Update on intensive motor training in spinocerebellar ataxia: time to move a step forward?

Giuseppe Lanza[1,2] (iD),
Jacopo Antonino Casabona[3], Maria Bellomo[3],
Mariagiovanna Cantone[4],
Francesco Fisicaro[5] (iD), Rita Bella[5],
Giovanni Pennisi[1], Placido Bramanti[6],
Manuela Pennisi[7] and Alessia Bramanti[6]

Abstract

Some evidence suggests that high-intensity motor training slows down the severity of spinocerebellar ataxia. However, whether all patients might benefit from these activities, and by which activity, and the underlying mechanisms remain unclear. We provide an update on the effect and limitations of different training programmes in patients with spinocerebellar ataxias. Overall, data converge of the finding that intensive training is still based either on conventional rehabilitation protocols or whole-body controlled videogames ("exergames"). Notwithstanding the limitations, short-term improvement is observed, which tends to be lost once the training is stopped. Exergames and virtual reality can ameliorate balance, coordination, and walking abilities, whereas the efficacy of adapted physical activity, gym, and postural exercises depends on the disease duration and severity. In conclusion, although a disease-modifying effect has not been demonstrated, constant, individually tailored, high-intensity motor training might be effective in patients with degenerative ataxia, even in those with severe disease. These approaches may enhance the remaining cerebellar circuitries or plastically induce compensatory networks. Further research is

[1]Department of Surgery and Medical-Surgical Specialties, University of Catania, Catania, Italy
[2]Department of Neurology IC, Oasi Research Institute – IRCCS, Troina, Italy
[3]School of Human and Social Science, University Kore of Enna, Enna, Italy
[4]Department of Neurology, Sant'Elia Hospital, ASP Caltanissetta, Caltanissetta, Italy
[5]Department of Medical and Surgical Sciences and Advanced Technologies, University of Catania, Catania, Italy
[6]IRCCS Centro Neurolesi Bonino-Pulejo, Messina, Italy
[7]Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy

Corresponding author:
Giuseppe Lanza, Via Santa Sofia, 78 – 95125, Catania, Italy.
Email: giuseppe.lanza1@unict.it

required to identify predictors of training success, such as the type and severity of ataxia and the level of residual functioning.

Introduction

The cerebellum is involved in control of several motor behaviours, such as speech, eye movements, limb coordination, balance, and gait. In particular, shaping and fine-tuning of movements are major functions. Correspondingly, a cerebellar lesion does not typically result in a pure motor deficit, but in a lack of coordination and poor motor performance (ataxia).[1,2] Ataxic gait is characterized by a disordered coordination between the head, trunk, and legs, resulting in impairment of postural adjustments, balance, and multijoint coordination.[3,4] These deficits lead to an increased step width, variable foot placement, irregular trajectory, and an instable, stumbling walking path, with an abnormal range of movement[5,6] and a high risk of falling.[7]

Because pharmacological interventions are rarely feasible options in neurodegenerative disorders,[8] physiotherapy and kinesitherapy are currently viewed as a major cornerstone in managing ataxic patients. Nonetheless, while the benefits of different motor training programmes have been demonstrated in other neurological disorders (i.e., stroke, Parkinson's disease), their application remains controversial in degenerative ataxias.[9–11] Indeed, motor training in these patients is significantly limited by critical involvement of the cerebellum in motor adaptation and learning,[4] and by

the type of the disease process and progression.[12–14]

To date, evaluation of motor training interventions for patients with degenerative ataxia have been undertaken by only a few small clinical studies. Observed improvement mainly involves an increase in postural stability and a decrease in independency on walking aids.[15,16] An example of this situation is that locomotion training on treadmills, with[17,18] or without body-weight support,[19] has been proposed especially for patients with more severe ataxia. Nonetheless, most of these studies did not focus on primary degenerative ataxia, but on non-degenerative or secondary forms of ataxia. Consequently, as highlighted by recent studies,[20,21] there is a requirement for a deeper basic education, more advanced knowledge, and publication of evidence-based guidelines on this issue.

Hereditary ataxias: a brief overview

General features

Hereditary ataxias are a group of genetic disorders that are characterized by a primary and gradually progressive degeneration of the cerebellum, spinocerebellar bundles, and the spinal cord. Classically, Anita Harding classified hereditary ataxias into autosomal recessive ataxias, X-linked

ataxias, mitochondrial ataxias, and autosomal dominant cerebellar ataxias,[22] which include spinocerebellar ataxia (SCA). To date, at least 40 clinical phenotypes of SCA have been identified, and they are caused by three nucleotide bases repetitions (so-called CAG triplet) in the corresponding gene. An increase in CAG triplets produces protein formation with a longer polyglutamic tract (polyQ), which leads to neural death and cerebellar degeneration.[23,24]

Symptoms of SCA typically start in adulthood and slowly progress over many years, culminating in brainstem failure. However, this is not the case for SCA6, which typically spares cranial motor nerves and has a better prognosis compared with the other forms (e.g., SCA1). There is considerable variability in disease features, partly due to differences in polyQ repeat expansion, which involves longer expansions associated with earlier onset and a broader range of symptoms. The neuropathology of SCA is also varied. In SCA1, SCA2, and SCA3, cerebellar and brainstem degeneration are nearly always prominent, whereas the basal ganglia and the spinal cord exhibit variable involvement.[25]

Diagnosis and differential diagnoses are often challenging for SCA. Useful investigations are brain and cervical magnetic resonance imaging, nerve conduction studies and electromyography, multimodal evoked potentials, electroencephalograms, and fundoscopy. However, a definitive confirmation is currently based on genetic testing.[26]

To date, there is no causative therapy for SCA. Management of SCA is multidisciplinary and includes neurologists, physiatrists, physiotherapists, speech therapists, occupational therapists, dieticians, psychologists, ophthalmologists, orthopaedic specialists, and kinesiologists. Nevertheless, the progressive course often weakens the patient's will and mood, usually leading to refusal to carry out motor activity and to prefer to maintain a sedentary lifestyle. This worsens the functional status and leads to premature loss of autonomy. Therefore, early recognition and treatment of these symptoms are mandatory to slow down disability and to improve quality of life.[27,28]

Most prevalent SCA

The age of onset of SCA1 ranges from childhood to late adult life, with a peak in the fourth decade. Earlier age at onset and larger expansion are associated with faster progression of SCA1. Of the polyQ SCAs, SCA1 progresses the fastest, and is associated with concomitant progression of cerebellar and non-cerebellar symptoms.

SCA2 presents with ataxia, slowed eye movements, and sensory-motor neuropathy, although extrapyramidal manifestations and cognitive impairment may also occur. The age of onset ranges from infancy to later adult life, with a mean onset in the mid-30s. As in SCA1, an earlier age at onset and larger expanded alleles are associated with faster progression of symptoms.

SCA3 (Machado–Joseph disease) is so clinically variable that some authors have classified it into the following subtypes: early-onset disease with extrapyramidal signs and spasticity, but minimal ataxia (Type 1); midlife progressive ataxia (Type 2); later-onset ataxia with neuropathy, amyotrophy, and loss of reflexes (Type 3); and parkinsonism with or without ataxia (Type 4).

SCA6 begins later in life, with a median age of onset in the early 50s. SCA6 is a relatively pure cerebellar syndrome, and does not appear to reduce the lifespan. Symptoms may be episodic in the shortest disease-causing repeat sequences and clinical dysfunction correlates with cerebellar atrophy.

Three other polyQ diseases can present primarily with ataxia: SCA7, SCA17, and dentatorubral-pallidoluysian atrophy.

SCA7 resembles SCA1, SCA2, and SCA3, but it is typically accompanied by severe retinal degeneration. SCA17 and dentatorubral-pallidoluysian atrophy are relatively rare, show more widespread degeneration than most SCAs, and are markedly heterogeneous in clinical features.[25]

Data source and selection

Search strategy

A selective, focussed PubMed-based literature review from January 1997 to February 2019 was performed by using a combination of the following keywords and MeSH terms: "cerebellar ataxia", "rehabilitation", "physiotherapy", "kinesitherapy", "adapted physical activity, "motor training", "postural exercise", "exergames", "virtual reality", and "complementary therapy". We also reviewed the articles listed in the references to locate further data.

Selection

Articles that met the following criteria were included: i) recruitment of patients with SCA; ii) original report (excluding conference abstracts); iii) prospective clinical trial that evaluated the effectiveness of physical therapy or other motor training programmes (e.g., computer-assisted, treadmill, videogame-based training); iv) high-intensity training over an extended time period; and (v) control design (case–control or intra-individual control design). We excluded the following: i) studies on patients with secondary cerebellar ataxias; ii) studies in preclinical or animal models; iii) studies that did not sufficiently report the statistical values required; iv) articles different from research studies (i.e., commentaries, letters, editorials); and v) papers not in English. After this process, 13 articles were identified (Table 1). The following data were considered: 1) study design; 2) sample characteristics, such as the number of participants, age, sex, presence/absence of treatment, and time of the day; 3) method used and its features; 4) outcome measures; 5) results; and 6) limitations.

Intensive motor training techniques

Physiotherapy and kinesitherapy

Recent studies have shown that postural, co-ordination, and walking exercises can improve ataxia, although the rehabilitative outcome mainly depends on the individual compensatory resources and the residual functional abilities.[29] In this context, the motor activity programme identifies two phases. 1) The preparatory phase aims to learn the patient's own body perception, spatial-time awareness, coordination, respiration, and simple motor movements. 2) In the operational phase, the patient progressively learns complex tasks and, by repetition of the activities learnt, enriches his/her sensorial experience, executive strategies, and anticipatory capabilities.[30] In this framework, adequate feedback and constant proprioception are mandatory because they improve dysfunctional capacities during the learning phase.[31]

Most studies have shown that motor recovery and adaptation subsequent to cerebellar degeneration involve synaptic plasticity. However, because of the limited diagnostic methods and the minimal scientific evidence, whether this process contributes to effective functional improvement of patients with ataxia is still unknown.[32] In the last decade, researchers have investigated the role and effect of different rehabilitative techniques on motor dysfunction, and have mostly focussed on exercises of balance, stretching, coordination, proprioception, and walking.[8]

Table 1. Main studies on intensive motor training in degenerative ataxia.

Authors, year[ref]	No. of patients	Type of ataxia (no. of subjects affected)	Age, years/range (sex)	Type of intervention(s)	Duration	Post-training	Outcome measures	Main findings
Gill-body et al., 1997[15]	2	Cerebellar atrophy (1) Post-surgical ataxia (1)	48 (M) 36 (F)	Balance exercises	6 weeks	No	Balance tests Posturography	↑ Balance ↑ Stability during gait
Pèrez-Avila et al., 2004[35]	87	Mild SCA2	Mean (SD): 38.1 ± 10.9; range: 17–69 (sex not specified)	Physical exercises based on coordination, balance, and muscular strength	6 months	No	Balance quantitative tests Neurological indices	↑ Static balance ↑ Neurological indices
Vaz et al., 2008[19]	2	Chronic ataxia	25 (F) 53 (M)	Treadmill training sessions, with progression in velocity and step length	20-minute session, three times a week for 10 weeks	No	Rivermead Visual Gait Timed up and go test Time to complete a balance task Walking speed, cadence, and stride length	↑ Parameters at baseline and subsequent phases. Significantly superior effects of treadmill training over baseline conditions on cadence.
Cernak et al., 2008[17]	1	Severe ataxia	13 (F)	Locomotor training with a treadmill	5 days a week for 4 weeks in a clinic	5 days a week for 4 months at home	FIM	↑ Ambulatory function, although the intensity and duration of training may be prolonged
Ilg et al., 2009[52]	16	Cerebellar degeneration (10) Degeneration of afferent pathways (6)	40–79 (8 M, 8 F)	Intensive coordinative physiotherapy	1 hour, 3 days a week for 4 weeks	No	Ataxia rating scales Individual goal attainment scores Quantitative movement analysis	↓ Ataxia ↑ Balance ↑ Limb coordination ↑ Gait speed and lateral sway
Freund and Stetts, 2010[18]	1	Severe ataxia	23 (M)	Trunk stabilization training Locomotor training using a treadmill Overground walking for balance, gait, and trunk muscle performance	28 sessions, two times a week for 10 weeks	10 60-minute sessions for the next 4 weeks	BBS Timed unsupported stance FAC 10-m walk test OPTIMAL Abdominis thickness Isometric trunk endurance tests	↑ Balance ↑ Gait ↑ Trunk muscle performance

Table I. Continued

Authors, year[ref]	No. of patients	Type of ataxia (no. of subjects affected)	Age, years/range (sex)	Type of intervention(s)	Duration	Post-training	Outcome measures	Main findings
Ilg et al., 2010[33]	14	Degenerative cerebellar disease	40–79 (8 M, 6 F)	Intensive exercises (static and dynamic balance; trunk-limb coordination; fall-preventing strategies; treating or preventing contractures)	Three sessions, 1 hour per week for 4 weeks	1 year of exercises at home	SARA BBS GAS ADL	↑ Balance ↑ Motor performance ↑ Coordination ↑ ADL
Miyai, 2012[32]	42	SCA6 (20) SCA31 (6) ICA (16)	Mean (SD): 62.5 ± 8.0 (sex not specified)	Physical therapy for balance and gait Occupational therapy for coordination and ADL	1 hour + 1 hour a week for 4 weeks	No	SARA FIM	↓ Ataxia ↑ Gait speed ↑ ADL Improvement in ataxia and gait speed lasted for 12 and 24 weeks
Miyai et al., 2012[34]	42	SCA6 (20) SCA31 (6) ICA (16)	Mean (SD): 62.5 ± 8.0 (22 M, 20 F)	Physical and occupational therapy focussing on coordination, balance, and ADL	2 hours on weekdays, 1 hour on weekends for 4 weeks	No	SARA FIM Gait speed and cadence FAC Number of falls ADL	↑ Ataxia (trunk more than limbs) ↑ Gait speed ↑ ADL Improvement was sustained at 12 and 24 weeks
Ilg et al., 2012[40]	10	Moderate degenerative ataxia	11–20 (5 M, 5 F)	Three videogames to exercise whole-body coordination and dynamic balance	Lab-based 2-week training	6 weeks of training at home	SARA Dynamic Gait Index Activity-specific Balance Confidence Scale	↑ Balance ↑ Coordination ↑ Posture ↑ Gait
Burciu et al., 2013[53]	19	SCA6 (6) Sporadic adult-onset ataxia (9) Autosomal dominant cerebellar ataxia type III (3) SCA14 (1)	54–71 (3 M, 3 F) 26–73 (8 M, 1 F) 42–51 (2 M, 1 F)F	Sensory-motor training Balance exercises	2 weeks	No	SARA International Cooperative Ataxia Rating Scale Voxel-based morphometry	↑ Balance ↑ Grey matter volume in the dorsal premotor cortex, and to a lesser extent, in the cerebellum

(continued)

Table 1. Continued

Authors, year[ref]	No. of patients	Type of ataxia (no. of subjects affected)	Age, years/range (sex)	Type of intervention(s)	Duration	Post-training	Outcome measures	Main findings
Santos de Oliveira et al., 2015[28]	11	SCA2 (2) SCA3 (8) SCA7 (1)	28–59 (5 M, 6 F)	Exercises to improve static and dynamic balance, and whole body movements Fall-preventing strategies	Twice per week, for 4 weeks	No	BBS	↑ Balance ↓ Risk of falls
Schatton et al., 2017[41]	10	Advanced degenerative ataxia	Mean (SD): 16.0 ± 7.4 (7 M, 3 F)	Home-based training with body-controlled videogames	12 weeks	No	SARA GAS Quantitative movement analysis	↑ Balance ↑ Coordination ↑ Posture ↑ Gait Benefits correlating to the amount of training

Abbreviations and symbols: No.: number; ↑ = increase; ↓ = decrease; M = male; F = female; ADL = Activity of Daily Living; BBS = Berg Balance Score; FAC = Functional Ambulation Category; FIM = Functional Independence Measure; GAS = Goal Attainment Score; ICA = idiopathic cerebellar ataxia; OPTIMAL = Outpatient Physical Therapy Improvement in Movement Assessment Log Transverse; SARA = Scale for the Assessment and Rating of Ataxia; SCA = spinocerebellar ataxia; SD = standard deviation

Ilg and co-workers[33] proposed activities of motor coordination in patients with SCA (three times per week for 4 weeks, 60 minutes each) that were evaluated on the following different scales: the International Cooperative Ataxia Rating Scale, the Scale for the Assessment and Rating of Ataxia (SARA), the Berg Balance Scale, and the Functional Independence Measure (FIM). These authors found an improvement in walking velocity and length of gait, which lasted for the following 8 weeks.[33] Miyai and colleagues[34] enrolled 42 older patients with SCA (mean age: 62 years) who received 4-week treatment on the basis of balance, coordination, and walking exercises in addition to 1 hour of occupational therapy. At the end of the experimental protocol, patients showed an improvement in score in the SARA and FIM.[34] Finally, Cernak and co-workers[17] showed an improvement in walking performance through a treadmill training programme that was performed three times per week for 20 minutes per session. Other authors that investigated short- and long-term effects of motor activity and physical exercise in patients with SCA concluded that long-standing improvement is possible with a constant and continuous motor activity.[35] However, once this activity is stopped, the clinical benefit is lost relatively soon.

Virtual reality and exergames

Immersive virtual reality is a recently developed technology that permits stimulation of senses and the possibility to interactively operate within a customized rehabilitative setting. This allows performance of different activities in real time, such as playing, walking, and manipulating objects.[36] When the senses are stimulated, they generate proper responses to which the body continuously adapts its motor and cognitive behaviour.[37] For these reasons, virtual reality has provided relevant clinical and scientific contributions, especially in the rehabilitation area.[38] Indeed, this technology can non-invasively improve motion, balance, coordination, and cognition. Therefore, virtual reality is often used as support for post-stroke upper limb recovery, as well as for degenerative and vascular-related cognitive deficits.[39] Videogames also enhance oculo-motor coordination, anticipatory capacities, and rapid movements to be executed in a virtual environment.[40]

On the basis of these considerations, a study[40] was conducted in 10 children with mild SCA (patients were able to walk autonomously) by using three common videogame consoles. The experimental protocol lasted 2 weeks and was based on specific whole-body movements that are useful for improving stability and preventing falling. The post-treatment results showed an improvement in the items of SARA related to posture, balance, walking, and coordination. The authors concluded that videogames play a relevant role within the rehabilitation programme of mild SCA,[40] although it was uncertain whether this approach might be applied in severe patients. A recent study[41] addressed this question by investigating patients with SCA in a wheel chair who were treated with a selection of videogames for 12 weeks. The authors found that an improvement at SARA was still observed. However, these preliminary data should be confirmed by further investigations.

With regard to the type of videogames, coordination sports are suggested in the initial stage, such as ping-pong, squash, badminton, and boules-type games. These games should be performed on an elastic carpet to further increase posture and coordination.[42] When ataxia becomes more severe, videogames or virtual reality should be combined with specific motor programmes aiming at preventing falls

and improving mobility, resistance, posture, balance, and muscular strength. For this purpose, static and dynamic balance exercises, as well as entire body movements, are proposed. These exercises can be executed even through console games (e.g., Ski Slalom and Tightrope walk).[20] At later stages, there is currently no efficacious intervention. In selected cases, some videogames that are used while patients are sitting down are still recommended, along with use of a treadmill that rhythmically reinforces the patient's balance and walk.[19]

Postural exercises

Postural instability is an initial clinical feature of SCA and significantly affects gait and mobility. Moreover, static and dynamic imbalance increases the probability of falling, with a risk of bone fractures and other complications. Finally, the fear of falling often leads to refusal of physical activity and consequent social isolation. SCA-related rigidity is a main cause of postural instability and is associated with postural destabilizing and other abnormal reactions.[43]

The rehabilitative approach of SCA-related postural disorders is currently based on the so-called "re-learning" of destabilizing responses (namely, by using moving platforms) and impaired activities of daily living (e.g., getting up from a chair, holding and throwing objects, and the standing position).[44] Treatment approaches should take into account podalic and visual receptor stimulation, and customization of treatment strategies. Some exercises are indeed designed to improve muscular strength and balance, such as those requiring use of a fitball as a wall squat, single wall squat, balance reversal lunge, balance push-up, ball pass, and balance oblique crunch.

Notably, postural instability may lead to chronic lumbar backache. Therefore, an important task of postural exercises is to favour stretching of lumbar muscles by using specific methods, such as Pilates, Mezieres, and Feeldenkrais.[45]

Adapted physical activity

Adapted physical activity (APA) includes group exercises aimed at secondary and tertiary prevention of disability and improvement of patients' lifestyle, well-being, and quality of life.[46] In APA programmes, simple, flexible, light, and variously coloured equipment (e.g., elastics, sticks, hula-hoops, bottles, balls, walls, carpets, mirrors, and one/two weights) are used to stimulate motor performance, coordination, and motivation. Accordingly, when APA is carried out regularly at the gym, it improves the psycho-physical status of patients with SCA. Additionally, listening to music while practicing further improves the effects by enhancing mood, motivation, and socialization.[47]

The training session includes the following phases: 1) warming-up; 2) aerobic exercises of moderate intensity; 3) strength exercises (e.g., series of a repetition of 10 exercises for each muscular group) and limb mobility (e.g., stretching); and 4) cooling down exercises to improve venous return and energetic restoration. Soft APA is also important for harmonic stimulation of the whole body. Therefore, APA should include mobility exercises of the head and shoulders, as well as muscle toning of abdominal and upper/lower limb muscles.[48]

Discussion

Summary of findings

As summarized in Table 1, intensive training in SCA is still based either on conventional motor stimulation or whole-body controlled videogames (exergames). Overall, the studies mentioned here provide evidence that, although a disease-modifying

effect has not been demonstrated, constant high-intensity motor training may be effective in degenerative ataxia, even in patients with severe disease. As a general rule, rehabilitation should provide a large selection of training strategies, which need be individually tailored according to each ataxia type, disease stage, and personal preferences. Such a customized approach helps to maximize functioning of each subject and might, at least in some cases, reduce ataxia-related complications.

The experience from these studies also indicates that exergame-based training and virtual reality can enhance the effect of conventional physiotherapy, helping subjects to achieve and maintain the required training intensity.[48] In particular, these skills are highly required in a number of situations where subjects have to adequately react under time pressure to dynamically changing environmental conditions and to accurately anticipate novel or unexpected events. In this scenario, exergames properly simulate "real-world" situations. However, there is a need for trained operators to initiate and supervise any exergame-based training. Professional expertise is required for selection of the appropriate exergame on the basis of the subject's coordinative ability and level of impairment, as well as the treatment goal that has to be achieved. This suggests that exergame-based training may be useless or even harmful if not adequately applied or supervised.[49]

A relevant aspect is the scales that should be used to quantify disease severity and the outcome measures. One of the most frequently used scales is the SARA,[50] which is quick and easy to score, has good metrological qualities, and does not require special training or technical equipment. The main disadvantages of the SARA are that it does not capture all symptoms at onset and does not cover extracerebellar or oculomotor symptoms.[51] However, the SARA can reliably monitor the effects of different rehabilitative methods.[43] A randomized trial in 42 patients with degenerative cerebellar disease that assessed the effect of an intensive programme (physical therapy and occupational therapy) showed improvement of the SARA score at 6 weeks, and this effect was still present 24 weeks later[34] Another prospective study evaluated static and dynamic balance exercises and coordination in 16 patients with degenerative cerebellar disease, and showed improvement of the SARA score [33] that lasted for up to 1 year.[52] In 10 patients with degenerative ataxia, use of Kinect® (with games chosen to specifically work on multi-segment coordination, dynamic balance, and arm or leg movements towards a target) improved the SARA score, especially when the rehabilitation programme was intense.[40] This finding suggested a dose-effect relationship for rehabilitation.

Proposed mechanisms

The neural mechanisms underlying motor training effects in degenerative ataxia are still largely unknown. A hypothesis for this mechanism is that degenerating cerebellum is still able to adapt its functioning, or alternatively, the learning deficit is compensated by other brain areas.

A voxel-based morphometry study in patients with cerebellar degeneration that was performed by Burciu and colleagues[53] showed that 2-week postural training resulted in a significant improvement of balance. More interestingly, comparison of grey matter volume before and after the training showed an increase primarily within the non-affected neocortical regions of the cerebellar-cortical loop, more specifically at the level of the premotor cortex. Grey matter changes were also observed within the cerebellum, although these modifications were less pronounced. The authors suggested that motor training might lead to activation and subsequent

plasticity of specific compensatory networks, and to a lesser extent, to functional hyperactivation of the remaining cerebellar circuitries.[53] Further imaging studies on different neurorehabilitative strategies will provide better understanding of the pathomechanisms underlying motor performance and learning. This will help to tailor physiotherapy and kinesitherapy to specific patients' needs.

Interestingly, multimodal integrated interventions targeting visual-perceptual abilities and motor skills are also effective in other clinical contexts, such as intellectual disability.[54] In particular, motor learning and memory-mediated mechanisms of neural plasticity might underlie improvement of hand–motor coordination, speed accuracy, and fine motor performance.[54] This suggests the presence of plastic adaptive changes, even in the adult brain with mild intellectual disability.

Finally, among non-pharmacological therapies, non-invasive brain stimulation (namely, transcranial magnetic stimulation and transcranial direct current stimulation [tDCS]) is an innovative and promising option that is currently used in several research and clinical settings.[55–67] In patients with SCA, the possibility to modulate cortical excitability and synaptic plasticity with non-invasive electrophysiological tools is a "cutting edge" topic in translational neuroscience. Because the cerebellum is closely connected with the cerebral regions subserving motor, associative, and affective functions, the cerebello–thalamo–cortical pathway can represent an intriguing target. Moreover, targeting the cerebellum might be a novel way to probe the excitability even of remote regions and their functions in normal subjects and in those with a wide range of neurological disorders.[68–70] A recent, randomized, single-blind, cross-over study[71] analysed the effect of cerebellar tDCS on lower extremity sensory and pain thresholds in 14 healthy

volunteers. This study showed that anodal tDCS was able to modulate pain processing in the ipsilateral leg. This finding suggests that cerebellar stimulation enhances plasticity and decreases pain perception. Translationally, this will be of pivotal importance when using high-intensity motor training because of the relevance of pain and its consequences (e.g., spasticity, spams, joint degeneration) in neurodegenerative disorders.

Pitfalls and limitations

Although clinically encouraging, the studies mentioned here have some weaknesses and limitations. First, a nomenclature flaw is present in some studies that included hereditary ataxic patients, but not subjects with a particular type of SCA. Second, coordinated multicentre efforts are necessary to accumulate larger cohorts, which should also be homogeneous in terms of selection of patients and disease severity. None of the available studies were large enough to allow recommendation of a standardized exercise protocol for a specific type of SCA. Third, the phenotypic and genetic variability in degenerative ataxia is large, including disease progression and comorbidity. Fourth, more studies should use a randomized controlled design to yield higher levels of evidence. Finally, different outcome measures were used among these studies. Therefore further research is required to specifically identify predictors of training success, such as the type of ataxia, the disease severity at baseline, and the level of residual cerebellar functioning. Indeed, studies with subgroup analysis comparing the outcome measures on different ataxia types are still lacking.

Conclusions

Rehabilitation of degenerative cerebellar diseases remains a challenge for clinicians

and researchers. However, notwithstanding the limitations, constant high-intensive motor training plays a role in the current management of SCA. In particular, most of the research that focussed on the short- and long-term effects of customized programmes of balance, coordination, proprioception, and postural exercises concluded that short-term improvement tends to be lost once motor stimulation is stopped. Therefore, clinical benefit should be maintained through constant activities. Additionally, application of videogames and virtual reality enhance balance, coordination, and walking abilities, whereas the efficacy of APA, gym, and postural exercises depends on the disease duration and severity. Progress in neurorehabilitation will lead to improved knowledge in this field and stimulate further studies that, ultimately, will improve quality of life of patients and caregivers.

Declaration of conflicting interest

The authors declare that there is no conflict of interest

Funding

ORCID iD

Giuseppe Lanza (iD) https://orcid.org/0000-0002-5659-662X
Francesco Fisicaro (iD) https://orcid.org/0000-0002-1579-8807

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