Multisensory Exercise Improves Balance in People with Balance Disorders: A Systematic Review*

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[Abstract] Objective: To examine the effect of multisensory exercise on balance disorders. **Methods:** PubMed, Scopus and Web of Science were searched to identify eligible studies published before January 1, 2020. Eligible studies included randomized control trials (RCTs), non-randomized studies, case-control studies, and cohort studies. The methodological quality of the included studies was evaluated using JBI Critical Appraisal Checklists for RCTs and for Quasi-Experimental Studies by two researchers independently. A narrative synthesis of intervention characteristics and health-related outcomes was performed. **Results:** A total of 11 non-randomized studies and 9 RCTs were eligible, including 667 participants. The results supported our assumption that multisensory exercise improved balance in people with balance disorders. All of the 20 studies were believed to be of high or moderate quality. **Conclusion:** Our study confirmed that multisensory exercise was effective in improving balance in people with balance disorders. Multisensory exercises could lower the risk of fall and enhance confidence level to improve the quality of life. Further research is needed to investigate the optimal strategy of multisensory exercises and explore the underlying neural and molecular mechanisms of balance improvement brought by multisensory exercises.

Key words: multisensory exercises; multisensory integration; balance; systematic review

Balance maintenance is essential for daily life. Balance can be defined as a stable state achieved by maintaining the body's mass center within manageable limits of stability^[1, 2]. Static balance is attained by keeping the center of mass within the base of support during standing and sitting^[2-4]. On the other hand, dynamic balance is more challenging because it requires maintenance of equilibrium of the body when both the center of mass and base of support are not constant^[2, 5]. Ability to maintain balance is the basis of

movement and performance of daily activities. Balance disorder refers to impaired or lost ability to accomplish equilibrium. The causes of imbalance include visual loss such as glaucoma, vestibular failure such as Meniere disease, somatosensory loss such as diabetic peripheral neuropathy, cerebellar lesions such as cerebellar stroke, and lesions involving basal ganglia and frontal lobes, etc. Balance disorders fall into three categories in terms of sensorimotor levels^[6]. The lowest-level sensorimotor dysfunction involves musculoskeletal dysfunction or multisensory disturbances such as visual, vestibular and somatosensory disturbances^[7]. The middle-level and the highest-level sensorimotor dysfunction separately involves faulty execution and selection of postural and locomotor responses^[7]. Middle-level dysfunction includes spastic, ataxic, dystonic, and choreic gaits, for instance, cerebellar ataxia^[7]. The highest-level balance disorders include subcortical disequilibrium, frontal disequilibrium and so on, e.g. Parkinson's disease^[7]. Moreover, balance disorder also increases the risk of fall^[8, 9] and even leads to fall-related injuries. According to WHO, roughly

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646 000 suffered from fatal falls each year, and the fall represents the second leading cause of unintentional injury-related death (2018)^[10]. Among people over 60 years, the rate of fall-related death is the highest around the globe^[10]. Though not fatal, approximately 37.3 million falls that require medical attention take place each year^[10]. To ameliorate balance disorders and reduce possible injuries, clinicians should understand the mechanism of balance disorders and thereby work out effective management.

Medication and surgery are seldom used for balance improvement and fall prevention. The main management for improving balance includes physical exercises, vestibular rehabilitation and multisensory exercises. They are three different training programs that are used to manage balance disorder^[11–13].

Physical exercises include aerobic exercise, stretching exercise and resistance training, among others^[11, 14, 15]. Those exercises train people's muscles, stretch their bodies, and challenge the ability to respond to different situations. Many studies have shown that physical exercises could bring beneficial effects on balance^[11, 14–16]. Vestibular rehabilitation includes adaptation, habituation, sensory substitution and optokinetic exercises^[17]. Vestibular rehabilitation aims to facilitate the compensation for vestibular function^[17]. It has been shown to be an effective treatment for reducing vertigo and improving gaze stabilization and balance^[12, 18]. Multisensory exercises consist of activities simultaneously stimulating at least two sensory modalities of multiple sensory systems including visual, auditory, tactile, vestibular, somatosensory systems and so on^[13, 19, 20]. Multisensory exercises may improve balance by enhancing central nervous system (CNS) ability to process and integrate sensory afferents and facilitating compensation for deficient sensory inputs^[20, 21]. And this process may rely on improved connectivity between numerous interconnected neural circuits that are regulated by the CNS.

Multisensory exercises and vestibular rehabilitation

both aim to promote balance by modulating CNS plasticity^[22, 23], while physical exercises aim at enhancing physical function^[16]. From the perspective of sensory inputs, multisensory exercises stimulate multiple sensory systems simultaneously^[13], but vestibular rehabilitation mainly stimulates the unisensory system such as vision or somatosensory sensation^[17]. Multisensory exercises can facilitate CNS compensation for multisensory afferents, vestibular rehabilitation is mainly aimed at patients with vestibular dysfunction to promote their vestibular compensation^[17]. The comparisons among three training programs are shown in table 1.

While a few studies have reported that multisensory exercises could positively impact on balance disorder^[24, 25], the effects of multisensory exercises on balance have not been systemically investigated. In this study, we conducted a systematic review with an attempt to look into the effect of multisensory exercise on balance disorder.

1 MATERIALS AND METHODS

1.1 Study Design and PICO

Patients with balance disorders under multisensory exercises were included in this systematic review. Comparators were patients with balance disorders undergoing other exercises or no multisensory training. In this study, balance function was the main outcome indicator.

1.2 Protocol of Systematic Review

The protocol for this systematic review was registered in PROSPERO (registration number: CRD42020151453). Protocol details were available from https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020151453.

1.3 Search Strategy and Study Selection

This systematic review was performed in accordance with the PRISMA statement^[26]. Two reviewers independently conducted the literature search. Electronic databases, including PubMed, Scopus and Web of Science, were searched to identify

Table 1 Comparison among physical exercises, vestibular rehabilitation and multisensory exercises

	Physical exercises	Vestibular rehabilitation	Multisensory exercises
Target population	Various disorders (e.g. stroke and dementia)	Vestibular dysfunction (e.g. BPPV and Menière's disease)	Balance disorders (e.g. eye disorders and type 2 diabetes)
Principles	Physical function: Train muscles Stretch bodies Respond to different situations	Unisensory stimulation: Vision (vestibulo-ocular reflex), somatosensory and vestibular sensation Habituation: Repeated exposure Sensory substitution: Visual or somatosensory sensation	Multisensory stimulation: Vision, hearing, touch, vestibular and somatosensory sensation, among others
How to improve balance	By enhancing physical function	By compensating for vestibular dysfunction	By enhancing multisensory integration

BPPV: benign paroxysmal positional vertigo

eligible studies published before January 1, 2020. We used the following search strategies: (1) (Multisensory OR Multi-sensory OR Multisensorial) OR (Crossmodal OR Cross-modal) OR (Crossmodal Sensory) OR (Multimodal OR Multimodality) OR Intersensory OR Multisystem), (2) (Exercis* OR Exercise) OR (Exercise Therapy) OR Train* OR Rehabilitat* OR Treat* OR Intervent* OR Program* OR Therap* OR Stimulation, and (3) Balanc* OR Equilibrium OR Gait OR Stability OR Stabilization OR Sway OR Instability OR Postur* OR (Gesture Control) OR (Movement Control). The “*” was the wild card. These search queries were combined by Boolean operator “And”.

The articles published in English were included and duplicates were excluded. Two reviewers (SZ and DL) assessed all the articles against the inclusion and exclusion criteria by reading title, abstract and the full-text. If any disagreement occurred, a third reviewer (DY) would be consulted, and a consensus was arrived at by referring to the inclusion and exclusion criteria.

The systematic review pooled the most up-to-date multisensory exercise that improves balance in people with balance disorders. A study was included if: (1) Participants included children, adolescents, adults and elders diagnosed with diseases that might affect balance, those with fall history or complained instability or assessment showed impaired balance function; (2) Multisensory exercise was the main intervention; (3) At least one outcome measure involved balance; (4) Included RCTs, non-randomized studies, case-control studies, and cohort studies; (5) Sample size >10. Moreover, studies were excluded if: (1) They were reviews, case reports, conference abstracts, comments, or letters; (2) Data were unavailable or insufficient; (3) They had overlapping dates or were animal studies.

1.4 Quality Assessment

The JBI Critical Appraisal Checklists for RCTs and for Quasi-Experimental Studies were used to assess the methodological quality of the included papers ($n=20$). The checklist for evaluating the RCTs consisted of 13 assessment criteria and the one for the quasi-experimental studies consisted of 9 assessment criteria. Each criterion was rated as “yes,” “no,” “unclear,” or “not applicable.”^[27]

Two reviewers (SZ and DL) independently assessed the quality of eligible studies, which were rated as “include,” “exclude,” or “seek further information.” In case of disagreement, a third reviewer (DY) was consulted to achieve a consensus. All disagreements with regard to the methodological quality of the studies were discussed and agreed upon by the team. The level of methodological quality was determined as follows: fair quality if less than 50% of the items were rated as “yes,” moderate quality if 51% to 80% of the items were rated as “yes,” and good quality if more than 80% of the items were rated as “yes.” No studies were

excluded based on methodological quality.

1.5 Data Extraction

The relevant data of the studies were extracted, including authors, publication year, country, design, sample population, sample size, age, intervention (frequency and duration) and outcome measures. Two reviewers (SZ and DL) separately extracted data which were input into a form. If any disagreement occurred, they reviewed the full text of the articles to reach an agreement.

1.6 Data Analysis

The authors intended a priori to complete a meta-analysis. However, the limited number of articles retrieved and substantial heterogeneity across the retrieved studies did not allow meta-analysis of the results for different study characteristics. In view of these, we only provided a qualitative synthesis of the results.

2 RESULTS

2.1 Study Selection and Characteristics

The electronic database search yielded 8460 records, of which 1726 were identified by Endnote as duplicates. Another 680 duplicate records were removed manually, leaving 6054 potentially relevant records for future screening. Upon reading the title and the abstract, we removed records that did not satisfy the inclusion criteria. Finally, 401 potentially eligible articles were subjected to full-text screening and 20 of them were eventually included in the systematic review (fig. 1). The study characteristics separately for

Fig. 1 Flow diagram of study selection process

RCTs and nonRCTs, included mean age, sex, types of disorder/disease, and most importantly, the types of interventions, range of length of interventions, a dose of intervention (i.e. No. of sessions), length of each session, mode of delivery, main result, etc.

2.2 Participants and Settings

The studies included in this review contained a total of 667 participants ranging from 10^[28] to 68^[29] participants per study (table 2). The mean age of the study samples ranged from 133.5±26.9 months^[30] to 84.8±4.1 years^[31]. Two studies collected and reported information about multisensory exercise, which included participants all females^[31, 32]. Of these participants, 30 were ataxic patients^[33], 73 were older adults with a history of falls^[20, 34, 35], 33 were older adults without fall history^[35, 36], 18 were older adults with visual impairment^[37], 16 were diabetics with peripheral neuropathy^[38], and 21 were patients with essential tremor^[39]. A total of 667 participants were included in the 20 studies, four studies were conducted in the United States, four in Canada, two in Brazil, and two in France, other studies in England, Indian, Sweden, and so on.

2.3 Intervention Programs

Table 2 presents the characteristics of the exercise training interventions. The total time spent in exercising during the multisensory exercise interventions varied from 0.5^[30, 40] to 180 h^[33], while the intervention duration ranged from 2^[41] to 16 weeks^[31]. Studies of intervention time showed that multisensory exercises worked within 6 weeks^[34, 38, 42], 8 weeks^[20, 39, 43], 12 weeks^[36, 37, 44] respectively. However, there are still studies which reported effective intervention duration was less than 6 weeks or more than 12 weeks. Six of the interventions were new systems or advanced equipment such as the Balance Freedom TM head-band system (Balance Int. Innovations GmbH, Switzerland), a performance scoring system, etc.^[28, 39–41, 43, 45]. Two of the interventions used games for multisensory training^[30, 35]. One study used a multisensory program with dance^[37]. One study involved cognitive training in addition to multisensory training^[46].

2.4 Group Comparison

One study^[46] used three groups: one control group (conventional training included balance tasks in seated, standing, and moving task situations), one group of individual Dual-Task Training, and one group of multisensory training. Five studies^[28, 33, 34, 39, 42] used only one group in their study design. The other studies used two groups (intervention group and control group). The main control groups included oral education, daily routine, conventional training, strength exercise, and other none-multisensory exercises (table 2).

2.5 Outcomes Measures about Balance

The measures used for balance assessment include the sensory organization test (SOT) ($n=3$), the timed up

and go test (TUG) ($n=4$), the Berg balance scale (BBS) ($n=3$) and the activities-specific balance confidence scale (ABC) ($n=4$). This systematic analysis showed that multisensory exercises were effective in improving balance in people with balance disorders. The balance performance was assessed by the SOT, TUG, BBS and ABC. The SOT^[47] examines the abilities to maintain standing balance under six different sensory conditions: (1) eyes are fixed on a fixed screen when standing on a fixed surface; (2) eyes close while standing on a fixed surface; (3) eyes are fixed on a moving screen when standing on a fixed surface; (4) eyes are fixed on a fixed screen while standing on moving surface; (5) eyes close when standing on a moving surface; (6) eyes are fixed on a moving screen when standing on a moving surface. The TUG^[48] measures the time taken to rise from an arm chair, walk 3 meters away, go back and sit down again. The BBS^[49] consists of 14 activities rated on a 0–4 point scale, with the maximum score being 56. The major activities are dynamic tasks ranging from simple items (e.g., sit-to-stand) to difficult items (e.g., turning 360°). A recent study suggested that only an over 8-point change in BBS could lead to clinically significant functional alteration^[50]. However, the change in BBS in our study was too small to produce a clinically significant change. Nonetheless, multisensory exercises pose no harm to balance performance in any way. The ABC^[51] is a 16-item questionnaire that examines balance confidence. Items are rated from 0% (no confidence) to 100% (full confidence). The activities' difficulty ranges from walking around house to walking on icy sidewalks. Higher ABC score implies better balance confidence during daily activities^[52]. Stronger self-assurance can break up the vicious circle between fear of fall and avoidance of physical activity.

2.6 Methodological Quality of Included Studies

The eligible studies are listed in table 2. The methodological quality assessment of 9 RCTs and 11 non-randomized studies are presented in tables 3 and 4. Eight RCTs scored "yes" for most items. Two studies were unclear randomization used for assignment of participants to treatment groups and the allocation to treatment groups concealed unclear too^[36, 45]. In one study, participants blind to treatment assignment were unclear^[40]. Only two studies answered yes for delivering treatment blind to treatment assignment^[31, 46]. Outcomes assessors in three studies were blind to treatment assignment by methodological quality assessment^[31, 40, 46]. Our study had no follow-up assessment because of time constraints^[46]. The randomization process was not clearly described in 11 non-randomized studies. Ten studies scored "yes" for most items, except for item 1^[33]. There was no control group in the four studies^[35, 37, 41, 43]. Two studies' outcomes measured whether a reliable way were unclear^[33, 35].

Table 2 Characteristics of eligible studies (n=20)

Author, year, country	Type of study setting	Experimental group	Experimental intervention	Control group	Control intervention	Treatment session details	Outcomes measurements	Main results
Allison, 2018, American	non-RCT	Fall-prone older adults (8-weeks intervention) n=20 Age=83±5 years	16 sensory-challenge balance exercise sessions performed with computerized balance training equipment	Fall-prone older adults (8-weeks baseline)	–	45 min× 2/week× 8 weeks	1. MSR center of mass gain and phase, position, and velocity variability 2. Clinical tests a. Sensory Organization Test b. Berg Balance Scale c. Activities-specific Balance Confidence Scale d. Limits of Stability test, e. Lower extremity strength and range of motion the Timed Up and Go Test	Abnormally elevated sensitivity to dynamic environmental stimuli in the fall-prone elderly was reduced following participation in a sensory-challenge balance exercise program. MSR is one of the mechanisms through which sensory challenge balance exercises may lead to improvements in postural control. Multisensory exercises were shown to be more efficacious than strength exercises to improve functional mobility.
Alfieri, 2010, Brazil	RCT	Community-dwelling elderly Intervention GMS: n=23 Age=68.8±5.9 years	Multisensory training (GMS)	Community-dwelling elderly Control GST: n=23 Age: 70.2±4.8 years	Strength training (GST)	1 h× 2/week× 12 weeks		
Allum, 2011, Canada	non-RCT	uncompensated unilateral vestibular loss patients Intervention group: n=7 Age=35–72 years	balance BF training	Healthy older adults Control n=12 Age: 59–86 years	Balance BF training	3/week× 2 weeks	Pitch angular displacements Roll angular displacements	The prospect for longer term (>1 week) effects of prosthetic training on balance control remains currently unknown.
Bellomo, 2009, Italy	RCT	elderly individuals GrHu group: n=20 Age=65±10 years	Multisensory train with Huber instrumentation	Elderly individuals Control GrCI group n=20 Age: 65±10 years	Classical rehabilitation including the lower limbs and spine	GrHu and GrCI: 30 min/ session× 3 sessions/ week× 3 months	BTS walk at normal speed (WA) and stabilometric test (StT) using the Dynamic Foot System energy cost (CE), oxygen volume TEF 4-min walk (assessments before training / after 3 months)	The multisensory training approach yields an improvement of balance in the elderly, which reduces the risk of falls and significantly improve quality of life. The observed improvement is significantly greater than that seen with the classical training program.
Davis, 2010, Canada	RCT	older adults Intervention group: n=32 Age Old: 63.7±4.3 years Young: 26.1±3.1 years	Vibrotactile, auditory and visual biofeedback of angular trunk displacement+ static and dynamic balance tasks	Older adults and young adults Control group: n=32 Age Old: 63.7±4.3 years; young: 26.1±3.1 years)	Biofeedback trunk displacement + balance training	30 min	90% range of angular trunk displacement	In some cases, biofeedback influenced balance in older adults, but not younger adults

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Author, year, country	Type of study setting	Experimental group	Experimental intervention	Control group	Control intervention	Treatment session details	Outcomes measurements	Main results
Fung, 2018, American	non-RCT	PD with impaired postural stability n=10 Age=70.7 years	Normal PD medication+ Dynamic WSBE with the SBS	--	—	Approximately 20 of rest between trials, directions then took a 5-min seated rest×24 trials	Dynamic WSBE LOS in both the A/P and M/L directions	The SBS can be a viable system for home-based balance rehabilitation and telerehabilitation. While the results of this study show the usability of the SBS system, future research will continue to evaluate the clinical impact of using the SBS.
Hafstrom, 2016, Sweden	non-RCT	Dwelling elderly n=40 Age=60–80 years	Multimodal balance-enhancing exercise program (BEEP)	--	—	16 min×4/ week× 6 weeks	One-leg standing time(OLST) Tandem stance with EC(Sharpened Romberg) Timed Up and Go speeds Walking speed Berg Balance Sclae(BBS) Modified step stool test Posturography with and without perturbations Questionnaire	Multimodal balance exercises offer an efficient, cost-effective way to improve balance control and confidence in elderly.
Kara, 2018, Turkey	non-RCT	Patients with Essential Tremor n=21 Age=63.5 years	Postural balance training	--	—	30 min/ week× 8 weeks	Postural Stability Test Limits of Stability Test Fall Risk Test Activities-Specific Balance Confidence Dynamic Gait Index Short Form-36	Balance training program is a feasible method that may have positive effects on balance performance and confidence, gait performance, and health-related quality of life in patients with ET.
Kim, 2013, American	non-RCT	Ambulatory older adults Intervention group: n=18 Age=68.28±3.74 years	VR-based exercise program	Ambulatory older adults Control group: n=14 Age: 66.21±3.87	Daily routine	60 min× 3/week× 8 week	Multimodal dynamometer muscle strength stepping tests	A VR-based exercise program may be a useful tool to improve decreased physical function in older adults as a home-based exercise.
Kristinsdottir, 2014, Iceland	non-RCT	Unsteady elderly people n=37 Age=80.8 years	Multisensory balance training	—	—	45 min× 3/week× 6 weeks	Sensory Organization Test Five-Times-Sit-to-Stand Test 30-m normal and fast walk with a turn, Ascending-Descending 11 steps Activities-specific Balance Confidence Scale	Combined vestibular, proprioceptive and fall-prevention training improves postural control, functional ability, confidence in ADL and might even decrease the risk of falling among elderly people

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Author, year, country	Type of study setting	Experimental group	Experimental intervention	Control group	Control intervention	Treatment session details	Outcomes measurements	Main results
Missaoui, 2013, France	non-RCT	Ataxic neuropathies $n=30$ Age=66±13 years		—	—	12 h× 3 sessions× 3/week× 5 weeks	Timed Up and Go test Berg Balance Scale Function Reach Test	Ataxic patients are impaired in balance and gait but can improve clinical balance parameters following training with a multisensory approach without limitation due to age or degree of sensory impairment.
Hackney, 2015, England	non-RCT	Older adults with visual impairment Fallproof group: $n=13$ Age=74.8±11.2 years	Activities of multimodal stimuli	Older adults with visual impairment Tango group: $n=12$ Age: 84.9±9.0 years	Dance steps	1.5 h× 2/week× 12 weeks	Berg Balance Scale (BBS) Sensory Organization Test (SOT) Postural sway, Dynamic Gait Index (DGI), Timed Up-and-Go Test (TUG) Gait speeds. Questionnaire	Adapted tango and FallProof could be effective and enjoyable long-term physical activities that benefit individuals with vision loss.
Lee, 2017, Canada	RCT	Non-injured elderly females Intervention group (ETG) ETG+ECG $n=24$ Age=60–80 years	Multisensory training	Non-injured elderly females Control group (ECG)	None	ETG: 60 min× 2/week× 3 weeks ECG: No	Dynamic Balance System (DBS) Berg Balance Test (BBT)	Three-week multisensory training program using CDBS was able to successfully reduce postural sway, thus improve balance control ability. Balance exercises are essential to improve balance ability for all ages
Lim, 2016, Canada	RCT	Healthy older adult Intervention group: $n=18$ Age=69±7 years	Stance and gait tasks+ multimodal biofeedback of trunk sway	Healthy older adult Control group: $n=18$ Age: 70±6 years	Stance and gait tasks +without biofeedback	3/week× 2 weeks	Trunk angular sway Task duration (assessed immediately and after 1-week, 1-month post-training)	There is little added benefit to balance training with biofeedback, beyond training without, in healthy older adults, transient use of wearable balance biofeedback systems as balance aides remains beneficial for challenging balance situations and some clinical populations
MyCoy, 2015, American	non-RCT	Children with FASD (fetal alcohol spectrum disorders) Intervention group: $n=11$ Age=137.0 months	STABEL training	Typical development (TD). Control group: $n=11$ Age: 133.5 months	STABEL training	30 min	Sensory attention Postural control	STABEL system was feasible for school-aged children with and without postural and balance control deficits

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Author, year, country	Type of study setting	Experimental group	Experimental intervention	Control group	Control intervention	Treatment session details	Outcomes measurements	Main results
Moreira, 2018, Brazil	RCT	Age > 65 years old adult women Intervention group: n=24 Age=84.83 years	Multisensory exercise	Age >65 years old adult women Control group: n=21 Age: 82.30 years	Strength exercise	50 min× 3/week× 16 weeks	Montreal Cognitive Assessment Berg Scale Timed Up and Go Test Physical Performance Test	The multisensory exercise programme improved the cognition and functionality of institutionalized older adults.
Majeed, 2013, India	RCT	Diabetic neuropathy Intervention group n=16 Age=65±2.12 years	Diabetes health education+ Multisensory training	Diabetic neuropathy Control group n=16 Age: 68±2.17 years	Diabetes health Education	30 min× 3/week× 6 weeks	Timed Up and Go Test(for balance) 6-min walk (for gait)	The study showed that multisensory exercises could improve balance in persons with Type 2 diabetes and peripheral neuropathy
Nematollahi, 2016, Iran	RCT	Older adults Intervention group: n=15 Age=63.8±3.82 years n=15 Age=64.7±5.00 years	Multisensory training Dual-Task Training	Older adults Control group: n=14 Age: 67.7±4.98 years	Conventional training	60 min× 3/week× 4 weeks	Fullerton Advanced Balance (FAB) scale, Gait stability ratio Walking speed	In a four-week period, all the training modes were effective in improving balance of older adults, with no significant superiority of one mode of training over another.
O'Callaghan, 2018, Ireland	non-RCT	Fall-prone older adults n=12 Age=70.74±2.8 years	CityQuest a. Sensorimotor control b. spatial navigation, c.obstacle avoidance d. balancecontrol	Healthy older adults n=15 Age: 71.0±4.89 years	-	40 to 60 min× 2/week× 5 weeks 10 training sessions	ABC mFES MiniBest SAFFE Trail Making Test Spatial Navigation Task Spatial Cognition Task	Multisensory training can affect structural changes in the older brain and have implications for programmes designed for the successful rehabilitation of perceptual and cognitive functions.
Yelnik, 2008, France	RCT	Hemiplegia after stroke unable to walk at least 2 weeks not exceeding 3 months and less than 80 years old Intervention group: n=33 Age=55.5±11.6 years	Multisensorial	Hemiplegia after stroke unable to walk at least 2 weeks not exceeding 3 months and less than 80 years old Control group: n=35 Age: 54.9±11.8 years	NDT	20 session× 5 days/week ×4 weeks 60-70 min/ session	Berg Balance Scale (BBS), Posturography Gait Functional Independence Measure Nottingham Health Profile (on day 0/30/90)	No evidence was found for the superiority of a multisensorial rehabilitation program in ambulatory patients with impairments beyond the time of inpatient therapy.

3 DISCUSSION

This systematic review studies evaluating multisensory exercise which improves balance in people with balance disorders (fig. 2). We identified a total of 20 moderate to high quality experimental studies representing a total of 667 participants. Most of these studies were conducted in the USA and Canada. Unfortunately, the limited number of articles retrieved and substantial heterogeneity across the retrieved studies did not enable us to conduct a meta-analysis. To our knowledge, this is the only systematic review exploring the effectiveness of multisensory exercise to improve balance in people with balance disorders.

3.1 Interventions Evaluated by Included Studies

The studies included in this review all but one^[29] found the superiority of multisensory exercises in patients with balance disorders. The interventions most commonly evaluated by included studies were multisensory exercises, which consist of activities simultaneously stimulating at least two sensory modalities of multiple sensory systems including visual, auditory, tactile, vestibular, somatosensory systems, and so on. Auditory stimulation mainly includes music, natural sound, voice, machine work sound, closing sound, etc.^[40, 41, 44]. Tactile was stimulated using vibratory stimulation above the perception threshold of the soles of both feet at 100 Hz frequency, baths in alternately cold and warm water, training by touching soft hardness, texture, or 1–2 mm vibrating items^[20, 33, 36, 40, 41].

Multisensory integration disorder refers to the abnormality in the integration of different sensations or modalities when relevant factors of balance are significantly altered, in addition to auditory and tactile stimulation, we can use fragrance to stimulate smell and food to stimulate taste for multisensory training. Four studies simultaneously stimulated vestibular, visual, and proprioceptive feelings for multisensory exercise^[29, 30, 34, 42]. Vestibular stimulation mainly includes head stationary; head tilt, nod, rotation, etc. Visual stimulation mainly includes closing

your eyes or wearing an eye mask, fixation of eyes, gaze range from small to large static, predictable and unpredictable movement, observing the color, brightness, etc. Somatosensory stimulation mainly includes solid ground, soft support surface (foam, sponge, etc.), rocking ground, etc. It is designed to improve foot dexterity through handling, collecting objects or writing with the toes. Furthermore, we found that visual and proprioceptive stimuli were more than vestibular, auditory, and tactile stimuli in multisensory exercise. It is worth mentioning that multi-modal biofeedback systems are applied to the research of multisensory exercise, overcome the aforementioned limitations of current biofeedback systems, and develop a multi-modal head-mounted biofeedback system that provides sensory information to the wearer by using: (1) bilateral audio bone-conducted signals; (2) an array of vibrotactile signals at the head; and (3) an augmenting visual signal^[40].

3.2 Mechanisms of Multisensory Exercises Improving Balance

From anatomical point of view, gray matter volume increased after multisensory exercises^[35]. Previous studies showed that the volume of the temporal lobe, cerebellum and hippocampus decreased with age^[53] and the reduced gray matter volume was associated with poor balance^[54]. Multiple areas in the brain are heavily involved in multisensory information processing, such as superior colliculus^[55] and the posterior parietal cortex^[56]. Our study suggested that multisensory exercises increased brain volume to enhance the ability to process multisensory information and maintain balance. Balance requires multisensory integration (MSI)^[21], i.e., the process by which multisensory inputs are combined by the nervous system to form a stable and coherent percept of the world, ensuing responses of the body^[57–59]. When sensory afferents from the environment are reduced, other sensory afferents will compensate for the reduction^[60]. MSI is modulated by both bottom-up and top-down factors^[61]. This study suggested that multisensory exercises might improve MSI by increasing bottom-up information inputs and

Fig. 2 Multisensory exercise improves balance in people with balance disorders

VOR: vestibular-ocular reflex; VSR: vestibulospinal reflex; VCR: vestibulocolic reflex

Table 3 Quality assessment of eligible non-randomized studies

Publications	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total
Missaoui 2013	Y	Y	Y	N	N	Y	Y	U	Y	6/9
Allison 2018	Y	Y	Y	N	N	Y	Y	Y	Y	7/9
Hackney 2015	Y	Y	Y	Y	N	Y	Y	Y	Y	8/9
McCoy 2015	Y	Y	Y	N	Y	Y	Y	Y	Y	8/9
Kristinsdottir 2014	Y	Y	Y	N	N	Y	Y	Y	Y	7/9
O'Callaghan 2017	Y	Y	Y	Y	N	Y	Y	U	Y	7/9
Kara 2018	Y	Y	Y	N	N	Y	Y	Y	Y	7/9
Fung 2018	Y	Y	Y	N	N	Y	Y	Y	Y	7/9
Kim 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9
Hafstrom 2016	Y	Y	Y	N	Y	Y	Y	Y	Y	8/9
Alum 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/9

Y, yes; N, no; U, unclear

Q1: Is it clear in the study what is the “cause” and what is the “effect” (i.e. there is no confusion about which variable comes first)?

Q2: Were the participants included in any comparisons similar?

Q3: Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?

Q4: Was there a control group?

Q5: Were there multiple measurements of the outcome both pre and post the intervention/exposure?

Q6: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?

Q7: Were the outcomes of participants included in any comparisons measured in the same way?

Q8: Were outcomes measured in a reliable way?

Q9: Was appropriate statistical analysis used?

Table 4 Quality assessment result of RCTs

Publications	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
Majeed 2013	Y	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	U	10/13
Alfieri 2010	U	U	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
Bellomo 2009	U	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	10/13
Lee 2017	Y	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	11/13
Lim 2016	U	U	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	9/13
Moreira 2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13
Yelnik 2008	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	11/13
Davis 2010	Y	Y	U	U	U	Y	Y	Y	Y	Y	Y	Y	Y	10/13
Nematollahi 2016	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	11/13

Y, yes; N, no; U, unclear

Q1: Was true randomization used for assignment of participants to treatment groups?

Q2: Was allocation to treatment groups concealed?

Q3: Were treatment groups similar at the baseline?

Q4: Were participants blind to treatment assignment?

Q5: Were those delivering treatment blind to treatment assignment?

Q6: Were outcomes assessors blind to treatment assignment?

Q7: Were treatment groups treated identically other than the intervention of interest?

Q8: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?

Q9: Were participants analyzed in the groups to which they were randomized?

Q10: Were outcomes measured in the same way for treatment groups?

Q11: Were outcomes measured in a reliable way?

Q12: Was appropriate statistical analysis used?

Q13: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

modulating top-down signals. Multisensory exercises stimulate multiple sensory inputs of various sources simultaneously to increase bottom-up information inputs^[13, 61]. If information of an object requires

integration of more than one sensory systems, it captures the attention of an information receiver more efficiently, and proves that bottom-up integration can “drive” attention^[62]. On the other hand, the bottom-

up information inputs can be modulated by the top-down signals of the brain^[63]. The mammalian brain is constantly learning from task-relevant sensory stimuli in the environment^[61] which changes the way of sensory cortex responding to the task-relevant sensory of stimulation^[64]. Learning-enhanced sensory responses are further facilitated by attention and task engagement^[65, 66].

Selective attention to important features of task-relevant stimuli can also enhance sensory responses^[67]. When multiple sensory systems are repeatedly stimulated by multisensory exercises, the brain might also learn from relevant sensory stimuli, put more attention on exercises-relevant sensory stimuli and modulate bottom-up inputs to improve balance.

Another possible mechanism is that multisensory exercises may enhance receptors' sensitivity of different sensory systems^[13]. Additionally, the ability for unisensory system processing might also get improved after multisensory exercises, since declined unisensory processing ability might impair balance performance^[68, 69].

3.3 Synthesized Findings

Analysis in terms of study type showed that, in both RCTs and non-randomized studies, multisensory exercises could effectively improve balance. Analysis in terms of intervention time showed that multisensory exercises worked within 6 weeks. Our analysis indicated that the optimal intervention time might be less than 6 weeks and multisensory exercises beyond 6 weeks are not necessary. And animal studies showed the time taken for vestibular compensation was no more than 7 days^[70, 71]. The intervention time should suffice to modulate central nervous plasticity. New neural networks may be activated and homeostasis may be achieved in the CNS. Moreover, the effect of multisensory exercises on balance might linger for a long time after the exercises ceased^[34, 37]. A follow-up study by Hackney *et al.* exhibited that the changes in SOT and BBS remained from the end of the intervention to one-month after the termination^[37]. And Kritinsdottir *et al.*^[34] found that the episodes of fall dropped during a time of 6-month. The long-term effect may be attributed to changes in the CNS effected by multisensory exercises. Multisensory exercises may elicit neurogenesis and synapse formation in the brain and new connections may develop between different brain regions. Besides, analysis showed no significant difference in balance improvement among patients with various etiologies. The result suggested that multisensory exercises are equally effective for patients with both central or peripheral nervous system disorders.

Multisensory exercises out-performed physical exercises in balance improvement^[36]. Alfieri *et al.* reported that after 3 months of training, multisensory

exercises decreased the time to complete TUG by 11.85%, while strength exercises shortened the time by only 3%, and the difference between the groups was statistically significant^[36]. The results suggested that multisensory exercises work better on dynamic balance than strength exercises, possibly because multisensory exercises could enhance multisensorial receptors' sensitivity^[72, 73]. On the other hand, the strength exercises mainly target muscle groups. Strength training could significantly slow movement of pressure center while multisensory exercises could shorten the distance over which pressure center moved^[36]. This suggested that multi-sensorial stimulation could help subjects develop optimal strategies for postural control, thereby minimizing body sway^[74].

Interestingly, we found that participants' mean age of the included studies were over 60 years old. As we know it, the incidence of balance disorders in older adults is higher than in young people. And aging progressively impairs sight, vestibular input, and somatosensory information, and reduces the number of muscle and nerve fibers, resulting in an impaired environmental perception and muscle strength^[1, 59, 75]. Besides, impaired multisensory integration makes the elderly people more vulnerable to fall^[76]. Patients with vestibular dysfunction were not included in our analysis, since they received vestibular rehabilitation, instead of multisensory exercises, as the major therapy.

3.4 Strengths and Limitations

The present systematic review was performed according to the PRISMA statement^[26]. This study had some limitations. We conducted analysis in terms of study type, intervention time and the underlying etiology of balance disorders, but gave up meta-analysis due to limited number of articles retrieved and substantial heterogeneity. Despite the comprehensiveness of our search, there is always a possibility that in a systematic review, we may have failed to uncover all available literature. Readers should also be aware that we have only included the strongest available evidence based on our critical appraisal of existing studies. Due to limited information about diseases of participants, we didn't conduct analysis on the basis of disease severity. Readers are further cautioned that the findings of studies included in this review reflect the effectiveness of outcome measures for balance and caution should be taken when attempting to generalize to those of other factors

To sum up, the findings of studies included in this review combined with knowledge of existing literature suggest that multisensory exercises may be a promising avenue for future research in terms of developing and evaluating interventions that target multisensory integration in balance disorder. We confirmed that the multisensory exercises were effective in improving balance in people with balance disorders. Multisensory

exercises could lower the risk of fall and enhance confidence level so as to improve the quality of life. Our results provided a new basis for the design of future training programs aimed to improve balance. Further research is needed to investigate the optimal strategy of multisensory exercises and explore the underlying neural and molecular mechanisms of balance improvement brought by multisensory exercises.

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Conflict of Interest Statement

All authors declare no conflicts of interest.

Author Su-ling ZHANG is a young member of the Editorial Board for Current Medical Science. The paper was handled by the other editor and has undergone rigorous peer review process. Author Su-ling ZHANG was not involved in the journal's review of, or decisions related to, this manuscript.

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