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REVIEW **Open Access**

Simulating space walking: a systematic review on anti-gravity technology in neurorehabilitation

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Abstract
Neurological disorders, such as Parkinson's disease (PD), multiple sclerosis (MS), cerebral palsy (CP) and stroke are well-known causes of gait and balance alterations. Innovative devices (i.e., robotics) are often used to promote motor recovery. As an alternative, anti-gravity treadmills, which were developed by NASA, allow early mobilization, walking with less effort to reduce gait energy costs and fatigue. A systematic search, according to PRISMA guidelines, was conducted for all peer-reviewed articles published from January 2010 through September 2023, using the following databases: PubMed, Scopus, PEDro and IEEE Xplore. After an accurate screening, we selected only 16 articles (e.g., 5 RCTs, 2 clinical trials, 7 pilot studies, 1 prospective study and 1 exploratory study). The evidence collected in this systematic review reported promising results in the field of anti-gravity technology for neurological patients, in terms of improvement in gait and balance outcomes. However, we are not able to provide any clinical recommendation about the dose and parameters of anti-gravity treadmill training, because of the lack of robust high-quality RCT studies and large samples.

Registration number CRD42023459665.

Keywords Anti-gravity technology, Anti-gravity treadmill, Neurological disorders, Neurorehabilitation

Introduction

Neurological disorders, such as Parkinson's disease (PD), multiple sclerosis (MS), cerebral palsy (CP) and stroke are well-known causes of gait and balance alterations [1]. Reduced mobility owing to neurological disorders is associated with multiple consequences on cardio-vascular and muscle-skeletal systems, limiting activities of daily living and patients' quality of life. In this context, innovative devices (i.e., robotics) are exploited in the neurorehabilitation field [2, 3]. In fact, robotic devices (such as exoskeletons and end-effectors) facilitate walking functions, even in patients with severe motor deficits due to brain damage [4]. However, these systems can limit joints movement due to the constraint of the robotic orthosis and may not allow normal gait patterns. As an alternative, NASA researchers have developed a new technology that mimics antigravity and uses differential air pressure to train astronauts to counteract muscle and bone loss. This technology consists of anti-gravity treadmills (A-GT), in which the lower half of the subject is surrounded by an air-tight, enclosed inflatable bag [5]. When the air compressor reaches the pressure

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in the chamber above atmospheric pressure, it creates an axial buoyant force, allowing gait training. Specifically, the air is released after the subject's weight calibration and the calibrated weight is used as a reference for selected unweighting during exercise [5]. In addition, the anti-gravity treadmills can be used by participants of all heights, thanks to vertical frame height adjustment. The body weight support system can sustain 80% of a person's body weight and can be adjusted progressively [6]. The safety and feasibility of A-GT was already investigated in healthy subjects, as well as in orthopaedics, post-surgical patients, and in neurological disorders [5, 7, 8]. The potential benefits of using A-GT in a neurorehabilitation context include early mobilization, walking with less effort to reduce gait energy costs and fatigue, decreasing the harmful impact on injured joints and maintain cardiorespiratory fitness [8]. One of the most used A-GTs in neurorehabilitation is the Alter G (AlterG Sports, AlterG Inc., California, USA). This helps to maintain normal muscle activation and gait patterns [9]. Thus, the use of A-GT could be an adjunctive rehabilitation treatment in those neurological patients who may manifest moderate motor deficits, allowing long-lasting aerobic training to promote neuroplastic processes. It is noteworthy that the use of A-GT could particularly involve vestibular pathways, reinforcing sensory and proprioceptive feedback, thus activating cortical areas (e.g., primary somatosensory cortex, motor cortex, insula, parietal and occipital lobes and frontal areas) [10]. In addition, aerobic exercise is a well-known way to improve neuroplasticity, as it promotes the release of neurotrophic factors like brain-derived neurotrophic factor (BDNF) [11]. However, it is still unclear whether A-GT could be beneficial and/or effective as an adjunctive innovative treatment in neurological patients. The main objective of this systematic review is to investigate the literature about the effects and potential benefits of A-GT training in neurological disorders, including PD, SM, CP, and stroke. These conditions collectively represent a significant proportion of neurological disorders worldwide and are associated with substantial gait impairment that is not easy to manage with conventional physiotherapy alone.

Methods

The protocol of this systematic review was registered on PROSPERO (https://www.crd.york.ac.uk/prospero) with the registration number CRD42023459665, following the Preferred Reporting Items for Systematic and Meta-analyses (PRISMA) [12]. Our research is aimed to explore the existing evidence on the effects and potential benefits of anti-gravity technologies in the context of neurorehabilitation.

PICO model

Search terms were defined according to PICO model (Population, Intervention, Comparison, Outcome) [13]. The population included patients affected by neurological disorders, such as stroke, PD, CP and MS; intervention included all anti-gravity existing technologies in the field of neurorehabilitation; the comparison included sham or placebo treatments, and/or conventional physiotherapy conducted in the control group, allowing for a comparative analysis of the effects of the active interventions. However, considering the limited literature available, we included multiple study designs for qualitative synthesis, such as non-controlled/randomised studies; and outcomes included any motor improvements shown by the patients and efficacy of treatment.

Search strategy and eligibility criteria

A systematic search, according to PRISMA guidelines [12] (see Supplementary material for PRISMA checklist), was conducted for all peer-reviewed articles published from January 2010 through September 2023, in order to search for the most recent literature. We chose to include articles from 2010 because of the growing interest in technology in neurorehabilitation. Our research was conducted on the following databases: PubMed, Embase, Cochrane Database, PEDro, Web of Science and IEEE Xplore. The following terms were used: ("neurological disorders") OR ("stroke") OR ("Parkinson's disease") OR ("multiple sclerosis") OR ("cerebral palsy) AND ("anti-gravity technology") OR ("anti-gravity treadmill") OR ("Alter G").

All articles were reviewed based on titles and abstracts by two investigators (M.B and R.S.C), who independently performed data collection to reduce the risk of bias (i.e., the bias of missing results). These researchers read the full-text articles deemed suitable for the study and in case of disagreement on the inclusion and exclusion criteria, the final decision was made by a third researcher (M.G.M). The inclusion criteria were: (1) patients with neurological disorders due to central nervous system impairment, including stroke, Parkinson's disease, multiple sclerosis, and cerebral palsy, since they collectively represent a significant proportion of neurological conditions worldwide and are associated with substantial gait impairment that it is not easy to manage only with conventional physiotherapy; (2) an applied approach to motor rehabilitation; (3) written in English; and (4) published in a peer-reviewed journal. We have excluded articles describing theoretical models, methodological approaches, algorithms, and basic technical descriptions. Additionally, we excluded: (1) animal studies; (2 conference proceedings or reviews; and (3) studies involving children affected by neurological disorders other than CP; (4) studies involving other neurological disorders that do not involve the central nervous system; (5) case reports and reviews. Our search strategy included some filters such as temporal range between 2010 and 2023. The searches were limited to the title and abstract in this phase. Additionally, we considered the reference lists of included papers for the screening to identify additional relevant papers not found by the search strategy. The list of articles was then refined for relevance, revised, and summarized, with the key topics identified from the summary based on the inclusion/exclusion criteria.

Data extraction and analysis

After full-text selection, the data extraction from the included studies was summarized in a table (Microsoft Excel – Version 2021). Data summarized were considered for the following information: assigned ID number, title of study, year of publication or presentation and first author, study aims and design, study duration, method and setting of recruitment, inclusion/exclusion criteria, use of a control group, use of devices, informed consent, conflict of interest and funding, type of intervention and control, number of participants, characteristics at the baseline, setting of intervention, type of outcome and time-points for assessment, adverse events, results and key conclusions. In addition, the agreement between the two reviewers (MB and MGM) was calculated through the kappa's score [14]. The kappa score, which establishes a threshold for substantial agreement at >0.81, was interpreted as reflecting excellent concordance between the reviewers. This criterion ensures a robust evaluation of inter-rater reliability, emphasizing the achievement of a substantial level of agreement in the data extraction process.

Data quality assessment

The quality of each article was rated by the two reviewers (MB and MGM) using a revised Cochrane risk of bias (RoB 2) [15] for 5 RCT studies [17–21]. RoB-2 consists of five domains: (i) bias arising from the randomization process, (ii) bias due to deviations from intended intervention, (iii) bias due to missing outcome data, (iv) bias in the measurement of the outcome, (v) bias in the selection of the reported result.

Moreover, we used ROBINS-I [16] for the other non-randomized studies [22–32]. ROBINS-I is a method used to assess the risk of bias in non-randomized research. This assessment tool considers seven domains of potential sources of bias: (i) bias due to unknown or uncontrolled confounding factors; (ii) bias due to selection of participants, (iii) bias due to classification of interventions, iii) bias due to measurement of variables, (iv) bias due to deviation from intended intervention; (v) bias due to missing data; iv) bias due to selection of measurement outcome; (vi) bias due to selection of reported results.

Synthesis of evidence

Our initial research revealed 240 results, then we excluded 120 articles due to eligibility criteria that were not fully respected. Finally, we removed duplicates and we included and analysed 16 articles dealing with A-GT in neurological disorders (see Fig. 1).

In details, we found 5 RCTs [17–21], 2 clinical trials [22, 23], 7 pilot studies [26–32], 1 prospective study [24] and 1 exploratory study [25]. Study populations of the included evidence range between 6 (the minimum) and 50 (the maximum) subjects affected by different neurological disorders. With regard to aetiology, we found: 5 articles (2 clinical trials and 3 pilot studies) about PD patients [22, 23, 26–28]; 1 pilot study on multiple sclerosis [29]; 7 articles on stroke patients [17–21, 24, 25], (5 RCTs, 1 exploratory study and 1 prospective study); 3 pilot studies [30–32] on children affected by CP (see Table 1).

Quality of the studies and risk of bias

We found a great heterogeneity among the included studies that could influence the interpretation of results. Firstly, our research identified various study design, such as RCTs [17–21], clinical trials [22, 23], and pilot studies [26–32]. Most of the studies did not specify randomization procedures or blinding of raters, due to their methodology (e.g., pilot, exploratory, and prospective studies). Indeed, seven studies [22, 23, 26] did not include controls in their study design, which affected the assessment of A-GT intervention effects. Secondly, outcome measures varied among studies; some authors administered clinical tests/scales, including Unified Parkinson's Disease Rating Scale (UPDRS) [26], Berg Balance Scale (BBS) [18, 19, 21], Tinetti POMA (Performance Oriented Mobility Assessment) [17, 18, 27], Balance evaluation systema test (BESTest) [32], 6-Minutes Walking Test (6MWT) [20–21,25,28], Functional Ambulation Classification (FAC) [17, 20, 24, 25], Timed Up and Go (TUG) [18, 19, 26, 28], 10-Metres Walking Test (10MWT) [18,2528] to assess both gait and balance functions. Only a few studies performed specific assessment procedures such as gait analysis [20, 30–32], electromyography (EMG) [22], near-infrared spectroscopy (NIRS) [29]. In addition, we found substantial variability in training protocols and settings of the selected studies, with even 3 studies [19–21] not explicitly describing the training protocol used. Most authors administered AG-T training alone [17–19, 21–32], apart from Sukonthamarn et al. [20], who combined conventional physiotherapy with A-GT. Lastly, the analysed papers reported a variable number of participants most of whom were in small sample sizes [24, 25, 28–30, 32]. Furthermore, we performed a risk of bias assessment via RoB 2 [15] in 5 RCTs [17–21]. The included studies showed good overall quality, except in one study

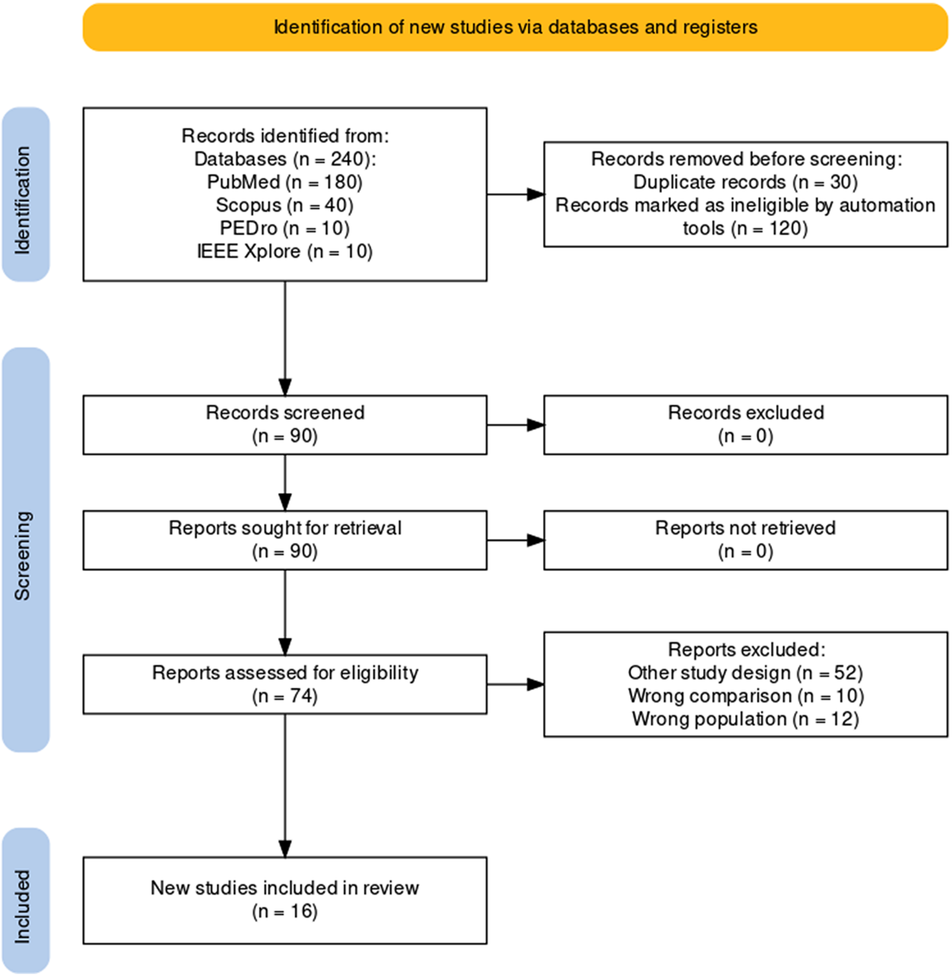


Fig. 1 PRISMA flow diagram

[19] where the result was “some concerns” following lack of blinding (domain 2). Otherwise, a low risk emerged, particularly in domains 1, 4, and 5 across all studies (see Fig. 2).

Risk of bias for the remaining eleven non-RCTs [22–32] was performed by using ROBINS-I [16], as reported in Fig. 3. We noticed that most of the included studies reported a moderate risk of bias, especially in the domains 2 [22, 23, 27, 28, 30, 32],4 [23–29, 32], 5 [22–25, 27–29, 31, 32], and 7 [22–29, 32]. In the majority of the studies, inclusion/exclusion criteria of the participants were not fully reported, or they were not explained clearly. In addition, the participants in the included studies reported low adherence to the treatment, even if adverse events were not reported. With regard to domains 5 and 7, we noticed that some concerns were present related to participants missing data, and to multiple analyses with small samples that can increase the overall risk of bias (see Fig. 4).

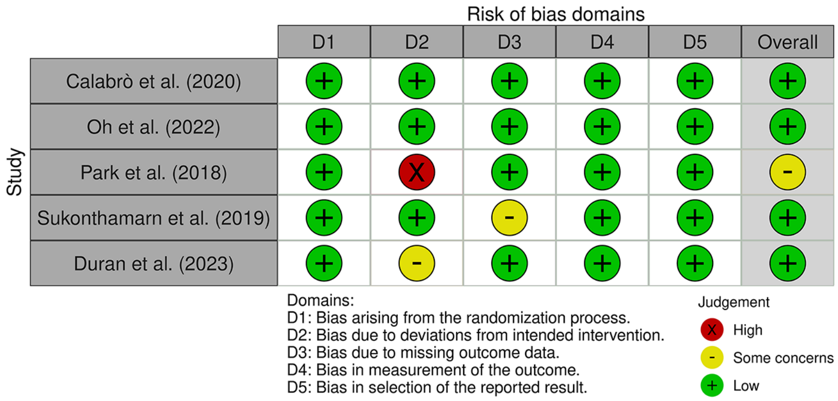
Description of intervention

All studies included in this systematic review administered A-GT training, comparing it with conventional treadmill, aquatic treadmill and/or conventional gait training/exercises. The A-GT training lasted from 20 to 60 min per session in each study, considering patients’ tolerance. Some authors [24, 25, 29] also performed a 20 to 30 min warm-up before A-GT session in order to prepare patients for further aerobic effort. The training periods reported by the authors ranged between 4 and 8 weeks, although Rigby et al. [27] performed the longest training period which lasted for 24 weeks. In general, the anti-gravity support during training was estimated with patients’ body weight, and it was slowly increased according to patients’ needs [17, 18, 23–28, 30–32]. However, there is a substantial heterogeneity of A-GT training protocols among the selected studies, as reported in Table 2. For example, Malling et al. [23] performed a specific training protocol in three blocks: motor, aerobic and mixed, using the A-GT. Furthermore, we found other differences among the included articles related to the %

Table 1 Description of study design, sample size and aetiology of neurological disorders

Reference	Year of publication	Study design	Neurological disorder	Sample size
Calabrò et al. [17]	2020	RCT	Stroke	50 with supra-tentorial ischaemic stroke compared to 25 healthy controls
Oh et al. [18]	2022	RCT	Stroke	30 patients with stroke
Park et al. [19]	2018	RCT	Stroke	27 patients with stroke
Sukonthamarn et al. [20]	2019	RCT	Stroke	31 subjects with stroke
Duran et al. [21]	2023	RCT	Stroke	39 subjects with stroke
Rose et al. [22]	2013	Clinical trial	PD	13 PD patients compared to 8 healthy controls
Malling et al. [23]	2016	Clinical trial	PD	13 PD patients compared to 17 healthy controls
Almutairi et al. [24]	2023	Exploratory study	Stroke	9 subjects (1 female and 8 males) affected by stroke
Almutairi et al. [25]	2023	Prospective study	Stroke	9 subjects (1 female and 8 males) affected by stroke
Baizabal-Carvallo et al. [26]	2020	Pilot study	PD	19
Rigby et al. [27]	2019	Pilot study	PD	10
Byl et al. [28]	2015	Pilot study	PD	12 PD patients randomly assigned to two treadmills
Willingham et al. [29]	2019	Pilot study	MS	6 adults with MS
El-Shamy et al. [30]	2017	Pilot study	CP	13 children with diplegic CP
Aras et al. [31]	2019	Pilot study	CP	29 children with spastic CP
Kurz et al. [32]	2011	Pilot study	CP	9 children with CP (one child with hemiplegic involvement and 8 with diplegic CP)

Legend: PD (Parkinson's disease), MS (Multiple Sclerosis), CP (Cerebral Palsy)



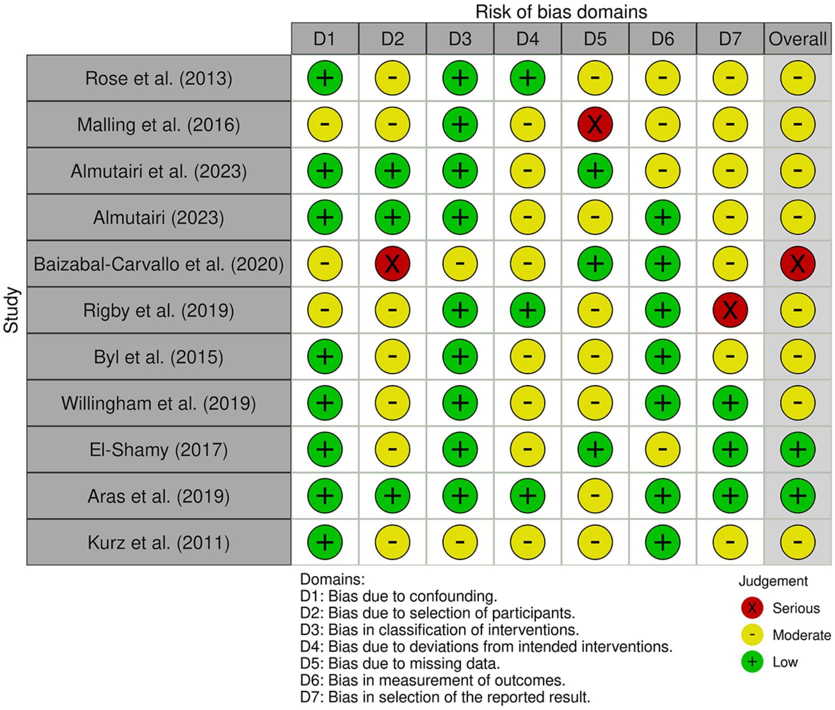
Risk of bias domains

Study	D1	D2	D3	D4	D5	Overall
Calabrò et al. (2020)	+	+	+	+	+	+
Oh et al. (2022)	+	+	+	+	+	+
Park et al. (2018)	+	X	+	+	+	-
Sukonthamarn et al. (2019)	+	+	-	+	+	+
Duran et al. (2023)	+	-	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
X High
- Some concerns
+ Low

Fig. 2 RoB 2 assessment of the 5 RCT studies



Risk of bias domains

Study	D1	D2	D3	D4	D5	D6	D7	Overall
Rose et al. (2013)	+	-	+	+	-	-	-	-
Malling et al. (2016)	-	-	+	-	X	-	-	-
Almutairi et al. (2023)	+	+	+	-	+	-	-	-
Almutairi (2023)	+	+	+	-	-	+	-	-
Baizabal-Carvallo et al. (2020)	-	X	-	-	+	+	-	X
Rigby et al. (2019)	-	-	+	+	-	+	X	-
Byl et al. (2015)	+	-	+	-	-	+	-	-
Willingham et al. (2019)	+	-	+	-	-	+	+	-
El-Shamy (2017)	+	-	+	-	+	-	+	+
Aras et al. (2019)	+	+	+	+	-	+	+	+
Kurz et al. (2011)	+	-	-	-	-	+	-	-

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
- Moderate
+ Low

Fig. 3 ROBINS-I assessment of the eleven non-RCTs studies

of unloading body weight support. Most of the authors [24–28] considered 50% of body weight unloading, which was gradually adjusted, according to the patients' needs. Specifically, Almutairi et al. [24, 25] performed a training protocol starting from 50% of unloading, which was gradually decreased by 2% in each session. In contrast, Oh et al. [18], considered an initial 30% of overload, which was gradually increased to 80% of the patient's body weight.

Effects of intervention

All the included studies [17–32] investigated the role of the A-GT in improving endurance, balance and gait functions. Authors administered A-GT training using the AlterG (Inc., California, USA) for the experimental procedures. In the control groups, six studies used conventional physiotherapy [17–21, 24, 25, 30], while three studies used gait training with other types of land and/or aquatic treadmills [27, 28, 31]. However, seven studies [22–26, 29, 32] out of the 16 [17–32], did not include a control group in their study design. The outcome measures included were mainly oriented towards measuring gait [17–22, 26–32] and balance [18, 21, 23, 24, 27, 28] functions, whereas cardiovascular function (e.g., heart rate, blood pressure and oxygen saturation) was assessed in three studies [21, 24, 28]. Additionally, Willingham et al. [29] evaluated muscle oxidative metabolism and endurance through NIRS and mechanomyography in people affected by MS. Another study [22] tested force and EMG signals in the lower limbs of PD patients, during A-GT training, whereas gait analysis was performed only by Sukonthamarn et al. [20] and Aras et al. [31] (see Table 3).

Legend: TUG (Timed UP and Go), UPDRS-III (Unified Parkinson's Disease Rating Scale), Tinetti POMA (Performance Oriented Mobility Assessment), 10MWT (10-Metres Walking Test), 6-MWT (6-Minutes Walking Test), FAC (Functional Ambulation Classification), TS (Tinetti Scale), HR (Heart rate), BBS (Berg Balance scale), MMSE (Mini-mental status examination), RATE (Robotic assisted treadmill exercise), ATE (Antigravity treadmill exercise), BESTest (Balance evaluation system test), NIRS (Near-infrared spectroscopy).

Moreover, the effects of A-GT training included improvements in global mobility, freezing of gait (FoG) [26, 28], balance [23, 28] and gait functions [22] in patients with PD. Willingham et al. [29], reported promising results on endurance and muscle oxidative state in individuals affected with moderate to severe MS. In post-stroke patients, authors reported improvements in gait speed, endurance [19, 24, 25], balance and walking functions [19, 20] and cardio-respiratory fitness [21]. However, balance functions measured with POMA score was less statistically significant than POMA gait score, as showed by Oh et al. [26]. In post-stroke patients, specific improvements in lower limb muscle activation were also achieved after A-GT, as demonstrated by Calabrò et al. [17]. The EMG data, analysed as root mean squares, showed that the activity levels of the gastrocnemius and

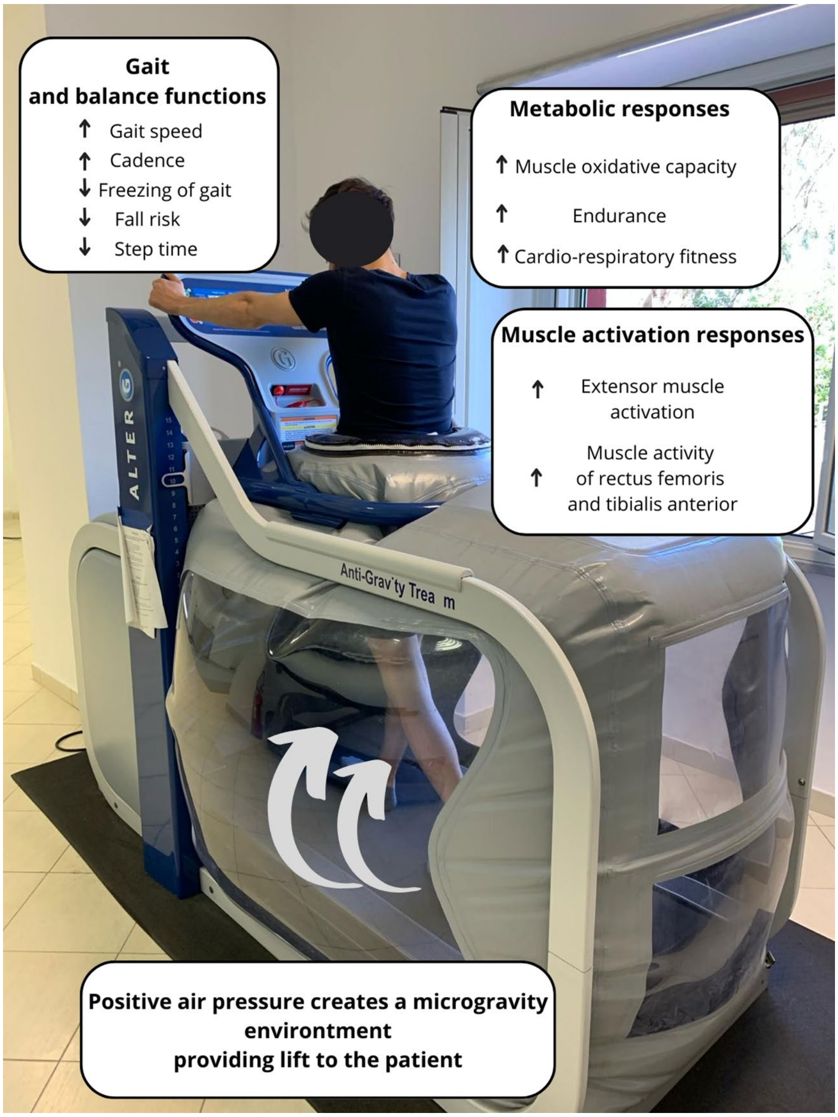


Fig. 4 ROBINS-I assessment of the eleven non-RCTs studies

rectus femoris muscles decreased during the early and mid-swing phases of the gait cycle, specifically at 50%, 60%, and 70% of the cycle. In contrast, the activity of the tibialis anterior on the unaffected side increased during the preparation for heel strike, at 100% of the gait cycle. [17]. Positive results were also documented in CP patients, especially for balance, gait and risk of falling [30–32]. (see Fig. 3).

Discussion

To the best of our knowledge, this is one of the few systematic reviews [8, 33] investigating the effects of A-GT training in patients affected by neurological disorders. We have found that few articles dealt with this topic and most of them present high risk of bias [22–29, 32] making interpretation and generalization of results difficult. In particular, the novelty of our systematic review is the investigation of literature about the clinical effects of using anti-gravity technology in the neurorehabilitation context. Other authors have previously addressed our topic in different patient populations, such as paediatric [8] and orthopaedic (i.e., lower limb surgery and athletes' injuries) [5–7]. Recently, a systematic review [33] highlighted the lack of larger RCTs and standardized training protocols using lower body positive pressure treadmills like Alter-G in neurological patients.

However, the authors did not include any articles about CP patients and did not perform a quality assessment or a risk of bias analysis for the included studies. These limitations should be considered when interpreting the results. In addition, Almutairi [33] considered also case reports in his analysis, which we excluded a priori due to their scarce scientific reproducibility. Moreover, we reported some clinical implications of using Alter-G in

Table 2 Description of anti-gravity treadmill training parameters and settings

Reference	Training parameters	Anti-gravity treadmill setting
Calabrò et al. [17]	One session a day of Alter-G (for 40 min), six days a week, for four weeks (for a total amount of 24 sessions).	BWS, physiotherapist assistance, and treadmill speed (TS) were checked and adapted to subjects' progress in terms of FAC scoring across the AlterG sessions
Oh et al. [18]	20 min a day, five times a week for 4 weeks	The initial overload was set to 30% of the body weight and then increased gradually. AGT was gradually increased to 80% of the patient's body weight.
Park et al. [19]	30 min, with 3 sessions per week for 4 weeks	NA
Sukonthamarn et al. [20]	30 min per day, five times per week	NA
Duran et al. [21]	30 min per day for three times a week for 4 weeks.	NA
Rose et al. [22]	three 1-h training sessions/week for 8 weeks	Patients started with 20% to arrive at 80% of anti-gravity support.
Malling et al. [23]	8-week control period followed by 8 weeks of motor intensive antigravity training	Authors administered three exercise modes: 1) Motor block: consisting of walking/running with 20–100% of body weight support changing inclination (0°-15°). 2) Aerobic block: 5–10 min of walking/running with 50% of anti-gravity support, considering the 70–80% of the estimated heart rate capacity. 3) Mixed block: performing 2 min intervals of walking at 3 km/h at 100, 80, 60, 40 and 20% BW and followed by running at 8 km/h at 20, 40, 60, 80 and 100% BW.
Almutairi et al. [24]	40 min for three times a week for six weeks	The first session on the A-GT chamber was set to unload 50% of the participant's body weight. The percentage of the unload decreased gradually by approximately 2% per session in the following sessions.
Almutairi et al. [25]	40 min, per three days a week for six weeks.	The first session on the A-GT chamber was set to unload 50% of the participant's body weight. The percentage of the unload decreased gradually by approximately 2% per session in the following sessions.
Baizabal-Carvallo et al. [26]	A-GT training biweekly for 4 weeks. Each session lasted 60 min according to patients' tolerance.	All patients underwent automatic weight estimation by A-GT, followed by a programmed body-weight reduction of 50% in all sessions. The treadmill velocity was adapted on the individual tolerance during each session, but all patients were able to tolerate progressively faster velocities and training time.
Rigby et al. [27]	four weeks, twice per week for 20 weeks	The A-GT was unloaded to 50% of the participant's body weight during all stages of exercise. Authors considered a small, 3% error difference between the predicted weight and measured weight on an A-GT at 50% of weight loading.
Byl et al. [28]	5 days, 40 min/session for 5 weeks	Each participant was un-weighted to approximately 50–60% of their body weight.
Willingham et al. [29]	40 min approximately twice per week for approximately 8 weeks (16 sessions total)	Anti-gravity support (35–70%) and treadmill speed (0.2–2.5 mph) were adjusted throughout the training program to maintain effort without exceeding a rating perceived exertion of 8.0.
El-Shamy et al. [30]	20 min/d, 3 d/wk	The treadmill was set at zero-degree inclination. Treadmill speed was set to 75% for patients' comfortable speed during over-ground walking. Verbal commands were given to the children to maintain upright posture.
Aras et al. [31]	20 treadmill exercise sessions for 45 min for five days a week for a total of four weeks	Anti-gravity support started at 60% and gradually decreased to a level that prevented the collapse of the knee in flexion during the stance phase. The treadmill speed was initiated at the average walking speed according to the child's walking pattern, weigh and endurance, then increased to the highest level tolerated.
Kurz et al. [32]	2 days per week for 6 weeks	Anti-gravity was set to 40% of body weight and gradually reduced to 10% by the end of the intervention. The speed of the treadmill was initially set at 90% of the child's over-ground walking speed and gradually increased.

both acquired brain injury (i.e., stroke and cerebral palsy) and neurodegenerative disorders (i.e., PD and MS).

Acquired brain injury

In this paragraph, we discuss our findings related to acquired brain injury, including post-stroke and CP patients. Balance and gait disorders are the most common deficits in patients affected by neurological disorders and the prognosis to regain ambulatory functions depends on the underlying pathology and its severity [34]. Generally, robotic device like end-effectors and exoskeletons are often used in rehabilitation after neurological damage, including stroke and CP [35]. According to Calabrò et al. [36], the use of robotic gait training in post-stroke patients increases the possibility of regaining an independent gait, and this should be considered as either "add on" treatment or even in substitution of the traditional rehabilitation. Otherwise, the treadmill

Table 3 Description of the reported interventions, outcomes and major findings

Reference	Neurological disorder	Intervention		Outcomes	Major findings
		EG	**CG**		
Calabrò et al. [17]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA)	Conventional gait training	FAC, TS,	Alter G gait training was superior to conventional gait training in modifying the temporal variables of gait and specific muscular activation patterns.
Oh et al. [18]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA)	Conventional gait training	Barthel Index, POMA, BBS, TUG, 10-MWT, MMSE	A-GT enhances dynamic balance and gait speed and effectively lowers fall risk in stroke patients.
Park et al. [19]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA) and Aquatic treadmill	Conventional treadmill	BBS, 10MWT, and TUG	aquatic treadmill and A-GT improved balance and gait abilities in stroke patients.
Sukonthamarn et al. [20]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA) combined with conventional physiotherapy	Conventional gait training	Gait analysis, 6-MWT, FAC	A-GT combined with conventional physiotherapy was superior to the control group in balance training.
Duran et al. [21]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA) or aquatic treadmill	Conventional gait training	6-MWT, BBS, cycle ergometer test	A-GT training has favourable effects on cardiorespiratory fitness in stroke survivors.
Rose et al. [22]	PD	Alter-G (AlterG Sports, AlterG Inc., California, USA)	NA	Force and electromyographic signals	Increased body weight support normalized extensor muscle activation abnormalities in PD patients.
Malling et al. [23]	PD	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	five repetition sit-to-stand test and a dynamic postural balance test	PD patients improved motor performance during balance related tasks.
Almutairi et al. [24]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	HR, blood pressure and oxygen saturation, FAC	The study showed that the A-GT was safe and feasible to use with chronic stroke.
Almutairi [25]	Stroke	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	6-MWT, 10MWT, FAC	Six weeks of A-GT gait training may potentially improve ambulation ability, gait speed, and walking endurance in individuals with chronic stroke.
Baizabal-Carvallo JF et al. [26]	PD	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	TUG, UPDRS-III	PD patients improved global mobility and freezing of gait.
Rigby et al. [27]	PD	Alter G (AlterG Sports, AlterG Inc., California, USA)	land TM, Acquatic TM	POMA. Purdue Pegboard Test and postural sway using the Limits of Stability Test	Aerobic exercise training on various treadmills had little effect on functional measures in adults with Parkinson's disease
Byl et al. [28]	PD	Alter G (Alter G Sports, AlterG Inc., California, USA)	GlideTrak treadmill	Heart rate, 10MWT, 6-MWT, Five Times Sit to Stand (FTSTS) and TUG	PD patients with mild to moderate symptoms improved mobility, balance and resilience without exacerbating pain, freezing or tremors
Willingham et al. [29]	SM	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	muscle oxidative capacity of medial gastrocnemius with NIRS, muscle endurance with mechanomyography during 9 min of twitch electrical stimulation in three stages (3 min per stage) of increasing frequency (2, 4, and 6 Hz) and 2-min walking test. Muscle strength (plantarflexion). Timed 25-foot walk test	A-GT improved only muscle oxidative capacity and endurance in people with MS who have moderate-to-severe levels of disability.

Table 3 (continued)

Reference	Neuro-logical disorder	Intervention		Outcomes	Major findings
		EG	CG		
El-Shamy et al. [30]	CP	Alter G (AlterG Sports, AlterG Inc., California, USA)	Conventional physiotherapy	Gait parameters (i.e., velocity, stride length, cadence, and percent of time spent in double-limb support), postural stability, and fall risk.	A-GT treadmill training may be a useful tool for improving gait parameters, balance, and fall risk in children with diplegic cerebral palsy.
Aras et al. [31]	CP	Alter G (AlterG Sports, AlterG Inc., California, USA)	partial body weight-supported treadmill exercise (PBW-STE), robotic-assisted treadmill exercise	three-dimensional gait analysis, open-circle indirect calorimeter, six-minute walking test, and Gross Motor Functional Measurement (GMFM)	Our study findings indicate that all three treadmill exercises have a positive impact on walking, and RATE and A-GT can be used more actively in patients with spastic CP.
Kurz et al. [32]	CP	Alter G (AlterG Sports, AlterG Inc., California, USA)	NA	walking speed, spatiotemporal kinematics, lower extremity strength, and the BESTest	A-GT treadmill training resulted in significantly faster walking speed, less time in double support, improved overall balance, and strength of the lower extremity anti-gravity musculature

Legend TUG (Timed UP and Go), UPDRS-III (Unified Parkinson's Disease Rating Scale), Tinetti POMA (Performance Oriented Mobility Assessment), 10MWT (10-Metres Walking Test), 6-MWT (6-Minutes Walking Test), FAC (Functional Ambulation Classification), TS (Tinetti Scale), HR (Heart rate), BBS (Berg Balance scale), MMSE (Mini-mental status examination), RATE (Robotic assisted treadmill exercise), ATE (Antigravity treadmill exercise), BESTest (Balance evaluation systema test)

training in post-stroke patients appeared to be less effective in improving gait distance and balance when compared with overground gait training, as suggested by Gelaw et al. [37]. Moreover, Bonanno et al. [38], investigated the effects of robotic gait training on walk and balance functions in CP. The authors found that CP children with more severe disability may benefit from exoskeletons (since they have better joint and trunk control), whereas less impaired CP children may be trained with end-effectors and VR devices (as they require spared motor function). As an alternative, the A-GT, like Alter-G, allows a body weight supported gait, thus maintaining normal gait patterns [39]. In this sense, the Alter-G mostly improved temporal parameters of gait, such as gait speed in both post-stroke [18, 25] and CP patients [30, 32]. Hence, Calabrò et al. [17] demonstrated that the A-GT training in post-stroke patients shaped biceps femoris and rectus femoris bilaterally, which are essential muscles in opposing gravity force. Notably, the activation of rectus femoris allows propulsive forces during stance phase and this may lead the improvements in temporal-spatial variables of gait [40, 41]. Furthermore, as suggested by some authors [42] the A-GT could improve neuroplastic processes in the brain stem and cerebellar white matter after the training. In fact, these brain areas are fundamental in postural control and motor learning. Specifically, the cerebellum plays a role in modulating the step cycle to adjust step patterns, whereas the basal ganglia and the frontal cortex are involved in regulating gait during rapid changes in environmental conditions [43]. Azizi et al. [10] showed that A-GT training may lead to improvement in neurophysiological (motor evoked potentials-MEPs) and neuroimaging (diffusion tension imaging-DTI) indices of the corticospinal and vestibulospinal tracts in CP children. The idea is that the Alter-G, through a micro-gravity environment, could boost high myelination, improving balance and gait abilities [8–10, 44]. However, the investigation of brain activation related to weight-supported walking remains a challenging question.

Neurodegenerative disorders

Neurodegenerative disorders, like PD and MS, can cause progressive neuronal loss that consequently worsens postural control and gait ability over time [45]. Generally, conventional rehabilitation approaches include aerobic treadmill training, core exercises to improve balance reactions and postural stability, and hydrotherapy to reduce muscle stiffness and improve gait function [46]. Moreover, combined physiotherapy exercise training (including aerobic, resistance, and balance training) has shown beneficial effects not only for balance, muscle strength, gait recovery, and endurance, but also for slowing the progression of motor impairments [47]. In our systematic review, we noticed that literature about the use of A-GT in PD patients mostly improved global motor functions, reducing tremors, and freezing of gait. In addition, the A-GT training could improve kinematic factors of lower limbs, as suggested by Rose et al. [22]. The authors found that an eight-weeks A-GT training in patients affected by PD can normalize the extensor muscle activation during weight-supported gait. In line with these assumptions, Malaya et al. [9] showed that healthy subjects performing Alter-G training showed EMG elicited responses in the medial gastrocnemius as well as in the rectus femoris, which are both involved in the lower limb extension during gait. Furthermore, Berra et al. [48] compared the effects of treadmill training plus body weight support system with overground gait training. They found that the reduced body loading during gait training was effective in improving global motor skills and functioning, measured with UPDRS. However, they suggested that both types of gait training can be considered effective at inducing improvements in kinematic gait parameters. Moreover, A-GT seems to have a role in inducing muscle metabolic and plastic changes, as suggested by Willingham et al. [29]. In fact, the authors found that A-GT in MS patients improved muscle oxidative capacity through the activation of biochemical pathways, which are required for mitochondrial biogenesis. It is noteworthy that the study of Willingham et al. [29] is the only one which investigated the effects of A-GT in patients with MS. However, recent studies conducted with MS patients, using a treadmill, robotic devices, and partial body weight support systems, demonstrated the effectiveness of such training on in improving gait functions and global mobility [49, 50]. Lastly, the aerobic exercise is a well-known neuroplastic promoter [51]. Recent evidence suggests a strict relationship between cardiovascular performance and brain plasticity. It seems that intensive aerobic training is related to increased volume in hippocampus and basal ganglia which are involved in the control of motor behaviour [52, 53]. Altogether, these issues may explain the promising results of the selected studies in improving gait parameters and related functions.

Implications for clinical practice and future perspectives

To summarise, although both acquired brain injuries and neurodegenerative diseases can lead to motor impairment, the mechanisms of injury, disease progression, and motor recovery strategies can be very different. The potential benefits of AlterG have been studied primarily in acquired brain injury (i.e., post-stroke and CP) and in PD, a neurodegenerative disorder [17–28, 30–32]. From a clinical perspective, both post-stroke and CP patients achieved better outcomes in temporal parameters of gait (i.e. walking speed and cadence) and cardiovascular function [17–21, 24, 25, 30–32]. In this sense, AlterG may provide a safe and controlled environment to practise walking, which could explain the improvements in gait speed and cardiac fitness. Similarly, AlterG has shown potential benefits in gait function in CP children, likely due to the reduction in gravity that allows these children to practise walking with less effort [30–32]. On the other hand, improvements in global mobility (UPDRS), fall risk (TUG and POMA), freezing of gait and tremor have been obtained in PD patients [22, 23, 26–28]. These outcomes fundamentally differ from those observed in individuals with acquired brain injury, owing to the distinct pattern of neurological impairment. Despite these evident differences, both neurodegenerative conditions and acquired brain injuries exhibit the potential for enhancing overall walking functionality through the implementation of A-GT. Nonetheless, critical inquiries persist concerning the scarcity of RCTs with larger participant cohorts. Specifically, elucidating the optimal disease stage for initiating such interventions and determining the appropriate treatment dosage would be advantageous. Furthermore, many investigations have predominantly focused on gait kinematics (i.e., spatial-temporal parameters), with limited attention paid to EMG analyses [17, 22], while kinetic data, including forces and joint range of motion, have been largely overlooked. Finally, elucidating the activation patterns of cerebral regions (functional brain connectivity) during AlterG treatment would provide valuable insights. Comparing these patterns with those observed in alternative body weight support systems would further enhance our understanding.

Limitations

This systematic review has some limitations that need to be acknowledged. One limitation is the absence of quantitative analysis. In particular, we found considerable heterogeneity among the included studies in terms of methodologies, outcome measures, and participant characteristics, thus conducting a quantitative analysis was not feasible. This limitation underscores the need for caution in generalising the findings and emphasizes the importance of interpreting the results within the context of individual study characteristics. The selected studies also presented other limitations, including small sample sizes, lack of control group and lack of long-term follow-up evaluations. Despite these limitations, our review relies primarily on qualitative synthesis, based on systematically summarizing and interpreting the findings of individual studies to elucidate common themes, patterns, and discrepancies across the literature. As a result, our review provided a comprehensive qualitative synthesis of the available evidence, offering valuable insights into the novel A-GT rehabilitation approach for specific neurological conditions (i.e., PD, MS, CP and stroke), identifying key implications for clinical practice and considerations for future investigation.

Conclusion

The evidence collected in this systematic review shows promising results in the field of anti-gravity technology for neurological patients. When used alone or in combination with other treatments, the device can lead to better gait and balance parameters than conventional physiotherapy alone. However, we are unable to provide specific clinical recommendations about the dose and parameters of A-GT training, because of the lack of robust RCT studies and large samples. Future studies with rigorous methodologies should focus on comparing to other non-harness body-weight support systems, in order to better understand the potential effects of anti-gravity technologies.

Supplementary Information

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Supplementary Material 1

Author contributions

Conceptualization, M.B.; methodology, M.B. and M.G.M; software, A.M.D.N. and M.B.; validation, all authors; formal analysis, M.B. and M.G.M; investigation, M.B; resources, R.S.C. and A.Q.; data curation, M.B. and M.G.M; writing—original draft preparation, M.B.; writing—review and editing, R.S.C.; visualization, all authors; supervision, R.S.C. and A.M.D.N.; project administration, R.S.C. and A.M.D.N.; funding acquisition, A.Q. All authors have read and agreed to the published version of the manuscript.

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Data availability

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Declarations

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Competing interests

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