoms. The authors concluded that the VR tool used ameliorated the dynamic stability and motor performance in the healthy young participants (60).

Kumar et al assessed a Virtual Center-of-Mass-assisted balance task (CoMBat) platform augmented with a Wii Balance Board and a Kinect sensor as a balance rehabilitation system in a group of hemiplegic patients. The system was programmed to switch tasks in adaptation to individuals' weight-shifting ability, while the patients adhered to ankle strategy to perform the different tasks. Patients' performance was improved in tasks of two difficulty levels. Additionally, the patients were able to understand the tasks and were willing to use the system again (61).

Held et al. studied the ARISE system, a novel technology based on virtual and auditory reality augmentation and real-time kinematics feedback, for dynamic balance rehabilitation in individuals with a stroke. They applied it on a 74 years old person with a stroke 7 years ago and found that the patient's kinematics changed compared to his gait pattern without the system. The system was ranked as excellent and according to the patient, it could be an adjunct to his rehabilitation program. This study is considered the first to show gait manipulation with the use of an augmented reality rehabilitation system providing feedback in real time (62).

Andreikanich et al developed a VR car race game and integrated it with a Kinect v2 tracking sensor. The in-game vehicle is controlled by inclinations of the player's upper body in all directions. The 9 healthy subjects who participated in the study concluded that they enjoyed the game, but the car was difficult to steer. Moreover, the researchers implemented 'Tanks' game, which already existed, and adjusted it so that the patients should apply the same torso movements. 6 male patients with spinal cord injury were recruited and after playing, it was inferred that the game was enjoyable and useful in vestibular rehabilitation. Such games appear motivating and fun to play (63).

Sengupta et al evaluated the game-based VR balance rehabilitation program 'Rhetoric' in patients with spinal cord injury in an experimental group of 21 young patients and a control group of 12 patients. Standard balance rehabilitation was applied on both groups, but the experimental group also received VR balance training. Users of the system have an avatar, the different parts of which are moved by mobilization of the user's same body parts. The 2 groups has no significant difference in the severity of the SCI. Additionally, no statistical significance was found in the intergroup analysis of the outcome measures used (BBS 0,396, FRS 0,294, POMA-B 0,238), suggesting VR as a complementary treatment for balance training in patients with spinal cord injury (64).

Meyns et al evaluated VR technology in sitting balance rehabilitation in young patients with cerebral palsy following lower limb operation. An intervention group (n=4) received conventional balance rehabilitation plus training with exergames. Specifically, 3 VR games were developed and the patients had to move a virtual target by moving their body over a Wii Balance Board. The control group received only conventional training. Following balance training, both groups showed an improvement in sitting balance and actually the intervention group appeared to have better results. However, the young patients did not report the exergames as more amusing than conventional training (65).

Rosiak et al conducted a non-randomized controlled group study to compare a hybrid VR rehabilitation unit with 2 VR games to static posturography with visual feedback in patients with peripheral vestibulopathies. The intervention group received the VR rehabilitation program, while the control group received static posturography training for 10 days. Statistically significant differences were found in posturographic parameters, and thus in postural sway, in both groups, while there was no inter-group difference. Additionally, statistically significant improvements occurred in both groups, while a greater improvement occurred in the intervention group (66).

Ayed et al evaluated the effect of 3 novel VR games on postural control of 2 older subjects during a 5-week rehabilitation program in an elderly house. A low recruitment, high adherence and amusement was reported in the study. No adverse effects were reported and the individuals' balance was improved as shown in the Tinetti test scores (67).

Head mounted display technology

Study	Study design	Technology used	Applies to	Sample	Outcome measures	Results
Lubetzky et al., 2018 (68)	Prospective cohort study	6 VR scenes developed for the Oculus Development Kit-2 (DK2) headset	Potential future use in patients with balance disorders	21 healthy individuals (mean age: 28 y.o.)	VRMS, DP, Excursion and Sample Entropy	Intra-class correlation in most conditions ranged from 0,5 to 0,7 for velocity and directional path, were low for excursion, over 0,5 for sample entropy when stability trainers are used and over 0,4 when subjects stood on the floor. Good test-retest reliability. Slight to moderate adverse effects were reported in the simulator sickness questionnaire
Lubetzky et al., 2020 (69)	Descriptive feasibility study	Novel application for the HTC Vive HMD- VR technology	Patients with central or peripheral vestibular loss	15 adult patients: 1 male (30 y.o.) with vestibular migraine, 2 males (27,5 y.o. on average) with mild intracranial injury, 7 males and 5 females (57 y.o. on average) with unilateral peripheral vestibular lesion	Simulator Sickness Questionnaire, DHI, VVAS, ABC, FSST, 8FUG	Statistically significant improvement in DHI (p=0,008), VVAS (p=0,02), ABC (p=0,02) and FSST (p=0,015) scores patients with peripheral loss. Patients with mild intracranial injury were also improved, while the male with vestibular migraine was not
Zaleski-King et al., 2020 (70)	Cross-sectional study	VR-adapted RDT presented via an Oculus Rift HMD	Patients with dizziness	Vestibular group: 28 patients with dizziness (mean age: 49 y.o.). Control group: 20 healthy persons (mean age: 34 y.o.)	SVV	Statistically significant SVV shift in the vestibular compared to the control group. SVV findings through the HMD were correlated with SVV

						findings using conventional methods
Lubetzky et al., 2018 (71)	Test-retest, blocked-randomized experimental study	'Moving room' and 'avoidance task' paradigms for postural control evaluation developed for the Oculus Rift VR-HMD	Patients with vestibular disorders	Vestibular group: 25 patients with vestibular disorders (mean age: 52,2 y.o.). Control group: 16 control patients (mean age: 52,9 y.o.)	AP and ML center-of-pressure DP and sample entropy	Higher directional path in the 'moving room' paradigm and lower directional path in the 'avoidance task' paradigm were found in the vestibular group in comparison with the control group. Sample entropy increased in less challenging environments.
Micarelli et al., 2017 (72)	Randomized controlled pilot study	Track Speed Racing 3D VR game displayed on a 'Revelation' VR HMD	Patients with vestibular loss	HMD group: 23 patients with vestibular hypofunction (mean age: 49,72 y.o.). Control group: 24 patients with vestibular hypofunction (mean age: 50,48 y.o.)	VOR gain (vHIT), posturography parameters, ABC, DHI, Zung Instrument for Anxiety Disorders, DGI	Statistically significant improvements in the eyes closed on X (p=0,0021), the eyes opened on X (p=0,0028), the eyes closed on Y (p=0,0032) and the eyes open on y (p=0,0035) conditions in the HMD group compared with the control group. Statistically significant VOR gain amelioration (p=0,0031), DHI (p=0,002) and ABC score (p=0,0036) in the HMD group compared with the control group
Viziano et al., 2019 (73)	12-month follow-up of a randomized controlled trial	Track Speed Racing 3D VR game displayed on a 'Revelation' VR	Patients with vestibular loss	47 patients with vestibular loss	VOR gain (vHIT), posturography parameters, ABC, DGI, DHI	VOR gain, ABC, DGI and DHI scores remained significantly improved in both groups compared to the pre-treatment values.

		HMD (from a previous study)				Better VOR gains in the HMD group. Posturographic parameters significantly improved only in the HMD group
Micarelli et al., 2019 (74)	Randomized study	Track Speed Racing 3D VR game displayed on a 'Revelation' VR HMD	Patients with vestibular loss and MCI	Group 1: 12 UVH patients with MCI undergoing conventional training. Group 2: 12 UVH elderly patients undergoing conventional training. Group 3: 12 UVH patients with MCI undergoing combined VR and conventional training. Group 4: 11 UVH elderly patients undergoing combined VR and conventional training.	VOR gain (vHIT), posturographic parameters, ABC, DHI, DGI, SSQ	Significant improvement (p<0,05) in posturographic parameters, ABC, DHI and DGI scales in all groups. Significant improvement (p<0,05) in all tests, including VOR gain in the groups receiving VR rehabilitation compared to the groups receiving only standard training
Park et al., 2018 (75)	Feasibility study	Saccadic VR exercise implemented on an Oculus developers kit 2 HMD with an infrared eye tracker	Patients in need of vestibular rehabilitation	18 healthy subjects (mean age: 26.5 y.o.)	SEE accuracy, power spectral density of beta activity (EEG), Beta-event-related desynchronization (EEG), functional connectivity (EEG)	A significantly better SEE accuracy was found in the F-on related to the F-off condition (p=0,039). Significant improvements in EEG recordings.
Nehrujee et al.,2019 (76)	Usability study	Smartphone-based HMD	Patients with vestibular loss	15 healthy subjects and 15 patients with unilateral vestibular loss (18-60 y.o.)	Subjective assessment of the usability of a system (SUS quest.) and SS (SSQ quest.)	VEGAS highly usable by both healthy individuals (SUS: 91.5 ± 4.41) and patients (SUS: 88.33 ± 11.44). 4 healthy individuals (~27%) (SSQ: 5.41 ± 12.43) and 14 patients (~94%) (53 ± 40.98) with symptoms of SS.
Tabanfar et al., 2018 (77)	Prospective, evaluator-blinded,	VR system including an iPhone 6 into a HooToo VR HMD	Patients with BPPV	Intervention group: 10 healthy individuals (mean age: 26,4 y.o.). Control group: 10 healthy individuals (mean age: 26,1 y.o.)	Epley maneuver performance scoring, NASA Task Load Index	Statistically significant difference (p=0,0001) between the two groups with an average score of

	randomized controlled trial					7.78±0.99 in the intervention group and of 6.65±1.72 in the control group. No significant results associated with the subjects' perceived workload, according to the NASA Task Load Index

8FUG: 8-foot up and go; ABC: Activities-Specific Balance Confidence Scale; AP: Anteroposterior; DGI: Dynamic Gait Index; DHI: Dizziness Handicap Inventory; DP: Directional Path; EEG: electroencephalography; FSST: Four-Step Square Test; HMD: Head Mounted Display; MCI: mild cognitive impairment; ML: mediolateral; Quest. : Questionnaire; SEE: Saccadic Eye Exercise; SSQ: Simulator Sickness Questionnaire; SUS: System Usability Scale; SVV: Subjective Visual Vertical; UVH: Unilateral Vestibular Hypofunction; VOR: vestibulo-ocular reflex; VR: Virtual Reality; VRMS: Root Mean Square of Velocity; VVAS: Visual Vertigo Analogue Scale; y.o.: years old

Lubetzky et al developed a VR platform comprising of two functional scenes ('Park' and 'City') and 4 moving dot scenes for the Oculus Development-Kit 2 headset, which aims to assist with testing for visual dependence. Twenty-one healthy young individuals were recruited and tested twice with a one-to-two-week interval. Each subject was tested in all virtual scenes in both sessions. The individuals' postural sway was assessed in each of the 6 conditions while standing on the floor and while standing on foam or a Both Sides Up (BOSU) ball. Slight to moderate adverse effects were reported in the simulator sickness questionnaire. Intra-class correlation in most conditions spanned from 0,5 to 0,7 for velocity and directional path, were low for excursion, over 0,5 for sample entropy when stability trainers are used and over 0,4 when subjects stood on the floor. Thus, the VR platform has a good test-retest reliability in this group (68).

Lubetzky et al developed a clinical app for the HTC Vive Head Mounted Display which focuses on sensory modulation, imbalance and dizziness on vestibular patients. The application introduces patients into 4 complex sensory environments (city, subway, airport, park) in a safe and graded manner. The amount of sensory information provided to the patients is regulated by the clinicians. Of the individuals involved, the 12 patients with peripheral loss had a statistically significant amelioration on the DHI (p=0,008), the VVAS (p=0,02), the ABC (p=0,02) and the FSST (p=0,015) scores. The 2 patients with mild intracranial injury were also improved, while the male with vestibular migraine was not. According to the researchers, virtual reality training can constitute a complementary vestibular rehabilitation program (69).

Zaleski-King et al applied a modified Rod and Disk Test (RDT) via a head-mounted display on 2 groups: an experimental group of 28 patients experiencing dizziness and a control group of 20 healthy patients. The goal was to assess the 2 groups for visual dependence as a function of the Visual Vertical (SVV). A dynamic visual background was displayed in the VR RDT of the experiment, which resulted in a statistically significant SVV shift in the vestibular group compared to the control group. Additionally, the SVV findings using the head mounted display in patients with dizziness were correlated with SVV findings using conventional methods in this population. The authors conclude that such a low-cost VR technology can by implemented to reliably estimate the SVV in patients with dizziness (70).

Lubetzky et al used the VR technology to develop 2 tests for the evaluation of balance control in patients with vestibular disorders: a 'moving room' paradigm, with 'stars' scenes moving anteroposteriorly or mediolaterally, for static balance assessment and an 'avoidance task' paradigm, with a 'park' scene, for dynamic balance assessment. 25 patients with a vestibular loss and 16 control patients were recruited. A higher directional path in the 'moving room' paradigm and a lower directional path in the 'avoidance task' paradigm were found in the vestibular group in comparison with the control group. Sample entropy increased in less challenging environments. The authors conclude that virtual reality applications can be implemented to investigate postural mechanisms (71).

Micarelli et al studied a 3D VR game on a VR headset on a group of patients with vestibular disorders. They were randomly subdivided into 2 groups, an HMD group with 23 patients who underwent an HMD-based and a conventional vestibular rehabilitation program and a control group with 24 patients who only underwent conventional training. The trial took place during a 4-week period and statistically significant improvements were found in the eyes closed on X (p=0,0021), the eyes opened on X (p=0,0028), the eyes closed on Y (p=0,0032) and the eyes open on y (p=0,0035) conditions in the HMD group compared with the control group. Additionally, a statistically significant VOR gain amelioration (p=0,0031), DHI score (p=0,002) and ABC score (p=0,0036) were found in the HMD group compared with the control group (72).

Viziano et al examined the same 47 patients on a 12-month follow up study of the previous study. VOR gain remained significantly improved in both groups compared to the pre-treatment values, although lower than the VOR gains immediately after the 2017 study. Better VOR gains were found in the HMD group. Posturographic parameters were significantly improved only in the HMD group. The ABC, DGI and DHI scores were significantly improved in both groups in comparison to pretreatment scores (73).

Micarelli et al also aimed to study the same VR system on patients with vestibular loss and mild cognitive loss. A randomized study was conducted and 4 groups of participants were formed. Groups 1 and 2 underwent conventional vestibular training, while groups 3 and 4 underwent a combination of VR and conventional balance rehabilitation. After 4 weeks of intervention, all groups showed a significant improvement ($p < 0,05$) in posturographic parameters, ABC, DHI and DGI scales. A significant improvement ($p<0,05$) was found in all tests, including VOR gain in the groups receiving VR rehabilitation compared to the groups receiving only standard training. Thus, the aforementioned system could help improve balance, VOR and quality of life in patients with vestibular hypofunction and a mild cognitive loss (74).

Park et al used a VR headset with an infrared eye tracker to create a VR environment for vestibular training. A saccadic eye exercise under two conditions was implemented. On the first condition a feedback of the eyes position was provided (F-on), while on the second condition no feedback was available (F-off). 18 healthy persons took part. A significantly better SEE accuracy was found in the F-on related to the F-off condition (p=0,039). EEG recordings were also conducted and significant improvements were calculated in the power spectral density of beta frequencies in the F-on condition in the central, frontal and occipital areas. Beta band event-related desynchronization was significantly more distinct in the F-on condition and significantly abundant functional connectivity was found in the F-on condition. Considering these, eye tracking headsets could be implemented in balance rehabilitation (75).

Nehrujee et al. developed the VEGAS, a smartphone-based 3D VR headset and 2 VR games aimed for vestibular assessment and rehabilitation. The 2 games follow the principles of conventional training and have different levels of difficulty, intending to facilitate head movements and gaze enhancement by retinal slip. The VEGAS was found to be highly usable by both healthy individuals (SUS: 91.5 ± 4.41) and patients (SUS: 88.33 ± 11.44). Additionally, 4 healthy individuals (~27%) (SSQ: 5.41 ± 12.43) and 14 patients (~94%) (53 ± 40.98) displayed symptoms of SS. An assessment of head movement performance with VEGAS was also completed. The VEGAS is considered the first smartphone-based HMD applied on vestibular rehabilitation. Exercises for balance, gait, gaze and habituation can be realized either at subjects' home or at hospital (76).

Tabanfar et al developed a smartphone application aimed to assist BPPV patients with home performance of the Epley maneuver. A randomized controlled trial was conducted, where 10 healthy individuals received the smartphone intervention and 10 control healthy individuals guidance from an instructional handout. A statistically significant difference (p=0,0001) occurred between the two groups with an average score of 7.78 ± 0.99 in the intervention group and of 6.65 ± 1.72 in the control group. No significant results were associated with the subjects' perceived workload, according to the NASA Task Load Index (77).

Platform technology

Study	Study design	Technology used	Applies to	Sample	Outcome measures	Results
Fung et al, 2018 (78)	Usability study	Smarter Balance System: Smartphone-based wearable tele-rehabilitation system comprising of a smartphone and a custom wearable belt with 4 vibration motors and a control module	Patients with Parkinson's disease	10 patients with Parkinson's disease	AP and ML LOS	Significantly augmented AP and ML LOS after the session
An et al, 2020 (79)	Case series	Smarter Balance System: Smartphone-based wearable tele-rehabilitation system comprising of a smartphone and a custom wearable belt with 4 vibration motors and a control module	Patients with Parkinson's disease	2 patients with Parkinson's disease (75.5 ± 4.9 y.o.)	LOS, SOT, FES, ABC, DGI	AP and ML LOS improved. No significant changes in SOT, ABC, FES, DGI scores
Bao et al, 2018 (80)	Randomized controlled study	A smartphone balance trainer including two Apple iPods (a sensing and a user interface unit), a "tactor bud" accessory and an elastic belt	Community-dwelling healthy older individuals	12 community-dwelling healthy older persons (mean age: 75,6 y.o.) randomly divided into an experimental (6 persons) and a control group (6 persons)	ABC, SOT, 5STS, FSST, Mini-BESTest, FRT, Gait Speed Test, TUG, TUG with Cognitive Task	Significant amelioration in the Mini-BESTest, SOT, Five Times Sit to Stand Test in the experimental related to the control group. No significant changes between the 2 groups in the rest of o.m.

Cesaroni et al, 2019 (81)	Analytical, descriptive cross-sectional study	BRU posturography (force platform and virtual reality googles)	Patients with vestibular migraine	Experimental group: 26 patients (17-68 y.o.) in the intercritical phase of vestibular migraine. Control group: 30 healthy individuals (18-72 y.o.)	LOS, sway velocity, pressure center displacement area	Significant differences in sway velocity (p<0,05) in 9 of 10 sensory environments and in the displacement area of the COP (p<0,05) in 8 of 10 sensory environments between the 2 groups. Intergroup LOS not statistically different (p=0,121)
Proffitt et al, 2018 (82)	Quasi-experimental, randomized cross-over trial	3D interaction game applied on an Oculus Rift HMD combined with the Microsoft Kinect tracking system	Patients post-stroke	14 healthy individuals (mean age: 30 y.o.) and 5 patients post-stroke (mean age: 56 y.o.)	Demographic and brief technology use Quest. Semi-structured interview questions in the end of the trial	No significant adverse effects. 3 individuals from the healthy group reported nausea and dizziness. The whole post-stroke group in need of hands-on aid for posture control
Ulozienė et al, 2017 (83)	Usability study	'VIRVEST': VR headset and a Myo armband or a gamepad. A mobile phone or tablet app is implemented by the physician to control the VR environment	Patients with vestibular disorders	41 healthy young individuals	SVV, SUS, VAS for VR-induced dizziness	Significantly high SUS scores for the Myo (82,5) and the gamepad (95) (p<0,01). Median Visual Analog Scale at 0,7
Phu et al, 2019 (84)	Observational pre- and post-intervention study	BRU system	Older individuals at high risk of falls	195 adults with a history or risk of falls (median age: 78 y.o.) divided into 3 groups. BRU group: 63 persons. EX group: 82 patients. Control group: 50 patients	5STS, TUG, gait speed, posturographic parameters (using the BRU), FES, handgrip strength, adherence	Similar improvement and adherence rates in the BRU and EX groups. Significant improvements in gait speed (p=0,021), TUG (p<0,001), LOS (p=0,008), FES (p=0,013) and handgrip strength (p=0,021) in the 2 groups compared with the control

						group. Significant amelioration in 2 other posturographic parameters in the BRU group
Hondebrink et al, 2017 (85)	Observational retrospective trial	'CAREN' (computer-assisted rehabilitation environment)	Patients with peripheral vestibular disorders	17 patients (mean age: 52 y.o.)	DHI	Significant amelioration on median DHI values and a more than 25% improvement occurred in 13 participants
Bergmann et al, 2018 (86)	Single-blind, two-parallel-armed randomized control study	VR-augmented RAGT	Stroke patients	Intervention group: 10 subacute stroke patients (mean age: 62 y.o.). Control group: 10 subacute stroke patients (mean age: 65 y.o.)	Dropout rate and questionnaire (acceptability), IMI and individual mean walking time (participants' motivation), response to interventions and completion rate (outcome measures feasibility)	VR-augmented RAGT highly acceptable with one drop-out, while 4 drop-outs occurred in the standard RAGT group. Mean walking time significantly higher in the intervention group ($p<0,03$), while IMI scores high in both groups. Significantly less pressure and tension in the intervention group ($p<0,01$) and lower than in the standard RAGT group ($p=0,005$)

5STS: 5 times sit to stand test; ABC: Activities-specific Balance Confidence; AP: Anteroposterior; BRU: Balance Rehabilitation Unit; COP: Center of Pressure; DGI: Dynamic Gait Index; DHI: dizziness handicap inventory; EX: Otago Exercise Program; FES: Falls Efficacy Scale; FRT: Functional Reach Test; FSST: Four Square Step Test; HMD: Head Mounted Display; IMI: Intrinsic Motivation Inventory; LOS: limit of stability; Mini-BESTest: Mini Balance Evaluation Systems Test; ML: Mediolateral; o.m.: outcome measures; Quest.: questionnaire; RAGT: Robot-assisted gait training; SOT: Sensory Organization Test; SUS: System Usability Scale; SVV: Subjective Visual Vertical; TUG: Timed Up and Go test; VAS: Visual Analog Scale; y.o.: years old

Fung et al developed the Smarter Balance System, which incorporates feedback from proprioceptive and visual stimuli to support patients with Parkinson's disease with balance rehabilitation. They conducted an unsupervised session of 24 dynamic weight-shifting balance exercises on 10 subjects with Parkinson's disease in a clinical setting and evaluated the group's anteroposterior and mediolateral limits of stability, which augmented significantly after the session. Additionally, the patients could precisely perform the exercises (78).

An et al. further evaluated the Smarter Balance System in 2 individuals with Parkinson's disease. The 2 patients performed dynamic weight-shifting balance exercises in the medial-lateral and posterior-anterior axis at home for 6 weeks. Several outcome measures were assessed at the beginning, after 6 and after 10 weeks. Specifically, patients' limits of stability in the posterior-anterior and the medial-lateral axis improved after 6 and 10 weeks, while scores in the Sensory Organization Test, Activities-specific Balance Confidence, Falls Efficacy Scale and the Dynamic Gait Index did not change significantly. The authors conclude that further research needs to be conducted (79).

Bao et al. recruited 12 community-dwelling healthy older individuals to evaluate the efficacy of long term stability rehabilitation with the use of a novel smartphone balance trainer. The participants were randomly assigned to an experimental group (n=6) that performed certain exercises with vibrotactile sensory augmentation through the balance rehabilitation platform, and a control group (n=6) that performed a more conventional balance rehabilitation. Training took place for 8 weeks. A statistically significant amelioration was found in the Mini Balance Evaluation Systems Test and the Sensory Organization Test in the experimental related to the control group. A statistical significance was also reported in the Five Times Sit to Stand Test duration in the experimental group, while there were no significant changes between the 2 groups in the rest of outcome measures (80).

Cesaroni et al recruited 26 individuals in the intercritical phase of migrainous vertigo and 30 healthy control individuals to assess their static balance by using Balance Rehabilitation Unit (BRU) VR posturography. A statistical significance difference was found in sway velocity ($p<0,05$) in 9 of 10 sensory environments and in the displacement area of the center of pressure ($p<0,05$) in 8 of 10 sensory environments between the 2 groups. The limit of stability between the 2 groups was not statistically different ($p=0,121$). Thus, sway velocity and displacement area of pressure center can be implemented as parameters in VR posturography to assess patients in the intercritical period of vestibular migraine (81).

Proffitt et al developed a VR game for a paired Oculus Rift HMD and Microsoft Kinect sensor platform in an effort to provide post-stroke patients with a means of tele-rehabilitation. The game enables users to complete different tasks into a 3D recycling plant virtual environment. They recruited 14 healthy subjects and 5 post-stroke patients to test the game and no significant adverse effects were observed. Three individuals from the healthy group reported nausea and dizziness, while the whole post-stroke group was in need of hands-on aid for posture control. According to the authors, this was the first effort to investigate a combined HMD with a full-body rehabilitation game, but its utility as a tele-rehabilitation tool may be limited due to the physical support that post-stroke patients need while they are using it (82).

Ulozienė et al tested VIRVEST, a VR platform that helps estimate the Subjective Visual Vertical. The latter was assessed in four different (static, dynamic and VR real world) conditions projected through a headset and the users utilized Myo armband or a gamepad to define it. Forty one healthy individuals were recruited and Subjective Visual Vertical values were calculated and compared to those found in similar studies in the past. The System Usability Scale values for the Myo (82,5) and the gamepad (95) controllers were high and a statistically significant difference ($p<0,01$) was found. Finally, no significant dizziness was observed with a median Visual Analog Scale at 0,7 (83).

Phu et al aimed to compare VR training with the Balance Rehabilitation Unit (BRU) to the Otago Exercise program (EX) concerning postural control in a group of older individuals at risk or with a history of falls. The BRU group, which received BRU training, and the EX group, which received EX training showed similar improvement and adherence rates and improved significantly in comparison to the control group in gait speed ($p=0,021$), TUG ($p<0,001$), limits of stability ($p=0,008$), FES score ($p=0,013$) and handgrip strength ($p=0,021$). The BRU group, additionally, had a significant amelioration 2 other posturographic parameters (84).

Honderbrink et al implemented the 'CAREN' system, a VR platform combined with sinusoidal vertical passive body movement to assess vertigo alleviation on 17 patients with chronic peripheral vestibular dysfunctions. At follow-up, a statistically significant amelioration was found on median DHI values and a more than 25% improvement occurred in 13 participants. According to the authors, this is the first study assessing passive whole body sinusoidal oscillations in vestibular rehabilitation (85).

Bergmann et al aimed to investigate the acceptability of robot-assisted gait rehabilitation (RAGT) with and without VR technology, along with the feasibility of different outcome measures to facilitate a larger future study planning in stroke patients. Ten control patients received RAGT and ten patients received VR-augmented RAGT. VR-augmented RAGT was highly acceptable, with one drop-out, while 4 drop-outs occurred in the standard RAGT group. The mean walking time was significantly higher in the intervention group ($p<0,03$), while IMI scores were high in both groups. Significantly less pressure and tension were reported in the intervention group ($p<0,01$) and were lower than in the standard RAGT group ($p=0,005$). Finally, the Functional Ambulation Classification (FAC) appeared as a potential outcome measure for a future study (86).

Discussion

This study evaluates the involvement of modern technology and virtual reality in the diagnosis and treatment of individuals with dizziness and/or impaired postural control, during the last six years. Forty-three studies were included after search of MEDLINE. Different research papers reinforce the use of virtual reality/mHealth/eHealth applications as adjunct treatment options or even as monotherapies in the aforementioned group of patients. It is notable that throughout the studies described, investigation of the implementation of such applications is conducted in many major groups of diseases affecting postural control, highlighting the vivid research interest and the severity of these conditions. Such are vestibular disorders, strokes, Parkinson's disease, spinal cord injuries and cerebral palsy. There are also studies recruiting community-dwelling healthy older persons, healthy young individuals and children.

Balance is one of the most ancient human senses, mediated not only by the vestibular system, but also by many other neural systems and circuits. This complexity renders the investigation of balance control in humans notably arduous and poses the necessity of implementation of new tools. Technology has brought a new horizon in this effort and it is clear throughout this study that novel virtual reality applications related to diagnosis and treatment of balance disorders are tested and implemented in a daily basis.

A great interest on the utility of common gaming consoles, such as the Nintendo Wii, Nintendo Wii Fit and Sony PlayStation 2 EyeToy, in the evaluation and rehabilitation of balance disorders emerged during the first decade of our century (87), (88). Applications of such gaming consoles are still evaluated in several studies, but newer technologies have also arrived, as highlighted throughout the current literature review.

Notably, development of Serious Games is constantly growing, since they embody the three primary conditions for rehabilitation that is task-oriented training, repetitiveness and intensity (89). The appearance of smartphones have equipped every user around the world with an enormous amount of smartphone applications, including many applications for the management of dizziness and balance disorders. These applications may address to physicians, medical students and patients. Additionally, head mounted displays, which provide the users with 3D virtual reality environments, modern sensors systems, Internet-based applications and novel platforms combining several different tools are being evaluated and used.

As a matter of fact, all these modern technology applications have been studied only during the last few years, but their potential seems tremendous. Virtual-reality-based vestibular training focuses on neuroplasticity and the principles of restoration, adaptation and habituation, thus enforcing motor learning, like conventional rehabilitation does (90).

Modern technologies offer certain advantages to research and management of balance disorders. The affordability and accessibility, combined with the enriched environments that they offer, are features that render virtual reality applications popular in current research and vestibular rehabilitation at home or in the clinic. Since they provide a safe environment, vestibular training can assume different difficulty levels, with a capacity to adjust stimuli intensity and repetition (91). Another possibility that virtual reality offers, is feedback supply to the vestibular patient. Specifically, individuals with vestibular loss often fail to retain balance control in challenging environments, such as in the darkness or on uneven grounds, due to deficient visual and proprioceptive stimuli. Virtual reality-assisted balance rehabilitation can assist patients with overcoming this difficulty, by providing auditory, vibrotactile and visual biofeedback, and thus with inducing postural corrections (101). The latter promote patients' adherence, participation and motivation (92), (93).

Nevertheless, use of virtual reality is often impeded by cybersickness symptomatology. Otherwise known as simulator sickness or virtual reality sickness, cybersickness is a clinical entity encountered in virtual reality applications, such as flat-screen monitors and head-mounted displays (94). It is more commonly associated, however, with stereoscopic 3D head mounted displays (95). Simulator sickness is akin to kinetosis (motion sickness) and presents with dizziness, exhaustion, vertigo symptoms, confusion, headaches, nausea and epigastric discomfort (96), (97). As technology advances, virtual reality headsets tend to become highly realistic and immersive, leading to clear virtual environments with precise motion tracking and subsequently to elimination of sensory input conflict and minimization of cybersickness symptoms (94), (98), (99).

In a former article by Lange et al in 2009 the following classification of tele-rehabilitation in medicine is proposed: 1.sensor-based, which utilizes sensors, e.g. accelerometers, to assess patients, 2.image-based, with visual communication in real time and 3.virtual-reality-based tele-rehabilitation, which employs electronic games and VR technologies in the evaluation and rehabilitation of patients (100). Having explored a significant part of the literature for the realization of this review, it appears that modern technology enables the combination of more than one technological tools to create diagnostic and/or rehabilitation systems for patients with balance disorders.

In this review, a novel classification is proposed based on the technologies utilized in the diagnosis and training of these patients. Of course, the different technological systems are usually combined, making it difficult to safely distinguish the distinct categories. The classification includes: 1.mHealth applications, 2.Internet-based and telemedicine platforms, 3.sensors systems, and 4.head mounted display systems, and 5.novel platforms. Sole HMD systems or combinations of HMDs with smartphone applications are included in the fourth category. Combinations of smartphone applications with sensor systems or any other combination of modern technologies are included in the fifth category.

Classification of the novel technologies used in vestibular rehabilitation and diagnosis
mHealth applications
Internet-based and telemedicine platforms
Sensors systems technology
Head mounted display systems
Platforms

In an effort to group the articles presented in this review, several major grouping categories arise. That way, the articles will be categorized according to the age populations involved and the studied diseases. The studies involved shall be further segregated based on the use of the interventions as therapeutic or diagnostic. Additionally, the studies will be further categorized based on the outcome measures implemented and on whether these outcome measures are subjective or objective. Furthermore, the studies will be divided into observational and experimental ones and the observational studies will be further subdivided into cohort, cross-sectional and retrospective studies. Experimental studies are characterized by randomization of the interventions provided to different groups and offer a minimization of study biases and high validity of the results. Finally, the articles will be grouped based on the duration of follow-up, as short-term follow-up and long-term follow-up studies.

It is clear in the aforementioned studies that the different interventions may be implemented in many different patient populations suffering from symptoms of dizziness, vertigo and instability. It should always be kept in mind that patients with distinct diseases, as much as different individuals in a certain disease group, have distinct needs and wants and the treatment provided should be patient-oriented at every time. Thus, when individuals with certain health problems present with balance disorders, a personalized diagnostic or treatment tool may be implemented. Modern technological applications have been proved of value in several of these diseases and may often be indicated.

Several different populations based on their age distribution were studied throughout the involved studies. Adults with different health care problems including balance disorders were predominantly studied. Specifically, 25 articles studying samples of adults with a mean age between 18 and 64 years old (47, 48, 52, 54, 55, 59, 60, 61, 63, 64, 66, 68, 69, 70, 71, 72, 73, 75, 76, 77, 81, 82, 83, 85, 86) and 12 articles studying samples of older adults with a mean age of 65 and above (49, 50, 56, 57, 58, 62, 67, 74, 78, 79, 80, 84) were included in this review. Only one study with community-dwelling older women aged over 65 years old was included (51). Since children and adolescents may also suffer from syndromic or acquired balance disorders, three studies assessing vestibular interventions in relevant patient samples are hereby presented (46, 53, 65). Finally, two articles studying mHealth applications on medical students were detected (44, 45).

Through this review, it is clear that mHealth and eHealth applications have been applied and studied on a great range of different clinical entities leading to vestibular symptomatology. The studies involved concern either patients or healthy individuals. Regardless of that, the patient populations aimed by these applications will be further discussed.

To begin with, novel technologies aim at patients with BPPV (44, 45, 47, 77), Meniere's disease (57), vestibular migraine (81), patients with unilateral or bilateral peripheral vestibular loss (71, 85), unilateral peripheral vestibular disorders (58, 66, 72, 73, 76) and unilateral peripheral vestibular disorders and mild cognitive impairment (74). In addition, such technological applications have been designed for individuals with either peripheral or central vestibular disorders (46, 48, 49, 60, 68, 69, 70, 75, 83), chronic dizziness without an identified underlying disease (50), for stroke survivors (52, 54, 59, 61, 62, 82, 86), patients with Parkinson's disease (55, 56, 78, 79), with spinal cord injury (64) and patients with either spinal cord injury or a past stroke (63). Other applications range from community-dwelling older individuals without a clear vestibular pathology (51, 67, 80, 84), to children with dizziness and motion sickness (53) and children with cerebral palsy (65).

It should be again emphasized that eHealth, mHealth and virtual reality applications may be used for therapeutic or diagnostic reasons, although therapeutic applications are the commonest ones. Throughout this review, two studies concerned therapeutic mHealth applications (44, 45), while three studies concerned diagnostic mHealth applications (46, 47, 48). However, the two studies on Internet-based applications reported solely concerned therapeutic interventions (49, 50). Among the sensor system technological tools, fifteen studies concerning therapeutic interventions (52, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67) and only one diagnostic tool was reported (51). Articles on head mounted display technology referred to treatment tools on seven occasions (69, 72, 73, 74, 75, 76, 77) and to diagnostic applications on three occasions (68, 70, 71). Six studies on therapeutic applications of platform technology were cited (78, 79 80, 82, 85, 86) and two on diagnostic applications (81, 83). Finally, one sensor system (54) and one platform (84) had a role in both the diagnosis and treatment of vestibular disorders.

Next, the different outcome measures used in the articles involved will be discussed. A great number of distinct outcome measures are implemented in the involved articles, according to the different studied objectives. Herein, certain of the most important of these outcome measures used in the research of vestibular diagnosis and rehabilitation will be highlighted, as seen in the different studies.

The Dizziness Handicap Inventory (DHI) (49, 50, 55, 58, 69, 72, 73, 74, 85), the Timed-Up and Go test (TUG) and the Expanded Timed Get Up and Go test (ETGUG) (51, 52, 54, 58, 80, 84), the Dynamic Gait Index (DGI) (51, 59, 72, 73, 74, 79) and the Berg Balance Scale (BBS) (52, 54, 55, 64) are very commonly used outcome measures in vestibular research. Additional outcome measures include the Functional Reach Test (FRT) (52, 53, 64, 80), Gait Speed (51, 80, 84), the Activities specific Balance Confidence (ABC) (69, 72, 73, 74, 79, 80), the 5 Sit To Stand test (5STS) (80, 84), the Sensory Organization Test (SOT) (79, 80) and the Four Square Step Test (FSST) (69, 80).

Posturographic parameters are commonly used in research, too (51, 66, 72, 73, 74, 84). Postural sway parameters may be investigated (52, 81), along with different Center Of Pressure (COP)/ Center Of Mass (COM) values (54, 56, 57, 61, 66, 81) and mediolateral/ anteroposterior trajectories, direct path and Limits Of Stability (LOS) (57, 68, 71, 78, 79, 81). Such outcome measures can be assessed with the use of posturography or sensor system, like Xbox Kinect or Nintendo Wii Balance Board.

Nystagmographic evaluation, e.g. smooth pursuit, ocular vergence and saccades, is also usually performed (53, 75). Further assessment may include VOR gain (58, 72, 73, 74), Subjective Visual Vertical (SVV) (46, 53, 70, 83) and visual acuity (53, 58), while the Head Impulse test (HIT) and the Head Shaking Test (HST) may be implemented (53). Visual Analog Scales (VAS) may be used, like the Visual Vertigo Analog Scale (VVAS) (53, 69), the VAS for participants' amusement (65) and the VAS for VR-induced dizziness (83).

In order to investigate the past or present falls risk, a history of falls can be taken (51), along with a Falls Efficacy Scale (FES) (79, 84) and a number of falls assessment (59). Subjective outcome measures, such as Subjective Slalom Run Performance (60), the ease of use and learn of therapeutic games (63), the suitability of a system (56) and medical students' satisfaction (45) can be implemented.

Additionally, scales, such as the Vertigo Symptom Scale- Short Form (VSS-SF) (49, 50, 66) and the System Usability Scale (SUS) (62, 76, 83) and questionnaires, like the Simulator Sickness Questionnaire (SSQ) (68, 69, 74, 76), the System usability-related questionnaire (61), the acceptability questionnaire (86) and questionnaires for mHealth apps evaluation (48) are quite common. Finally, the adherence of the participants (67, 82), the sample entropy (68, 71), Epley Maneuver Performance Scoring (44, 77) and telemedical diagnosis of BPPV (47) can be assessed.

Throughout this review, a major problem, concerning the papers studying modern technological applications in the diagnosis and rehabilitation of balance disorders, arises.

Specifically, it appears that there are many pilot studies with small sample sizes, large age spanning and often with heterogeneous populations. In addition, a lack of randomization is often realized. Most studies also lack a long-term follow-up, so that the effects of vestibular rehabilitation through modern technologies cannot be evaluated after a longer period of time. The study of Viziano et al constitutes an exception (73). Thus, in the future, it is of importance to design larger, randomized studies with a long-term follow-up.

Specifically, three observational cohort studies (56, 60, 68), three observational cross-sectional studies (46, 70, 81) and one observational retrospective study (85) are involved. It is of interest that numerous feasibility and usability studies that lack randomization are met throughout the bibliography and notably five feasibility (47, 51, 65, 69, 75) and six usability studies (48, 61, 63, 76, 78, 83) are involved in this review. Most of these usability studies aim to assess the subjective opinions of the users relative to the applications examined. Additionally, four case reports/ case series are included (53, 62, 67, 79). Finally, fifteen randomized experimental or quasi-experimental studies are hereby reported, which provide the highest level of evidence among the aforementioned study protocols (44, 45, 49, 50, 52, 57, 59, 71, 72, 73, 74, 77, 80, 82, 86).

Short-term follow-up remains an important limitation of most of the studies regarding therapeutic vestibular tools. This leads to uncertainty whether the results obtained from the different study protocols can have long-term benefits for the patients involved. A plethora of studies presents a maximum follow-up interval of 3 months. Notably, fifteen articles had a maximal follow-up time of one month (52, 57, 60, 61, 62, 63, 64, 68, 69, 71, 74, 75, 76, 78, 82) and thirteen articles a follow-up interval between one and three months since the first clinical assessment of the participants (53, 54, 55, 56, 58, 59, 65, 66, 67, 72, 79, 84, 86). Four studies reported a follow-up of up to six months since the first subjects' evaluation (49, 50, 80, 85). A single study (73) was included, which was a one-year follow-up evaluation of a randomized controlled trial (72). Therefore, the crucial importance of designing studies with long-term follow-up protocols should be once more emphasized, so that impact of the different interventions can be evaluated over time.

In conclusion, traditional diagnosis and treatment of vestibular disorders tend to be replaced or supplemented, in most cases, by novel technological tools, such as mHealth, eHealth and Virtual Reality applications. Several articles are included in this review, so that the complete spectrum of the implementation of technology in the everyday clinical practice of neuroaudiologists be delineated. Interestingly, a wide range of central and peripheral vestibular disorders are aimed at and studied in a great variety of clinical trials. Apart from the short-term efficacy of such interventions, however, this review also emphasizes the need for the realization of more randomized studies with larger samples and long-term follow-up.

References

(1) Cawthorne T. Vestibular Injuries. Proc R Soc Med. 1946 Mar;39(5):270-3.

(2) Khan S, Chang R. Anatomy of the vestibular system: a review. NeuroRehabilitation. 2013;32(3):437-43.

(3) Angelaki, D. E., & Cullen, K. E. (2008). Vestibular System: The Many Facets of a Multimodal Sense. Annual Review of Neuroscience, 31(1), 125–150.

(4) Angelaki, D. E., Klier, E. M., & Snyder, L. H. (2009). A Vestibular Sensation: Probabilistic Approaches to Spatial Perception. Neuron, 64(4), 448–461.

(5) Lopez, C., Lenggenhager, B., & Blanke, O. (2010). How vestibular stimulation interacts with illusory hand ownership. Consciousness and Cognition, 19(1), 33–47.

(6) Smith, P. F., Geddes, L. H., Baek, J.-H., Darlington, C. L., & Zheng, Y. (2010). Modulation of Memory by Vestibular Lesions and Galvanic Vestibular Stimulation. Frontiers in Neurology, 1.

(7) Figliozzi, F., Guariglia, P., Silvetti, M., Siegler, I., & Doricchi, F. (2005). Effects of Vestibular Rotatory Accelerations on Covert Attentional Orienting in Vision and Touch. Journal of Cognitive Neuroscience, 17(10), 1638–1651.

(8) Hilber, P., Cendelin, J., Le Gall, A., Machado, M.-L., Tuma, J., & Besnard, S. (2018). Cooperation of the vestibular and cerebellar networks in anxiety disorders and depression. Progress in Neuro-Psychopharmacology and Biological Psychiatry.

(9) Han BI, Song HS, Kim JS. Vestibular rehabilitation therapy: review of indications, mechanisms, and key exercises. J Clin Neurol. 2011;7(4):184-196.

(10) Deveze A, Bernard-Demanze L, Xavier F, Lavieille JP, Elziere M. Vestibular compensation and vestibular rehabilitation. Current concepts and new trends. Neurophysiol Clin. 2014 Jan;44(1):49-57.

(11) Curthoys IS, Halmagyi GM. Vestibular compensation: a review of the oculomotor, neural, and clinical consequences of unilateral vestibular loss. J Vestib Res. 1995 Mar-Apr;5(2):67-107.

(12) Lacour M, Bernard-Demanze L. Interaction between Vestibular Compensation Mechanisms and Vestibular Rehabilitation Therapy: 10 Recommendations for Optimal Functional Recovery. Front Neurol. 2015 Jan 6;5:285.

(13) Lacour M. Restoration of vestibular function: basic aspects and practical advances for rehabilitation. Curr Med Res Opin. 2006 Sep;22(9):1651-9.

(14) Grill E, Heuberger M, Strobl R, Saglam M, Holle R, Linkohr B, Ladwig KH, Peters A, Schneider E, Jahn K, Lehnen N. Prevalence, Determinants, and Consequences of Vestibular Hypofunction. Results From the KORA-FF4 Survey. Front Neurol. 2018 Dec 7;9:1076.

(15) Moncada LVV, Mire LG. Preventing Falls in Older Persons. Am Fam Physician. 2017 Aug 15;96(4):240-247.

(16) Florence CS, Bergen G, Atherly A, Burns E, Stevens J, Drake C. Medical Costs of Fatal and Nonfatal Falls in Older Adults. J Am Geriatr Soc. 2018 Apr;66(4):693-698.

(17) Tjernström F, Zur O, Jahn K. Current concepts and future approaches to vestibular rehabilitation. J Neurol. 2016 Apr;263 Suppl 1:S65-70.

(18) Cooksey FS. Physical medicine. Practitioner 1945; 155:300–305.

(19) Cooksey FS. Rehabilitation in vestibular injuries. Proc Roy Soc Med 1946; 39:273–278.

(20) Brandt T, Daroff RB. Physical therapy for benign paroxysmal positional vertigo. Arch Otolaryngol. 1980 Aug;106(8):484-5.

(21) Epley JM. The canalith repositioning procedure: for treatment of benign paroxysmal positional vertigo. Otolaryngol Head Neck Surg. 1992 Sep;107(3):399-404.

(22) Shepard NT, Telian SA, Smith-Wheelock M. Habituation and balance retraining therapy. A retrospective review. Neurol Clin. 1990 May;8(2):459-75.

(23) Lacour M, Helmchen C, Vidal PP. Vestibular compensation: the neuro-otologist's best friend. J Neurol. 2016 Apr;263 Suppl 1:S54-64

(24) Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB. Disorders of balance and vestibular function in US adults: data from the National Health and Nutrition Examination Survey, 2001-2004. Arch Intern Med. 2009 May 25;169(10):938-44.

(25) Hilton MP, Pinder DK. The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo. Cochrane Database Syst Rev. 2014 Dec 8;(12):CD003162.

(26) Cabrera Kang CM, Tusa RJ. Vestibular rehabilitation: rationale and indications. Semin Neurol. 2013 Jul;33(3):276-85.

(27) Schmid A, Duncan PW, Studenski S, Lai SM, Richards L, Perera S, Wu SS. Improvements in speed-based gait classifications are meaningful. Stroke. 2007 Jul;38(7):2096-100.

(28) Patel M, Tilling K, Lawrence E, Rudd A, Wolfe C, McKevitt C. Relationships between long-term stroke disability, handicap and health-related quality of life. Age and Ageing 2006;35:273-9.

(29) Hansson EE. Vestibular rehabilitation – For whom and how? A systematic review. Adv Physiother. 2007; 9: 106-116

(30)Nussbaum RL, Ellis CE. Alzheimer's disease and Parkinson's disease. N Engl J Med. 2003 Apr 3;348(14):1356-64.

(31) Acarer A, Karapolat H, Celebisoy N, Ozgen G, Colakoglu Z. Is customized vestibular rehabilitation effective in patients with Parkinson's? NeuroRehabilitation (2015) 37:255–62.

(32) Wilkinson D, Podlewska A, Sakel M. A durable gain in motor and non-motor symptoms of Parkinson's Disease following repeated caloric vestibular stimulation: A single-case study. NeuroRehabilitation. 2016;38(2):179-82.

(33) Andreikanich A, Cardoso T, Dias P, Santos BS, Amorim P, Zagalo H, Marques B, Margalho P, Lains J, Faim F, Coelho M. An Exploratory Study on the use of Virtual Reality in Balance Rehabilitation. Annu Int Conf IEEE Eng Med Biol Soc. 2019 Jul;2019:3416-3419.

(34) Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. Dev Med Child Neurol. 2013 Jun;55(6):509-19.

(35) Woollacott MH, Shumway-Cook A. Postural dysfunction during standing and walking in children with cerebral palsy: What are the underlying problems and what new therapies might improve balance? Neural Plast 2005; 12: 211–219.

(36) Aggarwal R, Tully A, Grantcharov T, Larsen CR, Miskry T, Farthing A, Darzi A. Virtual reality simulation training can improve technical skills during laparoscopic salpingectomy for ectopic pregnancy. BJOG. 2006 Dec;113(12):1382-7.

(37) Jiandani N, Nair SR, Shukla H. Efficacy of Virtual Reality Exposure Therapy in the Management of Symptoms Associated With Post Traumatic Stress Disorder. Value Health. 2014 Nov;17(7):A572.

(38) Raghav K, Van Wijk AJ, Abdullah F, Islam MN, Bernatchez M, De Jongh A. Efficacy of virtual reality exposure therapy for treatment of dental phobia: a randomized control trial. BMC Oral Health. 2016 Feb 27;16:25.

(39) Doupis J, Festas G, Tsilivigos C, Efthymiou V, Kokkinos A. Smartphone-Based Technology in Diabetes Management. Diabetes Ther. 2020 Mar;11(3):607-619.

(40) Szekely A, Talano R, Bagyi P. Smartphones, tablets and mobile applications for radiology. Eur J Radiol 2013;82:829–836.

(41) Eysenbach G. What is e-health? J Med Internet Res. 2001 Apr-Jun;3(2):E20.

(42) WHO Global Observatory for eHealth. (2011). mHealth: new horizons for health through mobile technologies: second global survey on eHealth. World Health Organization.

(43) Levac D, Glegg SM, Sveistrup H, et al. A knowledge translation intervention to enhance clinical application of a virtual reality system in stroke rehabilitation. BMC Health Serv Res. 2016;16(1):557.

(44) Organ B, Liu H, Bromwich M. An iPhone-assisted particle repositioning maneuver for benign paroxysmal positional vertigo (BPPV): a prospective randomized study. J Am Board Fam Med. 2015 Jan-Feb;28(1):118-20.

(45) Dlugaiczyk J, Thiemer M, Neubert C, Schorn BA, Schick B. The aVOR App Increases Medical Students' Competence in Treating Benign Paroxysmal Positional Vertigo (BPPV). Otol Neurotol. 2018 Jun;39(5):e401-e406.

(46) Brodsky JR, Cusick BA, Kawai K, Kenna M, Zhou G. Peripheral vestibular loss detected in pediatric patients using a smartphone-based test of the subjective visual vertical. Int J Pediatr Otorhinolaryngol. 2015 Dec;79(12):2094-8.

(47) Shah MU, Lotterman S, Roberts D, Eisen M. Smartphone telemedical emergency department consults for screening of nonacute dizziness. Laryngoscope. 2019 Feb;129(2):466-469.

(48) de Joode LEGH, Martin EC, Stultiens JJA, Leue C, Delespaul P, Peeters F, Erdkamp A, van de Weijer S, Blom H, Bruintjes T, Zwergal A, Grill E, Guinand N, Perez-Fornos A, van de Berg

MR, Widdershoven J, Kingma H, van de Berg R. The DizzyQuest: to have or not to have… a vertigo attack? J Neurol. 2020 Dec;267(Suppl 1):15-23.

(49) van Vugt VA, van der Wouden JC, Essery R, Yardley L, Twisk JWR, van der Horst HE, Maarsingh OR. Internet based vestibular rehabilitation with and without physiotherapy support for adults aged 50 and older with a chronic vestibular syndrome in general practice: three armed randomised controlled trial. BMJ. 2019 Nov 5;367:l5922.

(50) Geraghty AWA, Essery R, Kirby S, Stuart B, Turner D, Little P, Bronstein A, Andersson G, Carlbring P, Yardley L. Internet-Based Vestibular Rehabilitation for Older Adults With Chronic Dizziness: A Randomized Controlled Trial in Primary Care. Ann Fam Med. 2017 May;15(3):209-216.

(51) Hall CD, Clevenger CK, Wolf RA, Lin JS, Johnson TM 2nd, Wolf SL. Feasibility of a Low-Cost, Interactive Gaming System to Assess Balance in Older Women. J Aging Phys Act. 2016 Jan;24(1):111-8.

(52) Karasu AU, Batur EB, Karataş GK. Effectiveness of Wii-based rehabilitation in stroke: A randomized controlled study. J Rehabil Med. 2018 May 8;50(5):406-412.

(53) Alves CC, Silva ALS. Pediatric Vestibular Rehabilitation: A Case Study. Pediatr Phys Ther. 2019 Oct;31(4):E14-E19.

(54) Noveletto F, Soares AV, Mello BA, Sevegnani CN, Eichinger FLF, Hounsell MDS, Bertemes-Filho P. Biomedical Serious Game System for Balance Rehabilitation of Hemiparetic Stroke Patients. IEEE Trans Neural Syst Rehabil Eng. 2018 Nov;26(11):2179-2188.

(55) Severiano MIR, Zeigelboim BS, Teive HAG, Santos GJB, Fonseca VR. Effect of virtual reality in Parkinson's disease: a prospective observational study. Arq Neuropsiquiatr. 2018 Feb;76(2):78-84.

(56) Albiol-Pérez S, Gil-Gómez JA, Muñoz-Tomás MT, Gil-Gómez H, Vial-Escolano R, Lozano-Quilis JA. The Effect of Balance Training on Postural Control in Patients with Parkinson's Disease Using a Virtual Rehabilitation System. Methods Inf Med. 2017 Mar 23;56(2):138-144.

(57) Hsu SY, Fang TY, Yeh SC, Su MC, Wang PC, Wang VY. Three-dimensional, virtual reality vestibular rehabilitation for chronic imbalance problem caused by Ménière's disease: a pilot study. Disabil Rehabil. 2017 Aug;39(16):1601-1606.

(58) Swanenburg J, Büchi F, Straumann D, Weber KP, de Bruin ED. Exergaming With Integrated Head Turn Tasks Improves Compensatory Saccade Pattern in Some Patients With Chronic Peripheral Unilateral Vestibular Hypofunction. Front Neurol. 2020 Jun 30;11:601

(59) Pedreira da Fonseca E, da Silva Ribeiro NM, Pinto EB. Therapeutic Effect of Virtual Reality on Post-Stroke Patients: Randomized Clinical Trial. J Stroke Cerebrovasc Dis. 2017 Jan;26(1):94-100.

(60) Wada Y, Nishiike S, Kitahara T, Yamanaka T, Imai T, Ito T, Sato G, Matsuda K, Kitamura Y, Takeda N. Effects of repeated snowboard exercise in virtual reality with time lags of visual scene behind body rotation on head stability and subjective slalom run performance in healthy young subjects. Acta Otolaryngol. 2016 Nov;136(11):1121-1124.

(61) Kumar D, González A, Das A, Dutta A, Fraisse P, Hayashibe M, Lahiri U. Virtual Reality-Based Center of Mass-Assisted Personalized Balance Training System. Front Bioeng Biotechnol. 2018 Jan 12;5:85.

(62) Held JPO, Yu K, Pyles C, Veerbeek JM, Bork F, Heining SM, Navab N, Luft AR. Augmented Reality-Based Rehabilitation of Gait Impairments: Case Report. JMIR Mhealth Uhealth. 2020 May 26;8(5):e17804.

(63) Andreikanich A, Cardoso T, Dias P, Santos BS, Amorim P, Zagalo H, Marques B, Margalho P, Lains J, Faim F, Coelho M. An Exploratory Study on the use of Virtual Reality in Balance Rehabilitation. Annu Int Conf IEEE Eng Med Biol Soc. 2019 Jul;2019:3416-3419.

(64) Sengupta M, Gupta A, Khanna M, Rashmi Krishnan UK, Chakrabarti D. Role of Virtual Reality in Balance Training in Patients with Spinal Cord Injury: A Prospective Comparative Pre-Post Study. Asian Spine J. 2020 Feb;14(1):51-58.

(65) Meyns P, Pans L, Plasmans K, Heyrman L, Desloovere K, Molenaers G. The Effect of Additional Virtual Reality Training on Balance in Children with Cerebral Palsy after Lower Limb Surgery: A Feasibility Study. Games Health J. 2017 Feb;6(1):39-48.

(66) Rosiak O, Krajewski K, Woszczak M, Jozefowicz-Korczynska M. Evaluation of the effectiveness of a Virtual Reality-based exercise program for Unilateral Peripheral Vestibular Deficit. J Vestib Res. 2018;28(5-6):409-415.

(67) Ayed I, Ghazel A, Jaume-I-Capó A, Moya-Alcover G, Varona J, Martínez-Bueso P. Feasibility of Kinect-Based Games for Balance Rehabilitation: A Case Study. J Healthc Eng. 2018 Jul 9;2018:7574860.

(68) Lubetzky AV, Kary EE, Harel D, Hujsak B, Perlin K. Feasibility and reliability of a virtual reality oculus platform to measure sensory integration for postural control in young adults. Physiother Theory Pract. 2018 Dec;34(12):935-950.

(69) Lubetzky AV, Kelly J, Wang Z, Gospodarek M, Fu G, Sutera J, Hujsak BD. Contextual sensory integration training via head mounted display for individuals with vestibular disorders: a feasibility study. Disabil Rehabil Assist Technol. 2020 May 18:1-11.

(70) Zaleski-King A, Pinto R, Lee G, Brungart D. Use of Commercial Virtual Reality Technology to Assess Verticality Perception in Static and Dynamic Visual Backgrounds. Ear Hear. 2020 Jan/Feb;41(1):125-135.

(71) Lubetzky AV, Hujsak BD, Kelly JL, Fu G, Perlin K. Control Mechanisms of Static and Dynamic Balance in Adults With and Without Vestibular Dysfunction in Oculus Virtual Environments. PM R. 2018 Nov;10(11):1223-1236.e2.

(72) Micarelli A, Viziano A, Augimeri I, Micarelli D, Alessandrini M. Three-dimensional head-mounted gaming task procedure maximizes effects of vestibular rehabilitation in unilateral vestibular hypofunction: a randomized controlled pilot trial. Int J Rehabil Res. 2017 Dec;40(4):325-332.

(73) Viziano A, Micarelli A, Augimeri I, Micarelli D, Alessandrini M. Long-term effects of vestibular rehabilitation and head-mounted gaming task procedure in unilateral vestibular hypofunction: a 12-month follow-up of a randomized controlled trial. Clin Rehabil. 2019 Jan;33(1):24-33.

(74) Micarelli A, Viziano A, Micarelli B, Augimeri I, Alessandrini M. Vestibular rehabilitation in older adults with and without mild cognitive impairment: Effects of virtual reality using a head-mounted display. Arch Gerontol Geriatr. 2019 Jul-Aug;83:246-256.

(75) Park JH, Jeon HJ, Lim EC, Koo JW, Lee HJ, Kim HJ, Lee JS, Song CG, Hong SK. Feasibility of Eye Tracking Assisted Vestibular Rehabilitation Strategy Using Immersive Virtual Reality. Clin Exp Otorhinolaryngol. 2019 Nov;12(4):376-384.

(76) Nehrujee A, Vasanthan L, Lepcha A, Balasubramanian S. A Smartphone-based gaming system for vestibular rehabilitation: A usability study. J Vestib Res. 2019;29(2-3):147-160.

(77) Tabanfar R, Chan HHL, Lin V, Le T, Irish JC. Development and face validation of a Virtual Reality Epley Maneuver System (VREMS) for home Epley treatment of benign paroxysmal positional vertigo: A randomized, controlled trial. Am J Otolaryngol. 2018 Mar-Apr;39(2):184-191.

(78) Fung A, Lai EC, Lee BC. Usability and Validation of the Smarter Balance System: An Unsupervised Dynamic Balance Exercises System for Individuals With Parkinson's Disease. IEEE Trans Neural Syst Rehabil Eng. 2018 Apr;26(4):798-806.

(79) An J, Kim J, Lai EC, Lee BC. Effects of a Smartphone-Based Wearable Telerehabilitation System for In-Home Dynamic Weight-Shifting Balance Exercises by Individuals with Parkinson's Disease. Annu Int Conf IEEE Eng Med Biol Soc. 2020 Jul;2020:5678-5681

(80) Bao T, Carender WJ, Kinnaird C, Barone VJ, Peethambaran G, Whitney SL, Kabeto M, Seidler RD, Sienko KH. Effects of long-term balance training with vibrotactile sensory augmentation among community-dwelling healthy older adults: a randomized preliminary study. J Neuroeng Rehabil. 2018 Jan 18;15(1):5.

(81) Cesaroni S, Silva AMD, Ganança MM, Caovilla HH. Postural control at posturography with virtual reality in the intercritical period of vestibular migraine. Braz J Otorhinolaryngol. 2019 Aug 2:S1808-8694(19)30084-9.

(82) Proffitt R, Warren J, Lange B, Chang CY. Safety and Feasibility of a First-Person View, Full-Body Interaction Game for Telerehabilitation Post-Stroke. Int J Telerehabil. 2018 Aug 3;10(1):29-36.

(83) Ulozienė I, Totilienė M, Paulauskas A, Blažauskas T, Marozas V, Kaski D, Ulozas V. Subjective visual vertical assessment with mobile virtual reality system. Medicina (Kaunas). 2017;53(6):394-402.

(84) Phu S, Vogrin S, Al Saedi A, Duque G. Balance training using virtual reality improves balance and physical performance in older adults at high risk of falls. Clin Interv Aging. 2019 Aug 28;14:1567-1577.

(85) Hondebrink MS, Mert A, van der Lint R, de Ru JA, van der Wurff P. Motion-based equilibrium reprocessing therapy a novel treatment method for chronic peripheral vestibulopathies: A pilot study. Medicine (Baltimore). 2017 Jun;96(24):e7128.

(86) Bergmann J, Krewer C, Bauer P, Koenig A, Riener R, Müller F. Virtual reality to augment robot-assisted gait training in non-ambulatory patients with a subacute stroke: a pilot randomized controlled trial. Eur J Phys Rehabil Med. 2018 Jun;54(3):397-407.

(87) Lange BS, Flynn SM, Rizzo AA. Initial usability assessment of off-the-shelf video game consoles for clinical game-based motor rehabilitation. Phys Ther Rev. 2009:14(5);355-363.

(88) Lange B, Flynn S, Proffitt R, Chang CY, Rizzo AS. Development of an interactive game-based rehabilitation tool for dynamic balance training. Top Stroke Rehabil. 2010 Sep-Oct;17(5):345-52.

(89) Noveletto F, Soares AV, Eichinger FLF, Domenech SC, Hounsell MDS, Filho PB. Biomedical Serious Game System for Lower Limb Motor Rehabilitation of Hemiparetic Stroke Patients. IEEE Trans Neural Syst Rehabil Eng. 2020 Jun;28(6):1481-1487.

(90) Wall T, Feinn R, Chui K, Cheng MS. The effects of the Nintendo™ Wii Fit on gait, balance, and quality of life in individuals with incomplete spinal cord injury. J Spinal Cord Med. 2015 Nov;38(6):777-83.

(91) Sulway S, Whitney SL. Advances in Vestibular Rehabilitation. Adv Otorhinolaryngol. 2019;82:164-169.

(92) Kang HK, Kim Y, Chung Y, Hwang S. Effects of treadmill training with optic flow on balance and gait in individuals following stroke: randomized controlled trials. Clin Rehabil. 2012 Mar;26(3):246-55.

(93) Valenzuela T, Okubo Y, Woodbury A, Lord SR, Delbaere K. Adherence to technology-based exercise programs in older adults: a systematic review. J Geriatr Phys Ther. 2018;41(1):49–61.

(94) Saredakis D, Szpak A, Birckhead B, Keage HAD, Rizzo A, Loetscher T. Factors Associated With Virtual Reality Sickness in Head-Mounted Displays: A Systematic Review and Meta-Analysis. Front Hum Neurosci. 2020 Mar 31;14:96.

(95) Jukka H, Monika P, Jari T, and Göte N. Simulator sickness in virtual display gaming: a comparison of stereoscopic and non-stereoscopic situations. In Proceedings of the 8th conference on Human-computer interaction with mobile devices and services (MobileHCI '06). Association for Computing Machinery, New York, NY, USA, 2006; 227–230.

(96) LaViola JJ. A discussion of cybersickness in virtual environments. SIGCHI Bull. 2000 Jan 1;32(1):47–56.

(97) Kolasinski EM. Simulator sickness in virtual environments (ARI 1027). Army Research Institute for the Behavioral and Social Sciences, USA, 1995.

(98) Shin J, An G, Park JS et al. Application of precise indoor position tracking to immersive virtual reality with translational movement support. Multimed Tools Appl 2016; 12331–12350.

(99) White PJ, Byagowi A, Moussavi Z. Effect of viewing mode on pathfinding in immersive Virtual Reality. Annu Int Conf IEEE Eng Med Biol Soc. 2015 Aug 2015;4619-22.

(100) Lange B, Flynn SM, Rizzo AA. Game-based telerehabilitation. Eur J Phys Rehabil Med. 2009 Mar;45(1):143-51.

(101) Weber H, Barr C, Gough C, van den Berg M. How Commercially Available Virtual Reality-Based Interventions Are Delivered and Reported in Gait, Posture, and Balance Rehabilitation: A Systematic Review. Phys Ther. 2020 Sep 28;100(10):1805-1815.

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