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Video-based Gait and Balance Training at Home in Healthy Adults and Patients with Cerebellar Ataxia

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I. Zusammenfassung

Die Beeinträchtigung von Gang und Balance stellt für Patienten mit hereditärer zerebellärer Ataxie eine zentrale Herausforderung im Alltag dar. Patientenberichte und Studien konnten zeigen, dass Bewegungstherapie und Physiotherapie zu den wirksamsten bisher verfügbaren Maßnahmen gehören, um Mobilität, Sturzrisiko und Wohlbefinden zu verbessern. Video-basiertes Training hat als leicht zugängliche, selbstgesteuerte Trainingsmöglichkeit an Bedeutung gewonnen, insbesondere für Patienten mit eingeschränktem Zugang zu Therapiezentren. Standardisierte Leitlinien für derartige Trainingsmöglichkeiten fehlen jedoch bisher. Weitere randomisierte Studien sind daher erforderlich, um die optimale Struktur für eigenständige Trainingsmethoden im häuslichen Umfeld festzulegen.

Die vorliegende Dissertation untersucht den Einfluss eines dreiwöchigen, videobasierten Gang- und Balancetrainings, welches zu Hause durchgeführt wurde, bei gesunden Probanden und bei Patienten mit hereditären, degenerativen zerebellären Ataxien. Vorteile und Einschränkungen solcher Programme werden erläutert und es wird gezeigt, wie Trainingsintensität, Lern- und Gewöhnungseffekte und klinische Merkmale der Patienten (z. B. Krankheitsschwere) die Ergebnisse beeinflussen können.

In der ersten Studie wurden Trainingseffekte und Lern- bzw. Gewöhnungseffekte bei gesunden Teilnehmern verglichen, und in einem separaten Kollektiv die Vergleichbarkeit von unterschiedlichen Platzierungen von Smartphone Sensoren untersucht. Verbesserungen in Gang und Balance wurden sowohl in der Trainingsgruppe als auch in der Kontrollgruppe ohne Training gefunden. Da beide Gruppen die im Labor untersuchten Gang- und Standaufgaben wöchentlich zu Hause wiederholten, deutet dies darauf hin, dass sowohl das Training selbst als auch die reine wöchentliche Wiederholung der Aufgaben, also das regelmäßige Üben ohne zusätzliche Trainingsinterventionen, positive Effekte in der Gang- und Balanceleistung hervorrufen können. Hinsichtlich der Platzierung des Smartphones am unteren Rücken oder Bauch wurden keine Unterschiede in der Messgenauigkeit gefunden, sodass die Platzierung in zukünftigen Studien so gewählt werden kann, wie sie am praktischsten für die Patienten und für die Studiendurchführung ist.

Die zweite, randomisierte und kontrollierte Studie mit Patienten mit hereditären, degenerativen zerebellären Ataxien, zeigte keine statistisch signifikanten Unterschiede zwischen den beiden Trainingsgruppen (4 x 20min vs. 2 x 40min Training pro Woche) und der Kontrollgruppe. Explorative, gruppenseparate Analysen zeigten jedoch ausschließlich in der 2 x 40min Gruppe mit längeren, aber weniger häufigen Trainingseinheiten, Verbesserungen in verschiedenen Gangvariablen und einem Maß der Krankheitsschwere. Darüber hinaus wurden Wechselwirkungen zwischen der Krankheitsschwere und erhobenen

Balancevariablen, sowie zwischen dem Wohlbefinden und erhobenen Gangvariablen gefunden, was darauf hindeutet, dass diese Faktoren die Wirksamkeit von Interventionen, Gewöhnung oder Anpassungsprozessen beeinflussen könnten.

Zusammenfassend kann aus den Erkenntnissen beider Studien geschlussfolgert werden, dass die Intensität oder Herausforderung des Trainingsprogramms nicht ausreichend war, um generelle Verbesserungen bei Gesunden und bei Patienten mit leichter bis moderater Ataxie im Vergleich zur Kontrollgruppe hervorzurufen. Die Implementierung einer Basismessung vor Beginn des Trainings könnte Gewöhnungseffekte bei Gang- und Standanalysen minimieren. Zudem zeigte sich, dass tragbare Sensoren (z. B. Smartphones) sowohl am unteren Rücken, als auch am Bauch getragen werden können, sodass in Folgestudien die für Patienten praktikabelste Lösung gewählt werden kann. Sowohl Patienten mit höherer Krankheitsschwere, als auch solche mit höherem Wohlbefinden, zeigten signifikante Verbesserungen in Gang und Stand. Dies verdeutlicht, dass künftige Trainingsstudien neben körperlichen auch psychische Faktoren, wie das Wohlbefinden, stärker berücksichtigen sollten.

II. Summary

Progressive impairments in gait and balance are the main challenges for patients with hereditary cerebellar ataxia in everyday life. According to both patients' reports and studies, exercise and physiotherapy are among the most effective supportive measures to improve functional mobility, reduce fall risk and improve well-being. Video-based training has gained traction as an accessible, self-directed approach to improve motor skills, especially for populations with limited access to regular supervised interventions. However, standardized guidelines are lacking, and further randomized controlled trials are needed to determine the best structure for home-based training programs.

This dissertation explored the impact of a three-week, video-based training program at home targeting gait and balance in healthy individuals, and in individuals with hereditary degenerative cerebellar ataxia. It highlights the potential benefits and limitations of such training protocols, and sheds light on how different training intensities, task repetitions (habituation), and patient characteristics may influence outcomes. In the first study with healthy participants we found improvements after the training in gait and balance in both the training group, and the control group without additional training. Since both groups repeated the gait and balance assessments at home, we summarized that both the gait and balance training, as well as the sole repetition of assessment tasks, can lead to improved gait and balance outcomes. In the second study, a pilot randomized controlled trial was conducted with ambulatory patients with hereditary degenerative cerebellar ataxias. While no general difference was found between both training groups (4 x 20min training, and 2 x 40min training per week, for three weeks), and the control group, exploratory analyses within the separate groups revealed hints for improvements in gait and in disease severity in the 2 x 40min training group only. In addition, interactions between disease severity and stance outcomes, and between well-being and gait outcomes were found, suggesting that these factors may influence the effectiveness of interventions, practice or adaptation processes.

In summary, the intensity and challenge of the chosen training program was not sufficient to induce an overall improvement in both healthy participants and patients with mild to moderate cerebellar ataxia compared to a control group. We found that the implementation of a baseline measurement might help to reduce habituation effects of gait and balance assessment, and that wearable sensors (e.g., smartphones) can be worn comparably at both the lower back and lower belly, increasing the convenience for patients. For patients, disease severity, and well-being interacted with the performance improvements throughout the training period. Patients with higher disease severity scores and higher habitual well-being significantly improved in gait and stance. This highlights the need to assess and improve patients' well-being in future training studies.

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IV. Introduction

Understanding gait and balance is essential for enhancing, maintaining or improving mobility, independence, and quality of life across diverse populations. Research in healthy individuals provides a baseline for normal balance and movement patterns, which is crucial for identifying deviations and impairments seen for instance in movement disorders like ataxia. For patients with ataxia, who experience significant coordination and balance impairments, research can help to tailor interventions to help mitigating symptoms, enhancing functional abilities, and improving their quality of daily living.

The work presented here aims to give an overview about healthy and impaired gait and balance abilities, about possibilities to improve these functions by physical activity and about current limitations which need to be addressed in future research and daily life to reach these goals.

1 Gait and Balance

In healthy adults, gait and balance often take place almost unnoticed and receive little attention until aging or illness leads to an increased risk of falls. Consequently, most research on gait and balance focuses on older adults or clinical populations, while studies on young or middle-aged adults are comparatively rare. However, understanding gait and balance in individuals with impairments requires age-matched, healthy control groups as a baseline for comparison. These comparisons are crucial for identifying deviations and mechanisms underlying gait or balance disorders, paving the way for more effective interventions and prevention strategies.

1.1 Definition and Key Concepts

Gait, the most fundamental form of human locomotion, can be analyzed from various perspectives, including a biomechanical approach. In this view, gait is divided into phases known as "steps" and "strides." A stride begins when one foot makes initial contact with the ground and ends when the same foot contacts the ground again (see Figure 1, colored leg). In contrast, a step starts with the initial contact of one foot and concludes when the opposite foot makes contact. Thus, a single stride comprises two steps.

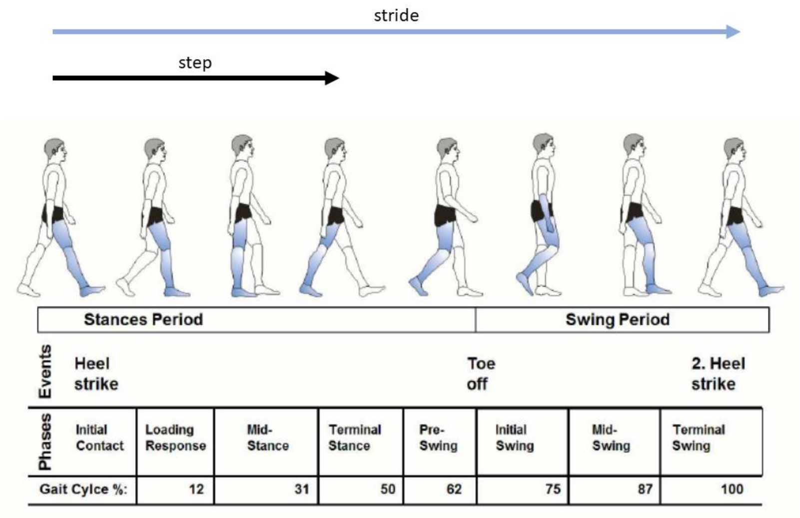

Figure 1: Visual description of one gait cycle (from: Noraxon MyoPressure Bilateral Gait Report, with permission)

Each stride is further divided into two main phases: the stance phase, where the leg remains in contact with the ground for approximately two-thirds of the cycle, and the swing phase, where the leg swings forward during the remaining third. Within these phases, specific positions, such as Heel Strike, Mid-Stance, and Toe-Off, are commonly used as key markers for gait analysis (Suppa et al., 2020). The duration of a gait cycle tends to remain consistent within an individual over time (Day & Lord, 2018).

Closely linked to gait is balance, or the ability to maintain the body in a desired position under varying environmental conditions. Balance plays a critical role in walking, but it is also an independent functional ability that can be assessed separately through specific tasks. These include static balance tasks, like maintaining stability while standing in one position, and dynamic balance tasks, which evaluate balance during movement, such as walking along a straight line or performing turning maneuvers.

Both gait and balance require fine-tuned activation of muscles. This fine-tuning takes place through detailed integration and interpretation of external and internal information (e.g., environment, body), production of goal-directed muscle force, and constant adaptation and correction of these processes. In order to achieve this, a wide range of neuroanatomical structures is involved, including those within the central nervous system as well as components of the peripheral motor pathway.

1.2 Neuroanatomical Structures

Various structures of the central nervous system are integral to gait and balance, including the cerebral cortex, thalamus, brainstem, basal ganglia, cerebellum, and spinal cord. They built complex circuits integrating input from sensory systems to the planning, initiation, and execution of movements, and its adjustments (MacKinnon, 2018). The input from sensory systems, e.g. proprioception, includes information about the external environment (e.g., movement of objects), and about the orientation and motion of the own body (e.g., relative positions of the body segments to each other). All this information is constantly being updated, creating feedback and feedforward loops, which help comparing the sensed outcome of movement with the desired outcome of movement (MacKinnon, 2018). As part of these circuits, the spinal cord hosts specialized neuronal networks known as central pattern generators (CPGs). CPGs are critical for generating continuous, rhythmic movements, such as those required for normal gait. These networks enable the largely cyclic and semi-automatic nature of walking, reducing the need for continuous and active input from descending pathways in the central nervous system once the initial step has been activated (Goetz, 2007). This automation is what distinguishes gait from many other motor activities. While normal gait is predominantly automated, more complex gait patterns, such as tandem or backward walking, require additional cognitive processing. These tasks engage higher-order neural systems to adapt motor output to novel or challenging conditions. The involvement of the peripheral motor system includes nerve fibers, the neuromuscular junction (motor endplate), muscles, and specialized sensory structures like muscle spindles with stretch receptors. These components collectively facilitate precise motor control by ensuring both the generation of motor commands and their accurate transmission to the musculoskeletal system.

Balance performance relies on a finely tuned interplay between several neural systems, with the most commonly associated brain structures being the basal ganglia, thalamus, hippocampus, inferior parietal cortex, frontal lobe regions, and cerebellum (Cabaraux et al., 2023). The cerebellum plays a pivotal role by compensating for errors during movement execution, ensuring smooth and coordinated adjustments. Additionally, the vestibular system in the inner ear detects changes in head position and movement direction, providing critical input for maintaining equilibrium. Sensory information from the environment, such as visual cues and somatosensory input from the feet and joints, contributes to postural control. Effective balance requires the rapid identification and correction of postural instability to prevent falls. This process involves continuous communication between sensory systems, motor outputs, and the cerebellum to adjust the body's position dynamically in response to external or internal perturbations. By integrating these systems, the body achieves the coordination necessary for both static postures and dynamic activities like walking, running, or navigating uneven surfaces. Muscle movements are orchestrated to maintain or correct posture as necessary. In particular, hip and leg muscles play important roles in locomotion (e.g., gluteus maximus, gluteus medius, vasti, soleus, and gastrocnemius, Pandy & Andriacchi, 2010).

1.2.1 The Cerebellum and its Role in Gait and Balance

Understanding the cerebellum's anatomical structure and its diverse functional roles helps exploring its contribution to gait and balance regulation, and to motor performance in general. The cerebellum is a critical structure in the brain, housing approximately 60-80 % of all its neurons (Manto & Pandolfo, 2002). This remarkable density is facilitated by its extensive surface area, which becomes apparent when the intricate folds (gyri) of the cerebellum are unfolded. This unique feature distinguishes the human cerebellum from that of other species and is often cited as a foundational element of our advanced motor and non-motor capabilities (Sereno et al., 2020). Such adaptations are thought to underlie complex behaviors and cognitive processes, reflecting the cerebellum’s evolutionary significance. Anatomically, the cerebellum can be divided into three main lobes: the anterior lobe, the posterior lobe, and the flocculonodular lobe. These lobes contain a total of 10 distinct lobules, with the specific distribution of lobules across the lobes following a regular pattern. Lobule I to V are attributed to the anterior lobe, lobules VI to IX to the posterior lobe and lobule X to the flocculonodular lobe. Unlike the cerebral cortex, the cerebellum exhibits a highly organized, three-layered cortical structure, which is uniform across the whole cerebellum. The three layers of the cerebellar cortex include the molecular layer, the Purkinje cell layer, and the granular layer, and contain five types of neurons. The uniformity in cellular organization across the cerebellum suggests that it may serve a consistent, overarching function, despite certain topographically focused functional attributions. This organization contrasts with the cerebral cortex, which exhibits more regional specialization. While the cerebellum receives input through many parts of the peripheral and central nervous system (e.g., proprioceptive information), the output relies solely on the cerebellar nuclei and projections reach cortical and subcortical targets (Goetz, 2007).

Within the cerebellum, the cerebellar vermis, anterior lobe, and lobules VI and VII are particularly important for maintaining gait and balance (Cabaraux et al., 2023). In detail, the cerebellar vermis and the cerebellar peduncles, transmitting information between the cerebellum, brainstem nuclei, and subcortical areas, are often associated with postural control. Vermis, paravermis and anterior lobe (lobule VI) are associated with locomotion in general, and the anterior lobe, as well as lobules 6 and 7, seem specifically involved in gait (Cabaraux et al., 2023).

However, the cerebellum is not isolated in its function; it interacts closely with other brain structures, including the cerebral cortex, brainstem nuclei, basal ganglia, and spinal cord. Together, these interconnected regions coordinate motor control, which encompasses motor preparation, execution, adaptation, learning, and the automation of movements (Cabaraux et al., 2023). These interactions are facilitated by intricate neural loops, which play a central role in integrating sensory and motor information. One prominent example is the cerebello-thalamo-cerebral loop, which is critical for merging motor and cognitive information. This loop highlights the cerebellum's role not only in coordinating complex motor tasks but also in supporting higher-order cognitive functions. Similarly, vestibulo-cerebellar interactions involve connections between the vestibular system and the cerebellum, enabling balance and spatial orientation. Disruptions in these interactions can lead to cerebellar oculomotor signs such as nystagmus or impaired smooth pursuit. The cerebellum's role in motor coordination is especially significant in the context of gait and balance regulation. Smooth and coordinated movement depends on the cerebellum's ability to predict and adapt motor actions in real time. One theoretical framework that elucidates this function is the concept of internal models (Ito, 2008). These models allow the cerebellum to simulate and refine motor commands by integrating sensory inputs from the external environment, enabling precise and adaptive movements. For instance, the motor cortex sends efferent signals to initiate movement, drawing input from regions like the premotor cortex, supplementary motor area (SMA), and anterior cingulate cortex (ACC). Simultaneously, sensory feedback informs and updates the cerebellum's internal model. This dynamic exchange occurs through feedback loops such as the cerebello-thalamo-cerebral and cerebral-ponto-cerebellar loops (Middleton & Strick, 2001; Palesi et al., 2017). These mechanisms enable the cerebellum to make rapid adjustments, ensuring smooth, precise, and coordinated actions. In addition to refining immediate motor output, the cerebellum facilitates the transition of movements from conscious, effortful control to automatic processing. This shift reduces the cognitive demand required for repetitive or well-practiced tasks, allowing individuals to perform them with minimal attention (Koziol et al., 2014). By retaining representations of movement patterns, the cerebellum supports both seamless transitions between movements and quick adaptations to changing conditions. In addition to the pure execution of movement, motor learning is also of great relevance for the optimization of movement efficiency, adaptation to new environmental conditions, and rehabilitation after injuries or neurological impairments. Motor learning plays a critical role in the transfer of skills to related tasks, enhancing overall motor versatility.

While this work focuses primarily on the motor functions of the cerebellum, which are central to gait and balance regulation, it is important to acknowledge its substantial non-motor roles. The cerebellum plays critical roles in cognitive, autonomic, and emotional functions, emphasizing its broad functional significance: It is for instance involved in executive function, visual spatial processing, linguistic skills and regulation of affect (Bellebaum & Daum, 2007; Schmahmann, 1997, 2019). This is also relevant in the context of motor learning, where the cerebellum adapts to refine motor actions and improve performance through training, as cognitive and affective deficits influence behavior and actions (Jacobi et al., 2021).

Additionally, a shared circuitry between cognitive and balance systems has been suggested (Cabaraux et al., 2023).

Cerebellar dysfunction can arise from a variety of causes, including focal damage, genetic disorders, and vascular events. Focal damage may result from traumatic brain injury, tumors, inflammation, or disruptions in blood supply via the cerebellar arteries, such as in cerebellar strokes. Additionally, genetic mutations can lead to progressive cerebellar degeneration, as seen in conditions like spinocerebellar ataxias. When the cerebellum is impaired, it manifests in a range of symptoms affecting both motor and non-motor functions. Motor symptoms include gait ataxia, speech impairments or involuntary eye movements for motor symptoms, while non-motor symptoms may involve deficits of executive functions, visuospatial cognition, linguistic functions, and personality changes. Regarding motor learning, Timmann et al. (2010) summarized in their review, that classical motor learning (e.g., eyeblink conditioning), emotional associative learning (e.g., fear-related learning), and cognitive associative learning (non-motor learning) are impaired in patients with degenerative cerebellar disorders. The severity and presentation of all the mentioned symptoms depend on the underlying cause of cerebellar impairment and in case of focal damage, to the extent of the damage. For example, results regarding impaired non-motor learning are inconsistent in patients with cerebellar diseases in general, even though clearer impairments have been found in degenerative diseases of the cerebellum (Berlijn et al., 2024).

2 Ataxia

2.1 Etiology and Classification

Ataxia is a term that refers to the impairment of movement coordination, translating to a "lack of order" in motor function. While various types and causes of ataxia exist (i.e., acquired ataxias, sporadic-degenerative ataxias, and hereditary ataxias, Jacobi & Minnerop, 2021), this work specifically focuses on hereditary degenerative cerebellar ataxias, which arise from gene-defect related dysfunction in the cerebellum.

Hereditary degenerative cerebellar ataxias are characterized by progressive neuronal loss within the cerebellum, driven by genetic factors. They can be further divided into autosomal recessive ataxias (e.g., Friedreich’s ataxia), x-linked ataxias (e.g., fragile x-associated tremor/ataxia syndrome), episodic ataxias (e.g., EA2), and autosomal dominant ataxias. Among the autosomal dominant inherited ataxias, spinocerebellar ataxias (SCAs) represent a prominent group of various subtypes, named numerically after their discovery (e.g., reaching from SCA1 as the first subgroup with the gene identified and associated protein characterized, Orr et al., 1993, to more recent ones like SCA49, Garg et al., 2024). Patients with SCAs typically experience significant difficulties with gait and balance, as well as fine motor coordination, slurred speech or double vision (Klockgether et al., 2019). With a prevalence of approximately 2.7 cases per 100,000 individuals, SCAs are considered rare diseases (Ruano et al., 2014). While SCAs are namely characterized by their affection of the cerebellum and its afferent and efferent connections, most SCAs involve broader neurodegenerative processes affecting the basal ganglia, spinal cord and peripheral nerves. The extent and nature of involvement vary across different types of SCAs, which led to an (informal) classification into ataxias commonly regarded as “pure cerebellar” ataxias (e.g., SCA6), and “non-pure cerebellar” ataxias (e.g., SCA3, which is the worldwide most frequent type of spinocerebellar ataxia). Nevertheless, even the pure cerebellar ataxias may show degeneration in other regions than the cerebellum (Jacobi, Reetz, et al., 2013; Marvel et al., 2022), further contributing to the variability in clinical presentation. Spinocerebellar ataxias are characterized by a high genetic and symptomatic heterogeneity, leading to a high range of phenotypes, including for instance involvement of eye movement, neuropathy or epilepsy, spasticity or macular degeneration (Marsden, 2018). Despite this, these ataxias share common features of motor impairment, including gait instability, poor coordination, and progressive disability.

2.2 Gait and Balance Abnormalities in Ataxia

Among patients with cerebellar ataxia, balance and walking are frequently reported as the most restrictive and challenging aspects of daily life (Gorcenco et al., 2024). Gait in cerebellar ataxia is characterized by widened base of support, increased variability (irregular steps), increased double limb support duration, reduced step and stride length, cadence, and speed (Cabaraux et al., 2023; Palliyath et al., 1998; Stolze et al., 2002); while in stance tasks they show higher trunk displacement, and instability (Marsden, 2018). These limitations contribute to an increased risk of falls and a marked reduction in quality of life. While individuals with cerebellar ataxia are often still able to adapt their gait in response to environmental changes – such as adjusting speed on a moving belt (Morton & Bastian, 2006) – their adaptability is notably impaired under additional physical challenges. For instance, when weights were added to their legs, patients demonstrated a diminished ability to adapt their gait compared to healthy controls (Ilg et al., 2008). Further evidence suggests that the severity of cerebellar impairment directly impacts motor adaptability. In conditions that challenge the vestibular and vestibulocerebellar systems – such as tasks requiring fine balance control or rapid adjustments – patients with cerebellar ataxia struggle considerably more than healthy adults (Jacobi, Rakowicz, et al., 2013). This difficulty extends beyond immediate adaptability and includes limited motor learning (Timmann et al., 2010), which is crucial for acquiring new movement strategies or transferring learned skills to novel contexts. Since the cerebellum is involved in those processes (Seidler, 2010), an impairment of transferring skills in patients with cerebellar ataxia is conceivable but has not yet been investigated.

Despite ongoing research efforts on gait in patients with cerebellar ataxias, a recent consensus paper concluded that the assessment of gait remains an area requiring further investigation (Cabaraux et al., 2023). This concerns for instance the tandem gait, which is incorporated in clinical disease severity scales, but no consensus is available on exact protocols evaluating tandem gait (e.g., training before execution, use of lines on the floor, instructions on arm position). Additionally, ecologically valid digital biomarkers with high sensitivity to early or even pre-ataxic stages remain to be defined and their availability improved.

2.3 Current Treatment Approaches

Currently, only one disease-modifying therapy is approved in the field of genetic or degenerative cerebellar disorders: Omaveloxolone has proven to slow disease progression in Friedreich's ataxia (FRDA, Lynch et al., 2021). However, this treatment option is limited to a specific disease group, is not available in every county, is relatively expensive, and its effectiveness is under debate in the medical community. Other pharmacological treatments have been tested without definite evidence of benefit (i.e., riluzole, valproic acid, varenicline and lithium carbonate), but more options are on the horizon, including genetic and epigenetic approaches (e.g., antisense therapies, reducing or silencing disease genes), as well as neuroprotective, anti-apoptotic/ anti-excitotoxicity, anti-neuroinflammatory approaches, mitochondrial enhancement, and neural replacement (Perlman, 2020).

Currently available treatment options include rehabilitation and symptomatic therapies such as physiotherapy, speech therapy, and occupational therapy, which aim to strengthen compensatory mechanisms, as well as non-invasive neurostimulation (transcranial magnetic stimulation and direct current stimulation), and symptomatic medication (e.g., treatment of motor dysfunction) (Perlman, 2020). The positive effect of physiotherapy and intensive balance training is well proven (Millar & Drake, 2023), while occupational therapy seems to improve global functional status only in combination with physiotherapy (Fonteyn et al., 2014). In addition, patients more frequently cited exercise as a reason for feeling better compared to symptomatic treatments, suggesting its prominent role in improving well-being from their perspective (Gorcenco et al., 2024). While physiotherapy was the most widely used kind of treatment according to a survey in patients with ataxia, challenges persist. Access to repeated or extended rehabilitative care is often limited, as outpatient visits and house-call prescriptions are not consistently feasible, and the frequent financial burden of repeated inpatient rehabilitation stays makes them difficult to sustain through insurance coverage.

This context underscores the pressing need for accessible and scalable solutions, such as home-based training programs. Such approaches could bridge the gap by enabling regular, guided exercises that are easily incorporated into daily life, helping to maintain motor function and improve overall well-being, even in the absence of frequent clinical care.

3 Outcome Measurement in Gait and Balance Research

Understanding and addressing gait and balance impairments, particularly in conditions such as ataxia, requires accurate and reliable tools for assessment. These measurements not only provide critical insights into the severity and progression of impairments but also serve as benchmarks for evaluating the effectiveness of interventions. In addition to tools used for patients, it is important to consider scales relevant for healthy individuals, as healthy individuals are frequently investigated in patient studies as control group, which also applies to the study presented here.

The current framework for clinical outcome assessments, as recommended by the US Food and Drug Administration (U.S. Department of Health and Human Services, 2020), emphasizes integrating novel quantitative performance-based assessments (PerfO), such as digital markers for gait and balance, with established clinician-reported outcomes (ClinRO) and patient-reported outcomes (PROs). This combined approach uses the strengths of objective digital measures along with clinical expertise and patient perspectives to provide a more comprehensive and nuanced understanding of patient outcomes in clinical research settings.

3.1 Clinician-Reported Outcomes (ClinROs)

Disease severity in cerebellar ataxia is typically measured clinically with the Scale for the Assessment and Rating of Ataxia (SARA, Schmitz-Hübsch et al., 2006) or the International Cooperative Ataxia Rating Scale (ICARS, Trouillas et al., 1997). Both scales rely on a trained rater, usually a neurologist, to assess clinical signs and symptoms such as gait, stance, speech, and limb coordination. The SARA was published in 2006 (Schmitz-Hübsch et al.), and is now among the most widely used scales for assessing ataxia severity. This generic measure evaluates key aspects of motor function, including gait, stance, speech, and limb coordination, to provide a comprehensive picture of ataxic symptoms. The SARA yields a total score ranging from 0 (no signs of ataxia) to 40 (most severe ataxia), with higher scores indicating greater functional impairment. The ICARS covers four domains (posture/gait, kinetic functions, speech function, and oculomotor function) with a total score between 0 (no signs of ataxia) to 100 (most severe ataxia). In addition to SARA and ICARS, standard neurological examinations include specific tests to assess various aspects of motor function, balance, and coordination. For instance, the Romberg test is commonly used to evaluate balance by observing the patient's ability to maintain a stable standing position with arms outstretched and eyes closed. The finger-to-nose and heel-to-shin tests assess limb coordination. As a general tool for evaluating balance, regardless of specific disease, the Berg Balance Scale is widely utilized to assess an individual's ability to maintain stability during various tasks. It measures balance through 14 functional tasks, such as standing up, reaching forward, and turning around. It evaluates the ability to maintain balance during static and dynamic movements. Each task is rated on a scale of 0-4, based on the level of independence and stability, with a total score ranging from 0 to 56. Higher scores indicate better balance.

Non-motor symptoms associated with cerebellar dysfunction were first described by Schmahmann and Sherman (1997) as cerebellar cognitive affective syndrome (CCAS). To assess CCAS, the Cerebellar-Cognitive-Affective-Syndrome Scale (CCAS-S: Hoche et al., 2018) has been introduced to capture dimensions executive function (e.g., working memory, abstract reasoning, linguistic functions, visual-spatial functions, memory, and learning). The score ranges from 0 to 120 (maximum points indicate no impairment) and a pass/fail criterion designates a participant as having definite CCAS if they fail three or more of the ten items. A different scale for non-motor deficits is the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005), which is a brief screening tool designed to assess cognitive function, particularly in individuals with suspected mild cognitive impairment. The test evaluates various cognitive domains, including attention, memory, language, visuospatial skills, and executive function. Scores range from 0 to 30, with higher scores indicating better cognitive performance; a score of 26 or above is generally considered normal. However, it is a general scale, widely used across various conditions beyond cerebellar ataxia.

Non-cerebellar symptoms in individuals with ataxia can be captured with the Inventory of Non-Ataxia Symptoms (INAS), which was was introduced in 2008 (Jacobi, Rakowicz, et al.). It assesses neurological features beyond the cerebellum, such as reduced vibration sense and hyper-/hyporeflexia, to reflect broader neurological involvement. Scores range from 0 (no non-ataxia symptoms) to 16 (maximum non-ataxia symptom load).

The Activities of Daily Living subscale of the Friedreich Ataxia Rating Scale (FARS-ADL, Subramony et al., 2005) evaluates the impact of ataxia on daily functioning. This scale captures the degree of difficulty patients experience in daily tasks, with scores between 0 (no impairment in activities of daily living) and 36 (severe impairment).

3.2 Patient-Reported Outcomes (PROs)

Next to demographic questionnaire, which can retrieve basic characteristics like age, sex, and years of education, patients with cerebellar ataxia are often assessed for their medical history, and estimated number of falls and almost falls. Symptoms of depression and anxiety can for instance be assessed with the Patient Health Questionnaire-9 (PHQ-9, Löwe et al., 2002), a tool that evaluates depressive symptoms in clinical populations, with the Hospital Anxiety and Depression Scale (German version: HADS-D, Hermann-Lingen et al., 2011), which measures anxiety and depression symptoms specifically in healthy participants, or with the Beck Depression Inventory (BDI, Beck et al., 1961), which has been widely used in both clinical and research settings, but since it additionally addresses motor impairments, it may be less suitable for patient populations with movement disorders, as their impairments might influence the assessment.

The “Fragebogen zur Allgemeinen Lebenszufriedenheit und Wohlbefinden“ (FAHW, Wydra, 2014) was employed to assess general habitual well-being. According to the scoring guidelines, total FAHW scores between 38 and 50 for men and between 35 and 47 for women are categorized as "average" representing a reference range of well-being in the general healthy population. No reference values are currently available for patients with cerebellar ataxia; however, average scores for rehabilitation patients range between 20 and 30 for men and 18 and 26 for women (Wydra, 2014).

Fall-related self-efficacy can be measured using the Activities-specific Balance Confidence Scale (ABC-D, Schott, 2008). The standard ABC-D scoring is based on percentage ratings from 0% (no confidence) to 100% (complete confidence) across different balance-related activities. Higher percentages indicate stronger confidence in balance and a lower perceived risk of falling. For healthy participants, the scale was modified to a 4-point response format (ranging from "not confident at all" to "absolutely confident") to enhance applicability. This adapted scale yields scores from 16 (maximum confidence) to 64 (minimum confidence), with lower scores indicating greater fall-related self-efficacy.

In patient groups, perceived changes are often assessed using a Patient Global Impression of Change (PGIC) questionnaire. This self-reported measure offers insight into subjective experiences and the perceived impact of, for instance, interventions.

In healthy participants, self-efficacy, optimism and pessimism can be assessed via the SWOP-K9 questionnaire (Scholler et al., 1999). It contained items on self-efficacy (SWOP-SE), optimism (SWOP-OP) and pessimism (SWOP-PS), with scores ranging from 5 to 20, 2 to 8 and 2 to 8, respectively.

3.3 (Digital) Performance-Based Outcomes (PerfO)

Performance-based outcomes encompass both clinician-rated assessments and independent tasks designed to capture digital data. This section first introduces commonly used tests and tasks for evaluating motor function, such as gait and balance assessments. Next, it outlines the parameters extracted from these tasks, which may include measures like stride length, gait speed, or stability.

3.3.1 Assessment Tools and Tasks

Although assessing gait may seem straightforward, it can be evaluated in various ways and through a range of different tools and tasks. In clinical or research settings, the Timed Up and Go Test (TUG, Podsiadlo & Richardson, 1991) is often used as a standard measure for functional mobility, timing the period required for the participant to stand up from a seated position, walk three meters, turn, return, and sit down. Although the TUG test is frequently categorized as a ClinRO, the rater's role is limited to recording the time needed to complete the task, which could also justify considering it a conventional PerfO. The task is conducted once, and lower times indicate greater mobility. Other tests in the field of cerebellar ataxia include the Dynamic Gait Index (DGI), in which 8 gait tasks with varying demands are assessed and scored by a rater (Shumway-Cook & Woollacott, 1996), the Functional Gait Assessment Score (FGA), which contains 7 of the 8 DGI items plus three new, more difficult, gait items (Wrisley et al., 2004), or the Timed 25-Foot Walk Test (25FWT), in which participants need to walk as quickly as possible but safely for 25 foot (Kieseier & Pozzilli, 2012). This test is utilized with adjusted times and distances across various studies (e.g., 6-Minutes walking test or 10-m walk test, 6MWT/10MWT etc.).

Regarding quantitative, digital measures, gait was most commonly assessed in a self-determined pace (Ilg et al., 2010; Seemann et al., 2024); however, in more recent studies different types of gait speed are used, as more prominent relations of gait variability and risk of falling were found for slow gait conditions in cerebellar ataxia (Schniepp et al., 2023) or fast speed conditions in Friedreich's ataxia (Milne et al., 2022). In clinical practice, the tandem gait test is commonly used to evaluate coordination and balance, requiring individuals to walk in a straight line while placing one foot directly in front of the other. It provides information on balance and gait stability, both of which are commonly impaired in hereditary degenerative cerebellar ataxia. Less commonly used tasks include tandem gait on a mattress (Ilg et al., 2016). More recently, turning tasks in an instructed task-based, supervised free, or real-life turning setting have also been analyzed as a relatively new addition to gait tasks (Thierfelder et al., 2021). In general, the distances covered during gait tasks are often constrained by the limitations of the measurement systems and laboratory settings, which makes it challenging to establish standardized conditions. Beyond lab-based gait tasks, recent studies have highlighted the benefits of assessing gait in real-life walking conditions – that is, in unsupervised, unconstrained settings that reflect patients' everyday environments. In these conditions, it is necessary to collect longer walking bouts, since the variability is increased in real-life conditions in comparison to lab-based conditions (Tamburini et al., 2018).

Balance is often assessed in clinical or research settings using the Berg balance score (BBS), in which 14 different tasks are rated by a trained examiner. Similarly, in the Mini-BESTest 14 items are rated to evaluate dynamic balance (Franchignoni et al., 2010). The Limits of Stability test (LoS, Clark et al., 1997) is conducted with a specific assessment tool using force plates, is connected to a computer, and patients are asked to shift their weight in eight different directions. More general tasks to assess digital, quantitative balance outcomes most commonly include stance tasks with varying degrees of difficulty. For example, Ilg et al. (2010) used a dynamic balance task, in which patients stood on a treadmill wearing a safety harness, and were challenged by a short acceleration of the treadmill. In a later study, Ilg et al. (2016) used the Romberg stance (feet together stance with arms outstretched) and assessed it with eyes open, eyes closed, and on a mattress. In a recent study, Shah et al. (2024) investigated six stance tasks in 53 patients with SCA summed up that natural stance with eyes closed and feet together stance with eyes open were the two most reliable and discriminative conditions to discriminate SCA patients from healthy controls. They conclude that tasks should be selected which are both feasible but yet challenging for the patient group. Stance tasks are usually performed for 30 seconds (Ilg et al., 2024; Shah et al., 2024).

For patients in more advanced stages of the disease – such as those requiring a wheelchair or constant use of walking aids – gait and balance measures lose their validity for assessing impairment. In these populations, upper limb impairments are more relevant indicators of disease progression and patient functionality. Little research has been conducted to assess upper limb impairments, though the need for such measures has been increasingly recognized (Németh et al., 2024).

In summary, more complex tasks hold a greater potential to detect subtle changes in motor performance as well as discriminate between early-stage ataxias/ pre-ataxic mutation carriers and healthy controls.

3.3.2 Extracted Performance Outcomes

The training effects observed in the tools and tests are evaluated using various outcome measures. Among the digital gait and balance biomarkers, several categories have been identified that effectively differentiate patients with ataxia from healthy controls (Serrao et al., 2018). For instance, kinematic measures, such as step width, step length and ankle joint of motion, show significant differences between these groups, as do kinetic measures of joint torques, upper body range of motion, and activation patterns of agonist and antagonist muscles.

Several outcome measures have been identified as critical for evaluating gait performance in patients with cerebellar ataxia. These measures focus on specific gait characteristics to shed light on the impact of the condition on movement and stability. Buckley et al. (2018) identified 14 commonly used gait variables, which have become standard metrics in gait research: velocity (average speed over a set distance), cadence (number of steps per second), step or stride length (average distance covered with one step/stride), base width/ step width (distance between the feet), step or stride time (duration of one step or stride), swing phase (leg not in contact with the ground), stance phase (leg in contact with the ground), double support phase (both legs in contact with the ground), and variability of step length, stride length, stride time, and speed. These variables are integral for analyzing gait patterns and assessing the effectiveness of interventions.

Recent studies have increasingly focused on gait outcome measures with high sensitivity to better characterize ataxic gait and detect subclinical changes. Among these measures, spatiotemporal variability metrics, particularly step length and step cycle time variability, have proven to be effective indicators of gait abnormalities associated with cerebellar ataxia (Ilg et al., 2016; Seemann et al., 2024). Such measures capture subtle changes in gait patterns that may not be evident with traditional metrics alone.

In balance tasks, the most commonly used features are sway area (usually measured as 95 % confidence ellipse area of sway), sway path (e.g., length of blue line in Figure 2), and sway velocity (path length covered per time) (Ilg et al., 2016; Shah et al., 2024).

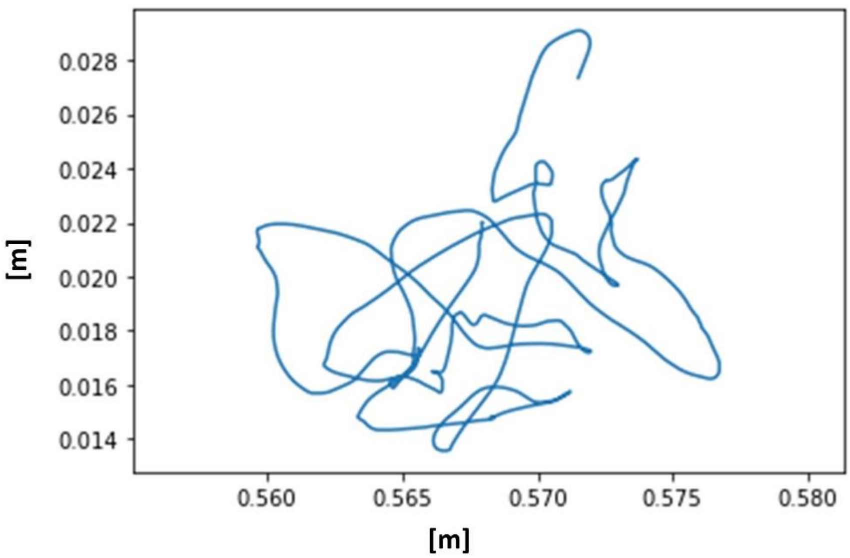

Figure 2: Representation of a sway path in the horizontal plane, with displacement values provided in meters.

3.3.3 Consensus Recommendations for Gait and Balance

Expert groups with members from all over the world have been collaborating to create a framework for future trials with ataxia patients, including recommendations for an optimized study protocol with defined tasks and outcome variables (Ilg et al., 2024). The recommended basic protocol includes three gait tasks (2-minute walk in a natural pace, 2-minute walk in a slow pace, and 1-minute walk in a fast pace for Friedreich's ataxia patients), in which variability of step length, lateral step deviation, foot rotation, double support time, and transverse and coronal trunk range of motion should be assessed. The three stance tasks include a 30-second normal stance with predefined foot placement, the same task with eyes closed, and 30-second feet together stance with eyes open. Recommended measures are sway area, root mean square sway, sway velocity and sway path. Last, a "T-turning" task is included in the protocol, in which participants are supposed to walk in a "T" (each side 5 m), two times with right turns and two times with left turns. Here, turning speed, duration, and lateral velocity change for stability should be measured.

For those participants in early disease stages or even pre-ataxic mutation carriers, more challenging tasks are supposed to be conducted in addition. These include a tandem walk (2 x 8 m) with the outcome measures lateral trunk range and variability of stride duration, a 30-second tandem stance with eyes open and a 30-second feet together stance with eyes closed, including the same outcome measures as the stance tasks in the basic protocol.

4 Measurement Instruments for Gait and Balance

Digital measures of gait and balance provide an observer-independent, objective, quantitative approach for detecting abnormalities, distinguishing between populations (e.g., healthy adults and patient groups), and assessing changes following interventions, such as training programs or clinical trials. In ataxia, several digital gait and balance measures have been found to be particularly sensitive to subtle changes, enabling the distinction between healthy controls and patients with hereditary degenerative cerebellar ataxia, and even between healthy controls and pre-ataxic mutation carriers (Ilg et al., 2016; Thierfelder et al., 2021). Longitudinal observations, however, are relatively scarce at the moment and the current Ataxia Global Initiative Working Group on Digital Motor Biomarkers suggested to increase the effort for international, longitudinal trials to determine trajectories of digital measures and capture biomarkers of disease progression (Ilg et al., 2024).

Various methods are available to measure digital gait and balance outcomes in both healthy individuals and patients. These include video-based motion capture, gait carpets (force plates), inertial measurement units (e.g., integrated into wearables or smartphones), and electromyography (EMG). Video-based motion capture, force plates and inertial measurement units can be regarded as the gold-standard, with providing highly accurate assessments that can detect subtle differences in gait and balance performance between healthy individuals and those with various conditions or across different age groups (Ilg et al., 2024). These advanced systems are capable not only of distinguishing between different stages or severities of disease but also of tracking changes in performance over time. This makes them invaluable tools for monitoring disease progression and evaluating the effectiveness of interventions in clinical and research settings. Video-based systems, such as the Vicon 3D system, capture movement through cameras and reflective markers to collect precise spatial data on body positions and motions. Their disadvantages include high cost, significant resource requirements, and limited portability. Force plates use capacitive pressure sensors to capture the distribution of pressure during gait and stance, providing insights into balance and weight transfer. They are very accurate in their spatiotemporal resolution, but limited to laboratory settings and on walkway length. Inertial measurement units (IMUs) record angular velocity, acceleration, and the earth's magnetic field, producing highly accurate data on movement dynamics. Those sensor-based measurements have shown more sensitivity in comparison to clinician-rated outcomes and lab-based gait measures (Seemann et al., 2024). When embedded in wearables or smartphones, IMUs are especially practical and have seen increasing use in recent years. A recent consensus guidance by the Ataxia Global Initiative Working Group on Digital-Motor Biomarkers (Németh et al., 2024) summarized that the emerging field of smartphone-based measurements hold the potential to be reliable, valid, and accurate outcome measures, and can improve adherence and measurement frequency. They suggested a basic protocol for future studies in this field. A notable advantage of IMUs is their ability to record free walking (real-life walking), which has been shown to yield more realistic gait patterns and improve both the accuracy and ecological validity of assessments. Disadvantages include the fact that metrics like velocity must often be inferred from acceleration data, which can introduce inaccuracies. Additionally, specialized algorithms are required to accurately extract and interpret gait and balance parameters, adding complexity to the analysis process. Smartphones used as wearable sensors are less precise but provide the greatest accessibility and ease of use, making them ideal for large-scale studies or at-home monitoring over longer time periods (e.g., to capture real-world data) where cost and convenience are prioritized.

Less common analysis tools, each with unique advantages, include EMG-based methods and gaming-based methods such as the Microsoft Kinect. EMG and surface EMG allow for the observation of muscle activation patterns during gait, providing valuable insights into neuromuscular coordination (Fiori et al., 2020; Mari et al., 2014). The Microsoft Kinect, originally developed for gaming, offers a low-cost, flexible option for at-home assessments. Although studies on its use with ataxia patients are limited, early results are promising, suggesting potential for reliable gait analysis in less controlled environments (Honda et al., 2020; Summa et al., 2020). However, its primary limitation is the small recording space, which results in a reduced captured walkway.

In summary, wearable IMU sensor technology has been recommended as the most appropriate technology to conduct multicenter gait and balance trials in ataxia, as its usage does not require special laboratories or staff. They are easy to use, portable, and suitable for recording longer gait distances and for daily life monitoring. Three sensors (lower lumbar spine, and on the top of each foot) seemed to be the optimal trade-off between data quality and participants burden (Ilg et al., 2024).

5 Practical Applications of Gait and Balance Assessments: Evidence and Relevance for Ataxia

This chapter explores how the tools, tasks, and outcome measures described earlier, can be practically applied in distinguishing patients with ataxia from healthy controls. Drawing from the literature, we highlight examples that demonstrate the utility of these assessments in clinical and research contexts, showcasing their ability to detect impairments, monitor progression, and evaluate the effects of interventions. The validity of motor biomarkers and digital performance outcomes designed to quantify ataxia-related motor deficits is often supported by comparisons and correlations with established clinical scales such as the SARA and ICARS (Schmitz-Hübsch, 2023).

Regarding gait tasks, Ilg et al. (2016) found that straight walking was able to distinguish healthy controls and patients in early ataxic stages, while in tandem gait conditions even pre-ataxic mutations carriers could be distinguished from healthy controls. Tandem gait is particularly sensitive to cerebellar dysfunction, as it requires a high degree of coordination and balance that many patients with cerebellar ataxia find difficult to maintain. Consequently, the tandem gait test is recognized as one of the most reliable clinical indicators for early detection of ataxia and related balance issues (Stolze et al., 2002). Also, the tandem gait test on a mattress successfully detected differences between pre-ataxic mutation carriers and healthy controls (Ilg et al., 2016). Similarly, turning tasks in an instructed task-based, supervised free, or real-life turning setting demonstrated strong potential for distinguishing between pre-ataxic mutation carriers and healthy controls and showed sensitivity to longitudinal changes over a one-year period (Thierfelder et al., 2021).

Regarding digital performance-based outcomes, gait velocity, mean step length, and step length variability are particularly valuable in monitoring disease progression in cerebellar ataxia (Ilg et al., 2018). Spatiotemporal gait measures and movement smoothness are increasingly recognized as effective tools for distinguishing between patients with cerebellar ataxia and healthy individuals, as well as for detecting subclinical changes in gait. Measures of variability, particularly those focusing on stride and step consistency, have shown high sensitivity in identifying gait abnormalities associated with cerebellar ataxia. Ilg et al. (2020) demonstrated that metrics such as the stride length coefficient of variation ($StrideL_{CV}$) and stride time coefficient of variation ($StrideT_{CV}$) are especially valuable in differentiating between patients and healthy controls during unconstrained walking. Among these metrics, lateral step deviation (LatStepDev) and spatial step variability compound measure (SPcmp) exhibited the highest effect sizes, highlighting them as particularly sensitive indicators of gait irregularities in patients with ataxia. This was supported by a very recent study of Seemann et al. (2024), who found that the mentioned measures of spatiotemporal variability, and in particular SPcmp, showed cross-sectional sensitivity and longitudinal sensitivity to change at one year, as well as high correlations to patient-reported outcomes (ABC-D) and clinician-reported outcomes (SARA). Additionally, research has shown that gait measures can discriminate between patients with the worldwide most frequent type of spinocerebellar ataxia (type 3, SCA3), and healthy controls at both preferred and slower walking speeds (Ilg et al, 2022). This differentiation has also been observed across other types of cerebellar ataxia, as well as between different stages of ataxia severity (Ilg et al., 2020), underscoring the diagnostic utility of these measures.

Gait variability has further implications for patient safety. Schniepp et al. (2023) identified increased gait variability as an independent risk factor for falls, highlighting the importance of assessing and monitoring variability measures to predict fall risk in patients with ataxia.

With respect to balance outcomes, differences in body sway were found for early ataxic stages as well as for pre-ataxic mutation carriers compared to healthy controls (Ilg et al., 2016). Shah et al. (2024) found the most discriminative features to be path length (total length of sway (acceleration) trajectory), sway range (range of the displacement (acceleration)), sway area (area of an ellipse covering 95% of the sway (acceleration) in both the coronal and sagittal planes) and root mean square sway (the root mean square (RMS) of the sway (acceleration) in both the coronal and sagittal planes).

6 Training Gait and Balance

Gait and balance performance decline with advancing age, the presence of diseases, or reduced physical activity levels. Physical training or motor interventions are primarily employed when there is a desire to improve these physical functions, typically focusing on patients or older adults who already experience impairments. Although younger or middle-aged healthy individuals do not necessarily require such interventions, as their functions are usually intact, it is a common procedure for studies to use incorporated control groups consisting of healthy participants (Ippisch et al., 2022; Jacobi, Rakowicz, et al., 2013; Kroneberg et al., 2024). Including healthy individuals as a reference group allows researchers to determine whether observed effects are universal or specific to certain conditions. A growing number of studies investigates the effects of home-based training compared to in-person training in various populations. Chaabene et al. (2021) concluded in their systematic review and meta-analysis on healthy older adults that even though supervised training programs are known to have larger effects, home-based training is effective to improve physical fitness (e.g., muscle strength, balance) in healthy older adults. Training effects were found to be stronger if the protocol included > 3 sessions per week and ≤ 30 minutes of training. However, in healthy, middle-aged populations, which could serve as a comparison group for patients with cerebellar ataxia, this remains a relatively underexplored area. Further studies have examined video-based physical therapy for various impairments and disorders, including shoulder joint replacement (Eriksson et al., 2011), rotator cuff tears (Türkmen et al., 2020), knee problems (Kim et al., 2016), cardiopulmonary diseases (Hwang et al., 2015), and stroke (Redzuan et al., 2012). The results of these studies indicated that those telerehabilitation methods have been well accepted, and a promising alternative to center-based exercise.

In the case of ataxia, the situation is markedly different. Training studies aimed at improving gait and balance are more frequent, as these functions are among the most affected in this population. Additionally, medication options for cerebellar ataxia are very limited, making therapeutic approaches like speech therapy, occupational therapy, physiotherapy, and physical activity the most common strategies for symptom improvement (Fonteyn et al., 2014; Ilg et al., 2014). According to patient surveys, exercise was the number one strategy to help them feel better, accompanied by physiotherapy, social interaction and relaxation (Gorcenco et al., 2024). While physiotherapy is the most common therapy for ataxia patients with the most profound evidence, there were several other forms of training being explored. Studies in this field vary widely in their training methods, duration, intensity, settings (e.g., inpatient, outpatient, or home-based), and outcomes assessed, making it difficult to compare results directly or establish standardized protocols.

In detail, training methods varied widely and included intensive coordinative training (Ilg et al., 2010; Ilg et al., 2009), balance training (Keller & Bastian, 2014), balance and coordination training with and without vibrotactile sensory augmentation (Jabri et al., 2022), gait training on a treadmill (Brito et al., 2024), cycling training (Barbuto et al., 2023), Tai Chi (Winser et al., 2022), exergaming (exercise-focused video games, Ayvat et al., 2022), and virtual reality training (Bonanno et al., 2024). All approaches demonstrated improvements in gait, balance, or clinical scores to varying extents.

Most studies employed long-term interventions ranging from 1 to 6 months (Ayvat et al., 2022; Barbuto et al., 2023; Bonanno et al., 2024; Jabri et al., 2022; Keller & Bastian, 2014; Milne et al., 2024; Winser et al., 2022), while a smaller subset examined short-term interventions lasting 5 days to 4 weeks (Brito et al., 2024; Ilg et al., 2010; Ilg et al., 2009). Again, both intervention types led to improvements, but due to the heterogeneity of the studies, it is difficult to determine whether one approach is superior or has stronger effects.

Training frequencies also varied significantly across studies. Common approaches included sessions of 60 minutes, 3 times per week (Ayvat et al., 2022; Ilg et al., 2010; Ilg et al., 2009; Winser et al., 2022), or 30 minutes, 5 times per week (Barbuto et al., 2023; Jabri et al., 2022). Other frequencies included 45 minutes, 3-4 times per week (Bonanno et al., 2024), 25 minutes daily for five days (Brito et al., 2024), 20–30 minutes on 4-6 days per week (Keller & Bastian, 2014), and longer sessions of 2 hours on 3 days per week or 1 hour on 5 days per week (Milne et al., 2024). However, only one of these studies provided a clear rationale for their chosen training frequencies (Milne et al., 2024), leaving this aspect open to further investigation.

The majority of the studies included outpatient programs which required participants to attend training sessions on-site (Ayvat et al., 2022; Bonanno et al., 2024; Brito et al., 2024; Ilg et al., 2010; Ilg et al., 2009; Milne et al., 2024; Winser et al., 2022), which creates practical challenges, particularly by adding the burden of frequent travel. Given that ataxia is a rare condition, not everyone has access to such facilities, especially those living in rural areas. This underscores the need for a more flexible solution that, for example, allows patients to engage in training at home. Evidence from multiple studies reinforces this idea, showing that continuity in training is essential for achieving long-term benefits (Ilg et al., 2010; Ilg et al., 2009), hence it may be beneficial for participants to establish a routine of practicing at home and integrating exercise into their daily lives to achieve long-term improvements in their health and performance. While some studies have examined the combination of outpatient programs and home-based training (Ilg et al., 2010; Ilg et al., 2009; Milne et al., 2024), there is limited research focusing solely on home-based training (Barbuto et al., 2023; Jabri et al., 2022; Keller & Bastian, 2014). Milne et al. (2017) summarized various types of rehabilitation programs for patients with genetic degenerative ataxia, whereof four studies also included a home-based training (Bunn et al., 2015; Chang et al., 2015; Félix et al., 2014; Keller & Bastian, 2014). However, the training of only two of the studies focused on balance exercises (Bunn et al., 2015; Keller & Bastian, 2014), while the other two addressed inspiratory muscle training and cycling. The authors of the systematic review also noticed that out of 17 selected studies only 5 were randomized controlled trials (Bunn et al., 2015; Chang et al., 2015; Kaut et al., 2014; Miyai et al., 2012; Seco Calvo et al., 2014), whereof one among the home-based trainings (Bunn et al., 2015). A few years later, He et al. (2021) concluded in their review about balance and coordination training in degenerative ataxias, that most home-based training programs yielded positive results. While the outcomes were not as good as those from conventional training methods, they still demonstrated improvements over baseline levels and indicated long-term benefits.

Technical advancements are increasingly enabling the translation of site-based assessments of clinical scores and interventions to home-based settings. This shift is particularly beneficial for patients with rare diseases like hereditary degenerative cerebellar ataxia, as it reduces the need for frequent travel to specialized centers, saving time and reducing physical strain. For example, tools such as the SARAhome and SaraHome have been developed to assess ataxia severity remotely (Grobe-Einsler et al., 2021; Summa et al., 2020). In line, home-based training interventions, supported by video-guided exercises or app-based platforms, are gaining popularity and provide a practical way for patients to integrate therapy into their daily lives. Such approaches hold significant potential for enhancing patient-relevant outcomes, improving quality of life, and facilitating personalized, continuous care in the management of hereditary degenerative cerebellar ataxias.

Training effects are supported by imaging studies that demonstrate reorganizational processes within the brain. Evidence suggests that the cerebellum exhibits a form of plasticity, meaning that even when affected by disease, it retains some capacity to reorganize and mitigate deficits (Mitoma et al., 2020). For example, as little as 90 minutes of balance training over two weeks has been shown to produce structural changes in cortical gray and white matter (Taubert et al., 2010). Training has been found to improve cerebellar circuitry function and increase cerebellar gray matter volume, although to a lesser extent than in healthy individuals. More substantial changes, however, have been observed in cerebral gray matter volume compared to healthy controls (Burciu et al., 2013). In patients recovering from cerebellar stroke, nearby cerebellar regions can compensate for impaired function. In contrast, in hereditary degenerative cerebellar ataxias, compensation appears to rely more heavily on unaffected cerebral structures, such as the premotor cortex (Burciu et al., 2013; Ilg et al., 2014).

The variety of tests and outcome measures used in existing studies complicates comparisons and meta-analyses. Standardized methodologies and protocols are crucial to ensure the validity of assessments and enhance the evaluation of short- and long-term interventions across diverse settings. In conclusion, there is a clear need for further research into home-based training for patients with hereditary degenerative cerebellar ataxia, particularly through randomized controlled trials (RCTs). These studies should focus on defining optimal training protocols, including content, duration, and frequency, to better tailor interventions to meet the needs of patients with gait and balance impairments. To address these issues and enable multicenter, international studies, the recommended consensus protocol on gait and balance outcomes for ataxia trials (Ilg et al., 2024) should be used in future studies.

7 Research Focus and Objectives

This dissertation aimed to investigate the effect of a three-week, video-based gait and balance training program at home in ambulatory patients with hereditary degenerative cerebellar ataxia. To accomplish this, two distinct studies were conducted. The first study was a feasibility study involving healthy participants. This study aimed to assess whether the training protocol is feasible and effective in a healthy population, and to evaluate how sensor placement (either on the front or back of the body) impacts the accuracy of movement measurements. Additionally, this study served as a preliminary test to identify any technical challenges that could arise when implementing the training program in a clinical setting. The second study applied a similar approach to a group of patients with mild to moderate hereditary degenerative cerebellar ataxia. This study aimed to investigate the impact of the chosen training protocol on gait and balance outcomes in this clinical population. Additionally, it examined whether different training parameters, such as the distribution of training frequency and duration, influenced the efficacy of the program. Furthermore, the study explored how baseline clinical variables, such as disease severity or well-being, might interact with training outcomes, providing insights into which patients could benefit most from this type of intervention.

In the first study, we found similar improvements for the intervention group, receiving a three-week, video-based training at home and performed weekly gait and balance tests at home, and the control group, which just repeated the weekly tests but received no intervention. In a different sample of healthy adults, the placement of wearable sensors (smartphone in a waist bag at the lower lumbar spine vs. at the lower belly) did not influence the measurement accuracy in normal gait. In conclusion, training and repeated task performance equally contributed to the improvement of the measured gait and balance variables, and wearable sensors (smartphones) can be worn both on the lower abdomen and the lower back in gait and balance analyses.

In the second study, the protocol was adapted based on the results of the first study. In detail, a baseline measure was conducted before the three-week training in order to reduce habituation effects, and the more convenient sensor placement at the front of the body was chosen for the smartphone used as wearable device. While the recording was conducted simultaneously with force plate, motion capturing system, and smartphone, similar to the first study, in the second study we only evaluated the force plate gold-standard outcomes to focus on the training effect rather than on the system comparison. Similar to the study with healthy participants, we found no difference between the control group, which received standard medical care, and the intervention group, which performed a three-week, video-based training program at home. The training program was adapted based on the abilities and needs of the patient population. Although the distribution of training sessions did not significantly influence gait and balance outcomes, an interesting trend emerged among patients with mild to moderate ataxia: those with greater disease severity and higher baseline well-being showed more notable improvements from pre- to post-intervention. Additionally, an exploratory analysis suggested that longer, less frequent training sessions (e.g., two 40-minute sessions per week) might be more beneficial than shorter, more frequent sessions (e.g., four 20-minute sessions per week).

Overall, the insights gained from these two studies contribute to a deeper understanding of the feasibility and effectiveness of short-term, video-based gait and balance training in patient and healthy populations. They provide valuable information on the potential of home-based, sensor-monitored interventions and lay the groundwork for future research into optimizing at-home rehabilitation for patients with hereditary degenerative cerebellar ataxia.

V. Study 1

1 Introduction

Gait disorders affect about 32 % of the elderly population and are associated not only with lower quality of life and increased fall risk but also with cognitive decline and depression (Mahlknecht et al., 2013; Verghese et al., 2006). When evaluating participants over time, and especially when assessing an intervention, it is important to distinguish the effects of the intervention from the habituation effects of performing a test multiple times. While such “practice effects” or habituation effects are well known in neuropsychological tests (Vincent et al., 2018; Weitzner et al., 2021), less knowledge is available on motor tasks, and specifically gait and balance. Meyer et al. (2020) found habituation effects of up to 50 % of the clinically meaningful detectable change in patients with multiple sclerosis, when performing functional mobility and gait tests on three consecutive days, and recommended that training tests should be performed before the actual assessment to mitigate the habituation effect. Similarly, Keklicek et al. (2019) found an habituation effect between the first and second trial in a balance test in healthy participants, supporting the need for training tests prior to observation in stance tasks. However, Salthouse et al. (2004), after analyzing six different cognitive tasks, reported that it might take up to seven years until no retest effect can be found.

Building on the importance of training effects in assessing gait and balance, it is crucial to consider how these outcomes are measured in real-world settings. Advances in wearable technology now allow for the monitoring of gait in everyday environments (Christensen et al., 2022; Su et al., 2021). One consideration in such measurements is the placement of sensors. In systematic reviews (Prasanth et al., 2021; Schniepp et al., 2016), pelvis, shank, and feet have been named as the preferred segments for wearable sensor placement. Studies using the pelvis mostly placed the wearable sensor or smartphone at the lower back (for review, see Hubble et al., 2015 or Ilg et al., 2024), since it is close to the center of mass and movement there reflects the movement of the rest of the body (Furrer et al., 2015; Kuntapun et al., 2020; Rucco et al., 2018). Likewise, standard gait measurement systems like Mobility Lab use one of their sensors at the lower back by default (L5 region). Differences in sensor placement have been assessed in several studies, but those studies only compared sensor placement on different segments of the body (e.g., pelvis vs. feet), not different placements on one specific segment (e.g., lower back or lower abdomen used as the “pelvis segment”) (Hsu et al., 2018; Lyu et al., 2022; Niswander et al., 2020). In everyday life or during studies, when using a smartphone as wearable sensor, carrying the phone on the front of the body may be preferred for easier handling (Su et al., 2021), especially for older adults or patients with motor impairments. It is necessary to understand if placing the device at the front or back of the body affects the results of the gait analysis, as improved user-friendliness would facilitate the implementation of the technology in clinical trials, and the remote recording of gait and stance in patient's everyday life.

In this study, a control group was examined that did not undergo the training intervention but completed weekly gait and balance tests, which were also assessed at the study visits. This approach allowed to distinguish between training and habituation effects in healthy adults, and contextualize prior findings from a three-week exercise intervention in healthy adults (Rentz et al., 2022), which is crucial not only for interpreting the outcomes of motor performance assessments but also for applying these findings to patient populations. Additionally, the present study investigated the accuracy of gait and balance outcomes using a smartphone placed on the front vs. on the back of the trunk in comparison a gold-standard standard method (force plate). This helped determine whether the back placement is necessary for more precise measurements, or if the patient-friendly front placement could be recommended for future patient studies without compromising accuracy, as it simplifies the feasibility of gait and balance assessments.

2 Materials and Methods

For the analysis of habituation effects, 26 healthy participants were recruited to perform weekly gait and balance tests (21 right-handed, 12 female, 38.3 ± 17.4 years old). For the re-analysis of training effects, this sample was compared to 25 participants from a previous feasibility study (Rentz et al., 2022), receiving home-based video training in addition to the weekly gait and balance tests (23 right-handed, 13 female, 44.1 ± 18.4 years old). The groups did not differ in their height, weight, educational level, or anxiety and depression score. For analyzing the impact of sensor placement on gait and balance analysis, 32 participants were recruited (37.1 ± 15.7 years old).

The training protocol was set up and recorded by an experienced physiotherapist, specialized on sports therapy, and based on sport-scientific knowledge of the physiotherapist and the author. The total training duration and session length were modeled after standard physiotherapy practices, which typically involve 6-12 sessions of approximately 20 minutes each, and based on literature, which suggests a drop in study compliance after three weeks (Haines et al., 2009). All exercises were conducted as part of the additional exercise program, designed to complement, rather than replace, individual training or physiotherapy. The exercises focused on three key aspects of gait and balance improvement: coordination, strength, and mobility. Each video/training session consisted of all three of these key aspects. Exercises were repeated throughout the whole training program, and the difficulty level increased. Coordination exercises were based on the key motor control and coordination skills defined by Hirtz (1985): Differentiation, orientation, reaction, balance, and rhythm ability. They were carried out in different variations and included fine motor exercises like “Rabbit and Hunter” (on one hand only the index and middle finger are extended, like a “peace” sign or like the ears of a rabbit, on the other hand, only thumb and index finger are extended, like a gun. The two signs shall be switched between the two hands as fast as possible, with the gun always pointing at the rabbit), as well as gross motor exercises like ball throws and catches in different positions, and coordinative skipping tasks, or combined the two aspects (stance tasks on different surfaces). Mobility exercises were included for the following reasons: With sufficient mobility, people can perform movements faster and more economically, which might also help to prevent falls. On the other hand, if mobility is restricted, this can lead to poor posture, increased risk of injury and limitations in everyday motor skills (Friedmann, 2009). Exercises included stretching muscles and moving all joints through their full range of motion. Regarding strength training, the exercises were specifically chosen to target the muscles most involved in gait and balance, like gluteus maximus, gluteus medius, vasti, soleus, and gastrocnemius (Pandy & Andriacchi, 2010). Some of the strength exercises were purely strength exercises, while others included aspects of coordination and mobility (e.g., lunges with turning the body sideways, conscious slow gait tasks). The content of one session was shortly repeated in the next session, to stabilize the learned skills, and increased in the level of difficulty in the following. Alternatives for an easier or more difficult version were mentioned in each video (e.g., using Swiss balls/ exercise balls instead of a common chair for sitting exercises).

2.1 Experimental Tasks and Procedure

Participants had two study visits (T1 and T2) in Düsseldorf, Germany. At the study site, participants of the habituation vs. training effects cohort performed gait and balance tests, consisting of three different gait tasks (normal, backward, and tandem gait) and four different stance tasks (feet together, tandem, single leg stance, and feet together stance with eyes closed) on a force plate (4.24 m, zebris Medical GmbH, Isny, Germany). In addition to the force plate, data were measured by a motion capturing system (Mocap System, Xsens Technologies B.V., 2024, Enschede, Netherlands) and individual smartphones of the participants (with the app JTrack Social installed, Far et al., 2021). The participants’ smartphones were placed in waist bags at the lower abdomen. Only in the group to test sensor placement, the waist bag was placed at the lower back and lower abdomen successively.

Participants were instructed to walk at a normal pace for the gait tasks and move as little as possible for the stance tasks. The maximum duration for a stance task was set to 30 s, but time was stopped if the participant held onto something or changed their foot position. During the three-week period at home, both groups repeated the seven gait and balance tests once a week at home. The intervention group additionally performed four trainings per week, 20 min each, containing mobility, strength, and coordination exercises, described above. The participants' self-efficacy, optimism and pessimism (SWOP-K9), general habitual well-being (FAHW), and their self-efficacy in relation to falls (ABC-D) were assessed via questionnaire. At the second study visit, participants repeated the gait and balance tests and completed the FAHW, SWOP-K9 and ABC-D questionnaires.

In the separate sample to test sensor placement, participants had only one study visit and performed normal gait across the force plate at their normal pace. This task was performed twice for two minutes each, once with the waist bag at the lower back and once with the waist bag in front on the lower abdomen.

2.2 Data Analysis

Differences in distribution of sex and handedness were assessed via chi-squared tests, while differences in age, height, weight, years of education, anxiety and depression scores were assessed via t-tests. A Mann-Whitney test was conducted to compare time spans between the two study visits and the number of missing data collection points at home.

To analyze whether changes in questionnaire scores and gait and balance variables have occurred between the two study visits, paired t-tests were conducted. Independent samples t-tests were used to compare mean differences between sensor placement at the front vs. back. Following the previous publication of the intervention group (Rentz et al., 2022), Bonferroni correction for multiple comparisons with *p*-values of less than 0.013 (force plate, mocap system) and 0.017 (smartphone) were used for gait, and $p = 0.025$ for balance tasks. For all other statistical analyses, a *p*-value of less than 0.05 was considered significant. To examine the relationship between sensor placement (difference between front and back) and body weight of the participants, Spearman's rank correlation was calculated. The Minimal Detectable Change (MDC) was calculated at the 90 % and 95 % confidence levels. The reliability of measurements was assessed using the intraclass-correlation coefficients (ICCs) with two-way random effects models.

Boxplots of all gait and balance variables were examined, and extreme outliers, defined as values greater than 3 times the interquartile range above the third quartile, were excluded.

To examine group differences and interaction effects, linear models with fixed and random effects were used as the statistical approach. A linear model using generalized least squares was applied to describe how group (intervention or control), and measurement time (study visit 1, T1, or study visit 2, T2) influenced the outcomes of questionnaire scores. A linear mixed-effects model was applied to assess how the gait or balance variables (cadence, stride time, and velocity for gait; sway area, and velocity for balance) were influenced by group, measurement time, and measurement system used (force plate, Mocap System or smartphone). The same model was used separately for the different gait and balance tasks (e.g., backward gait, tandem stance). Pairwise comparisons were used to highlight meaningful differences; however, they may not have captured all nuances of the interaction between factors. With a generalized least squares fitted linear model, the influence of the measurement system, and the placement of the waist bag (front, back) on the gait variables were described.

3 Results and Discussion

When comparing mean differences of questionnaires, and gait and balance outcomes of the first and second study visit, we found no improvements in self-efficacy, optimism and pessimism, general habitual well-being, and self-efficacy in relation to falls, but significant improvements in gait and balance outcomes in both the control group and the intervention group after the three weeks of training. However, there was no overlap regarding the involved variables between both groups: In the control group, participants performed better after three weeks of repeating the gait and balance assessments in five variables related to the more difficult gait tasks (backward and tandem gait), while they performed worse at the second study visit in the single leg stance. Participants of the intervention group also performed better in (a different set of) variables related to backward and tandem gait, but also in normal gait and tandem stance (eleven improvements in total). The highest overlap between the two groups was found in the backward gait measured with the force plate, where all corresponding variables in the respective other group showed trends for significance (significant before Bonferroni correction), indicating a tendency for habituation effects, which would be in line with literature (Keklicek et al., 2019; Meyer et al., 2020). The additional improvements in normal gait and tandem stance could be interpreted cautiously as indicator of a training effect of a short-term training of three weeks, which is stronger than the habituation effect. Especially in normal gait, this would be in line with other training interventions of similar duration, even though they addressed different populations (Alizadehsaravi et al., 2022; Yang et al., 2005). To contextualize the findings, the Minimal Detectable Change (MDC) was calculated and showed that the changes observed within each group applying paired t-tests were not large enough to exceed measurement error and variability.

While in the setting of the current study it was not possible to check whether and to what quality the measurements and training were carried out at home, except for oral feedback of the participants, the number of unsubmitted smartphone recordings of the gait and balance assessments at home were low and showed no statistical difference between the two groups.

Secondly, advanced statistical models (linear mixed effect models) provided detailed insights into gait and balance improvements or declines based on group, variable, and measurement system. A complex interaction of all the mentioned factors was found only in the feet together stance with eyes closed and eyes open. However, the resolution of the interaction showed increased sway area (worse performance) over time, contradicting a training effect. While similar results have been found for a control group in another study (Uematsu et al., 2023), it contrasts literature on groups that underwent training (Conner et al., 2023), potentially due to task familiarity and reduced focus. In all other tasks, interactions were found between some of the mentioned factors only. In tandem stance, the gait or balance outcome showed differences dependent on group, and measurement system used. A difference in sway area was revealed between intervention and control group when measured by smartphone (higher sway area in the intervention group) or Mocap System (higher sway area in the control group), as well as a difference between the measurement systems for sway area in both groups (higher sway area for Mocap System compared to smartphone and force plate, and for force plate compared to smartphone). Both results indicated that these two measurement systems are not yet highly comparable. Such differences in measurement systems are known (Karlinsky et al., 2022; Rashid et al., 2021; Reimer et al., 2022), and should be minimized in the future. In single leg stance, an interaction between variable, measurement time and measurement system used revealed differences in sway area between intervention and control group at T1 and an even greater difference at T2 (higher sway area in the control group). For normal gait, a general difference in step width between force plate and Mocap System (higher step width for force plate) and in step width between T1 and T2 in general, not depending on the group or measurement system (lower step width at T2), was depicted. This might indicate that participants were able to improve their gait stability, as indicated by lower step width, between the first and second study visit, independent of group affiliation, hinting towards a potential habituation effect. In backward gait and tandem gait, an interaction was found between the variable, group, and measurement system used, independent of the measurement time (T1, T2). In backward gait, the resolution of interactions revealed a difference in the step width between the two groups when measured with the Mocap System (lower step width in general for the intervention group) and a difference in step width between the force plate and the Mocap System in general (higher step width for the force plate). In tandem gait, the resolutions again revealed a difference in step width between the two groups (lower step width for intervention group, measured with the Mocap System), a difference in cadence between the two groups (higher cadence in the intervention group, measured with the smartphone), as well as a difference in step width between the force plate and the Mocap System in general (higher step width for the Mocap System in both groups). These results of backward and tandem gait hint towards an overall better gait performance of the intervention group, and to differences in measurement accuracy of the measurement systems used, likely attributable to the way these measurement systems operate (pressure capacitive sensors vs. acceleration-based sensors). Overall, the findings did not support the presence of a distinct training effect that exceeds mere habituation or practice effects. This could be because practicing the tasks may have been similarly or more challenging than training, leading to improvements through repetition.

To addresses differences between specific sensor (smartphone) placement at the pelvis (lower back vs. lower abdomen), it was investigated how measurement system and sensor placement interacted with the gait or balance outcome. These findings revealed that the placement of the sensor (front vs. back) did not have an overall influence on the outcome variable. This was supported by the lack of mean differences between smartphone and force plate values (same task, same variable), when compared between front vs. back sensor placement. The results supported the use of wearable sensors in a manner that is most convenient for participants, ideally leading to greater study adherence and lower drop-out rates. Additionally, this increased comparability to other studies which might have used a sensor placement at the lower back. Differences between front and back placement were only weakly correlated to body weight. As the sample of in average normal weighted adults included one underweight adult and three adults with obesity, a generalizability of these findings to a diverse and representative population was suggested. Gait and balance outcomes however showed differences, depending on which measurement system was used.

4 Conclusion

Understanding how unintended habituation or training effects in control groups could obscure a potential group-specific effect in the actual target population is crucial for accurately interpreting intervention outcomes (e.g., in patient groups when compared with healthy control subjects) and for ensuring the relevance of findings in a clinical setting. The reported findings helped to understand how much of the observed improvement might be due to specific training versus general familiarity with the tasks. While it cannot directly be inferred how these improvements would differ in patients, establishing this baseline in healthy subjects was a critical step toward interpreting studies comparing patient data to a control group more accurately.

Habituation effects were addressed by comparing an intervention group (Rentz et al., 2022), performing a three-week gait and balance training, to a control group without additional training. Both the training and habituation effects resulted in significant improvements in gait and balance after a three-week period of either weekly tests alone or a combination of training and weekly tests. However, these improvements remained below the calculated measurement error and variability. While the additional gait and balance training did not seem to generate a measurable additional benefit in healthy controls, the overall positive impact on motor function was promising. This indicated that even minimal interventions could possibly lead to detectable changes in gait and balance in healthy adults and that more intensive training may be necessary to produce distinct training effects. These insights are important for contextualizing patient data, as they provide a baseline for understanding how different types of interventions might influence outcomes in a clinical setting. Based on the results and limitations of the current study, for future investigations addressing video-based training at home, we recommended to implement monitoring of tasks performed at home (e.g., tracking, regular calls) and at least one baseline measure to reduce habituation effects. In addition, the analysis of the sensor placement (lower abdomen vs. lower back) showed comparable values in healthy adults, which leads to the conclusion that a smartphone as a wearable sensor could also be worn in the position on the lower abdomen, which is probably more comfortable and easier to access for study participants.

VI. Study 2

1 Introduction

Progressive impairments in gait and balance are among the main challenges for patients with hereditary cerebellar ataxia in everyday life. According to patients' reports, exercise and physiotherapy are among the most effective supportive measures that are currently available (Gorcenco et al., 2024). Targeted and intense training programs lasting one to six months, including gait and balance training, have shown potential to improve functional mobility, reduce fall risk, and improve well-being (Miyai et al., 2012; Rodríguez-Díaz et al., 2018). However, these in-person approaches are only suitable for a subset of patients, inciting the need for effective training and monitoring solutions that require little or no physical presence at the study center (Lavorgna et al., 2024; Manto et al., 2020). Shorter or home-based training regimens led to improvements in clinical disease severity scores and quantitative gait and stance parameters, e.g., after four weeks of coordinative training in patients with cerebellar and afferent ataxias in the short term (Ilg et al., 2009), and for cerebellar ataxia patients even in the long term (Ilg et al., 2010). However, insights into remote training interventions are limited. A systematic review on rehabilitation programs in patients with genetic degenerative ataxia (Milne et al., 2017) summarized that only four out of 17 studies included home-based training, and only two were randomized controlled trials. A recent study reported improvements in balance confidence, quality of life (mobility, self-care, usual activities), health status, gait speed and fall rate after a five-week home-based core stability exercises in patients with hereditary ataxias, but no change in clinically rated disease severity (Cabanas-Valdés et al., 2024). In comparison, quantitative gait and balance parameters are considered as more sensitive methods to depict functional improvements (Ilg et al., 2018; Thierfelder et al., 2021).

Defining training parameters (frequency, duration, intensity) is crucial for optimizing rehabilitation outcomes (Milne et al., 2024). Standardized guidelines for hereditary cerebellar ataxia are lacking, and further randomized controlled trials are needed to optimize home-based training programs.

Following current guidance documents (U.S. Department of Health and Human Services, 2020) and consensus recommendations for quantitative gait and balance outcomes and the use of smartphone sensors (Ilg et al., 2024; Németh et al., 2024), the study presented here integrated quantitative performance outcomes (PerfO) with clinician-reported outcomes (ClinRO) and patient-reported outcomes (PRO). An exploratory proof-of-concept randomized controlled trial (RCT) on the impact of home-based, video-based training on gait and stance performance of patients with hereditary degenerative cerebellar ataxia using digital motor biomarkers as PerfO in combination with ClinRO and PRO is presented. It analyzed whether the distribution of training sessions across the week, with consistent weekly training time and content, affects the training effect; and how clinical characteristics interact with training success. It was hypothesized that (a) video-based training at home results in significant improvements in gait and stance abilities, (b) shorter, more frequent training sessions lead to greater improvements compared to longer, less frequent training sessions, and (c) clinical characteristics, such as disease severity and baseline functional status, would be key determinants of individual training success.

2 Methods

2.1 Experimental Task and Procedure

Participants had confirmed hereditary ataxia, indicated by genetic diagnosis, positive family history, or early-onset symptoms, were able to walk without walking aids for at least 2 minutes and had no signs of secondary CNS disease. All patients participated in a one-week baseline phase without training (T0 to T1, screening and baseline visit). They were then randomly assigned to one of two three-week video-based training protocols or a control group with standard medical care only (Train20, Train40, Control), and completed a third study visit after the training (T2, post-training). After T2, participants in the control group were randomly reassigned to one of the two original training protocols and completed a fourth study visit (T3, post-control-training, after week 7). Data was subsequently merged with their respective training groups from the first phase, forming two larger groups (Train20+C, Train40+C).

Participants followed uniform, pre-recorded videos for training. Both training protocols had identical content and total weekly duration but differed in session frequency and length: Train20 performed 4 x 20-minute sessions per week, and Train40 2 x 40-minute sessions. The control group received standard medical care without additional training. Exercises included easy-to-perform coordination, strength, and mobility exercises to avoid an increased risk of falling during the unsupervised home-based setting. All participants maintained their standard medical care routine, including physiotherapy, prescribed medications, and other exercises.

The training protocol was set up in close communication with an ataxia physiotherapy expert and based on sport-scientific knowledge of the author. All exercises were conducted as part of the additional exercise program, designed to complement, rather than replace, individual training or physiotherapy. The total training duration and session length were modeled after standard physiotherapy practices, which typically involve 6-12 sessions of approximately 20 minutes each, and based on literature, which suggests a drop in study compliance after three weeks (Haines et al., 2009). The exercises focused on three key aspects of gait and balance improvement: coordination, strength, and mobility. Each video/training session consisted of all three of these key aspects. Exercises were repeated throughout the whole training program, and the difficulty level increased. For instance, protective steps (Doris Brötz & Synofzik) were introduced in forward and backward directions during session 1/12, revisited in session 3/12, and supplemented with sideward protective steps in the same session. Participants were encouraged to perform these exercises in a relaxed and focused state to maximize effectiveness. For the group assigned to 2 x 40-minute training sessions, two video segments were combined for each session (e.g., segments 1+2 and 3+4) to streamline the exercise program. Coordination exercises were based on the key motor control and coordination skills defined by Hirtz (1985): Differentiation, orientation, reaction, balance, and rhythm ability. They were carried out in different variations and included fine motor exercises like synchronous and asynchronous head and finger movement, toe and foot arch movements, and eye movement tasks, as well as gross motor exercises like foot tappings, throwing a ball, clapping and stamping at certain displayed numbers, crawling, and clapping tasks, or combined the two aspects (walking on the spot while performing head/eye movements). Estimating times spans was used to train orientation ability, relevant for timing capabilities for motor and non-motor functions in which the cerebellum is involved (Boven & Cerminara, 2023). Mobility exercises were included for the following reasons: With sufficient mobility, people can perform movements faster and more economically, which might also help to prevent falls. On the other hand, if mobility is restricted, this can lead to poor posture, increased risk of injury and limitations in everyday motor skills (Friedmann, 2009). Exercises included stretching muscles and moving all joints through their full range of motion. Regarding strength training, the exercises were specifically chosen to target the muscles most involved in gait and balance, like gluteus maximus, gluteus medius, vasti, soleus, and gastrocnemius (Pandy & Andriacchi, 2010). Some of the strength exercises were purely strength exercises, while others included coordination aspects: Stepping on a stack of books (while sitting), calf lifts and toe lifts, squats in front of a bed/table, weight shifting (while sitting), kneeling to lunge exercises, protective steps forward, backward, and sideward knee to elbow and leg raises (while sitting), deep sideward walks, and wall sits. More challenging coordination tasks were conducted sitting or lying on a mat, in order to minimize fall risk (e.g., weight shifting). Exercises across all three categories were progressively advanced from lying to sitting and then to standing positions during each session, whenever applicable.

2.2 Data Analysis

ClinRO: Cognitive impairment was assessed for descriptive purposes at T0 using the Montreal Cognitive Assessment Test (MoCA). Four dependent variables were assessed longitudinally at T0 and T2 (and T3): Severity of ataxia (SARA-score), presence or absence of non-ataxia symptoms (INAS-score), functional mobility (TUG), and impairment of daily life activities (FARS-ADL). A.R., who assessed the ClinRO, was blinded to group allocation.

PRO: Baseline demographics and variables were collected via questionnaire at T0: medical history, handedness, physical/sport activity (amount per week/day), amount of physiotherapy, occupational therapy and speech therapy per week, estimated number of (almost) falls (past six months and one week), and years of education (school plus further education). Depressive and anxiety symptoms were retrieved with the depression module of the Patient Health Questionnaire (PHQ-9). After the training, perceived change in gait and stance was retrieved via a Patient Global Impression of Change (PGIC) questionnaire. Longitudinally assessed dependent variables included questionnaires on habitual well-being (FAHW), and fall-related self-efficacy (ABC-D), at T1 and T2 (and T3).

Longitudinal, performance-based outcomes (PerfO) were derived from three gait and five stance tasks at each study visit: Normal gait (NG), backward gait (BG), tandem gait (TG), natural stance (NS), feet-together stance (FTS), tandem stance (TS), FTS with eyes closed (FTSec), and single-leg stance (SS), recorded with a force plate (zebris Medical GmbH, Isny, Germany). Participants walked without shoes at a self-selected pace, while the examiner followed at a safe distance to mitigate any possible falls. During the natural stance, participants were asked to stand in a natural, stable position. In tandem stance, participants were allowed to decide which leg to put to the front, and in single-leg stance, they self-selected the foot to balance with. NG was conducted for 2 minutes, BG and TG for 4 lanes (each 4.24 m), and each stance task was attempted for 30 seconds without support, with values under 30 seconds excluded from longitudinal analyses. We analyzed only tasks completed by at least 75 % of participants (Shah et al., 2024) (≥ 30 s for stance tasks, gait without support). Outcomes included the dependent variables stride time [s], double support proportion [%], mean velocity [m/s], external rotation of the feet [°], step width [cm], and step width SD [cm] for each of the gait tasks, and sway area [mm2] and sway velocity [mm/s] for each of the stance tasks. The primary outcome was NG velocity.

For all PerfO, intraclass-correlation coefficients (ICCs) with two-way random effects models were calculated to confirm stability and reliability of the gait and stance measures (PerfO) between T0 and T1 (screening and baseline visit). Changes within the whole group in PerfO between T0 and T1 were identified using dependent samples t-tests. Baseline comparisons of PRO and ClinRO between groups were conducted using independent t-tests (two groups) or a univariate ANOVA (three groups). Categorical variables were analyzed with chi-square tests. To investigate group differences in PerfO, ClinRO, and PRO across the intervention phase, a series of 2 × 3 ANOVAs was performed. These included the within-subjects factor 'time point' (pre, post), and the between-subjects factor 'group' (Train20, Train40, Control).

Each dependent variable was analyzed separately, testing for main effects of group and time point, as well as their interaction. Similarly, a series of 2 × 2 ANOVAs was conducted for comparisons between the larger training groups (Train20+C, Train40+C) across time (pre, post). For the primary outcome gait velocity, independent contrasts of improvement were calculated between the groups (independent t-tests). An exploratory analysis compared pre- and post-training values within each group using dependent samples t-tests. For all participants who had completed training (Train20+C plus Train40+C, n = 31), a linear mixed model was used to assess whether baseline values of ClinROs and PROs influenced changes in PerfO across the intervention phase (the sample size of n = 31 does not apply to FTS/FTSec, as not all participants were able to complete this task). The model included fixed effects for ClinRO/PRO, time point (T1, T2), and their interaction to examine their influence on change of performance outcomes over time. To account for the repeated measures design, a random intercept for individual subjects was included, capturing individual variability in baseline levels. This model was applied separately for all PerfOs. For those models that revealed a significant interaction effect, further analyses were conducted to resolve the interactions. Hence, estimated marginal means for gait or stance at each time point were calculated, specifically examining the effects at higher and lower levels of the clinical scores (one SD above and below the mean). Pairwise contrasts were conducted to further explore the differences between the estimated marginal means at T1 and T2.

3 Results and Discussion

34 participants with a mean SARA-score of 8.4 ± 3.5 and a mean disease duration of 9.2 ± 8.3 years completed the first two study visits, and 31 participants completed the training. TS, SS, and TG had completion rates of < 75 % and were not evaluated.

Most PerfO demonstrated good to excellent reliability (ICCs 0.69 - 0.96, 0.94 for primary outcome NG velocity), indicating consistent measurement across the two time points, and no significant difference was found between T0 and T1.

The three groups (Train20, Train40, and control group) showed similar distributions of age, sex, number of pure cerebellar ataxias (hereditary ataxias commonly regarded as “pure” cerebellar ataxias (e.g., SCA6, SCA14)), disease duration, age at disease onset, and all other baseline variables. In the two larger training groups, a higher balance confidence, and a higher educational level was found in Train40+C compared to Train20+C.

Contrary to the expectations and independent of the distribution of training sessions, the results revealed no changes over time (before and after training), dependent on groups (Train20, Train40, control). While other intensive training programs with smaller sample sizes reported significant improvements after four or five weeks of training (Cabanas-Valdés et al., 2024; Ilg et al., 2009), this study, as one of the few RCTs in the field of home-based training in hereditary cerebellar ataxia, indicated that a three-week training with a total volume of 240 minutes may not offer a sufficient volume to achieve comparable outcomes, particularly for participants with mild to moderate ataxia in whom a more intensive training might be required. Notably, other interventions may have incorporated tasks in their training that resemble those assessed in the PerfO and ClinRO. In our training program, we used general coordination, mobility, and strength exercises without including any of the specific tasks assessed on-site, to avoid any bias by a sole practice effect. The mean perceived difficulty of exercises in this study was rated as 2.76 ± 1.22 out of 10, possibly indicating that the exercises were not challenging enough (Keller, 2023) to provoke substantial improvements. However, when conducting home-based training without supervision, it is crucial to select exercises that do not increase the risk of falling for patients, leading to a more conservative exercise selection. In the PGIC (n = 30, range -3 to 3), 40% of the participants reported a 1 to 2-point improvement in both stance and gait; 56.7 % reported no change, and 3.3 % reported a 1-point worsening.

In addition, when comparing pre- and post-training values within each group in an exploratory approach, we found that longer, less frequent training sessions may be more effective than shorter, more frequent sessions (2 x 40-minute vs. 4 x 20-minute). In detail, the control group showed an improvement in NG step width, and group Train40 showed improvements in the primary outcome NG velocity, and in stride time, double support, and BG step width, which was supported by similar effects in the larger training groups: Group Train40+C showed improvements in NG velocity and stride time. A significant improvement was found in Train40+C for SARA-score (1.5-point reduction), which is similar to other, more intensive home-based programs (Bunn et al., 2015; Cabanas-Valdés et al., 2024). This change did not reach significance in the smaller Train40 group (1-point reduction). Mean progression rates in SCAs are 0.8 - 2.1 points/year (Jacobi et al., 2015), and a change of 1 SARA-point can already be considered as meaningful (Schmitz-Hübsch et al., 2010), although it has been challenged whether the delta SARA-score is an appropriate outcome from a patients’ perspective (Maas & van de Warrenburg, 2021). However, the reported results should be interpreted with caution since they are lacking a direct comparison with a control group. When comparing improvements in the primary outcome gait velocity (difference of T2 minus T1) between groups (control group vs. Train20, control group vs. Train40, and Train20 vs. Train40) the analyses revealed no significant differences. Specifically, there was a small effect size for control group vs. Train20, a medium effect size favoring higher improvement in Train40 compared to the control group, and a large effect size favoring higher improvement in Train40 compared to Train20.

Assessing ClinRO as continuous predictors on changes in PerfO (T1 to T2) among all participants who underwent training (n = 31), revealed that initial clinical assessments may influence performance changes. Participants with varying levels of impairment (SARA and ADL) experienced different outcomes in the feet together stance: When assessing how score levels one standard deviation above and below the mean influenced gait or stance at both time points, participants with higher clinical scores showed a significant improvement (decrease) in sway velocity after training. This is likely attributable to the increased challenge the task posed for them, offering greater potential for progress. In addition, although nearly all patients reported no depressive symptoms above the clinical cut-off (with one exception with a score of 19 in the PHQ-9), participants with higher well-being showed a significant improvement in gait velocity during normal gait, and in stride time during backward gait after training, compared to those with a lower well-being. Thus, mental well-being does not only seem to enhance quality of life (Lo et al., 2016) but may also be a critical factor in determining the effectiveness of interventions, such as physical training or practice, in improving motor function. This would be in line with a current study on Parkinson's Disease patients, in which high responders of training had the worst functional mobility status but also the highest balance confidence (Albrecht et al., 2024). However, the analysis in the current study assessed all participants together without control group comparison, so that it remains unclear if the effect stems solely from the training.

The study had some limitations that warrant consideration. While the sample size was relatively high compared to other studies addressing patients with hereditary degenerative cerebellar ataxias, it might still have limited the statistical power of the study, potentially masking smaller but relevant effects. Also, the large number of statistical tests and comparisons, which were not entirely independent, should be considered, as this could increase the likelihood of Type I errors. In addition, it was not possible to control how often or with what quality the training was performed, as this information was based solely on self-reports from participants. Study participants were instructed to adhere to their standard medical care routines, including physiotherapy, which may have introduced variability in treatment consistency and affected the overall outcomes. While we only measured gait at preferred speed, recently published research recommends incorporating different gait speeds to provide a greater challenge to cerebellar gait control (Ilg et al., 2024).

4 Conclusion

This RCT offered important insights into the effects of a 3-week video-based gait and balance training program at home. Although the training did not lead to general improvements across all participants, those with higher disease severity and better mental well-being experienced significant benefits, suggesting that these factors may influence the effectiveness of interventions, practice or adaptation processes. While the study found no significant overall effect of training volume distribution (2 x 40-minute vs. 4 x 20-minute), the data hint that it may be worth exploring the benefits of longer, less frequent training sessions in patients with mild to moderate hereditary cerebellar ataxias. This study yielded valuable insights toward the broader goal of defining effective yet feasible training protocols, and further highlighted the need to identify the minimal effective training protocol (duration, intensity) necessary to generate substantial improvements.

VII. General Discussion

In recent years, video-based training has gained increasing attention as an accessible, self-directed approach to improve motor skills, especially for populations with limited access to regular supervised interventions. This dissertation unites findings from two studies exploring the effects of such home-based programs on balance and gait performance in healthy adults and individuals with hereditary degenerative cerebellar ataxia – two groups with distinct motor needs and baseline abilities. While the former group aimed to prevent functional decline or improve performance, the latter sought to mitigate ataxia-related impairments, offering a unique comparative perspective on training adaptability and efficacy.

Patients with hereditary degenerative cerebellar ataxia experience coordinative motor impairment, especially gait instability. Physical training, including home-based intervention programs, has been shown to improve gait and balance measures. However, further research, particularly well-designed randomized controlled trials, is necessary to deepen our understanding of how to optimize these interventions. Specifically, research is needed to determine the minimum effective training intensity, the ideal distribution of training sessions across weeks, and how these factors can be tailored to meet the needs of different patient populations and various degrees of disease severity. These insights are crucial for developing evidence-based protocols that maximize the benefits of home-based interventions while minimizing the burden on participants.

This dissertation assessed the impact of three-week, video-based home training programs on gait and balance outcomes in both healthy participants and ambulatory patients with hereditary degenerative cerebellar ataxia. The insights gained from both studies provide valuable information on the effectiveness of home-based interventions for improving motor function in these populations. Specifically, the findings highlight the potential benefits and limitations of such training protocols, shedding light on how different training intensities, task repetitions, and patient characteristics may influence outcomes. Hereby, they contribute to a broader understanding of how to optimize gait and balance interventions for individuals with neurological impairments, and point the way to future research directions and the development of tailored training approaches.

Designing effective training protocols for patients with cerebellar ataxia remains inconsistent across studies, with a wide variety of approaches employed. For instance, Doris Brötz developed brochures with exercises specifically for this patient group (D. Brötz et al., 2007; D. Brötz & Synofzik) offering a valuable starting point for creating structured training programs. Beyond this, published home-based protocols vary significantly in complexity and delivery methods: Keller and Bastian (2014) used a six-week program comprising six exercises, personalized by a physiotherapist, and demonstrated both in person and through a DVD (4-6 sessions of 20 minutes per week). Jabri et al. (2022) implemented five exercises tailored to a moderate level of challenge, delivered via written instructions on an iPod. Bunn et al. (2015) provided eight basic balance exercises using written guidelines, while Cabanas-Valdés et al. (2024) adapted 14 core stability exercises originally developed for stroke survivors, supplementing instructions with photographs and written material following an initial home visit by a physiotherapist. Despite these efforts, the selection of exercises was generally not well-documented or justified, and only Keller and Bastian (2014) employed video-based instructions, which may offer unique benefits. Videos can potentially enhance both motivation and motor learning, as observing others' movements is known to engage mechanisms such as mirror neurons (Rodríguez et al., 2014). In Study 2, we designed exercise protocols drawing from three primary considerations: (a) Scientific Basis: Exercises were selected to target performance factors specifically relevant for improving motor function in cerebellar ataxia patients, (b) Expert Input: Collaboration with a physiotherapy specialist for cerebellar ataxias (Doris Brötz, Germany) ensured that exercises were tailored to the capabilities and needs of the target population, and (c) Practicality: Exercises were designed for unsupervised home-based performance with minimal fall risk and avoided overlap with gait and stance tasks assessed during study visits. The training program's total duration and session length were aligned with standard physiotherapy protocols, typically involving 6-12 sessions of around 20 minutes each. While in other movement disorders a minimum of four weeks of gait training was recommended (Mak et al., 2017), a decline in study compliance was found already beyond three weeks (Haines et al., 2009). The final protocol included a total of 10 mobility exercises, 12 strength exercises, and 20 coordination exercises, each with variations. Key exercises were repeated across the 12 sessions with progressive difficulty to reinforce motor learning, acknowledging that the extent of motor learning achievable in this patient group remains uncertain (see first section of the Introduction).

1 Sensor Placement and Measurement Instruments

When assessing gait and balance quantitively, the most commonly used measurement tools are video-based motion capturing, force plates, and inertial measurement units (e.g., in smartphones or wearables) (Ilg et al., 2024). In our studies, we used a force plate, a motion capturing system with IMUs and a smartphone in parallel to record gait and stance tasks. In Study 1, all three systems have been used to assess changes from pre- to post-intervention. As expected, we found higher reliability (intraclass correlation coefficient) in those outcomes calculated by force plate measurement and motion capturing system, compared to the smartphone. Similar, significant changes from pre- to post-intervention assessed within each group (exploratory approach) were mostly present in the force plate outcomes, followed by the motion capturing system, and only one significant change (before Bonferroni correction) in the smartphone outcomes. Differences between measurement systems have been studied in healthy populations (Karlinsky et al., 2022; Rashid et al., 2021; Reimer et al., 2022). However, to the best of the author's knowledge, these differences have not been specifically investigated in patients with ataxia.

In a recent consensus paper on gait and balance outcomes in ataxia, wearable IMU sensor technology has been recommended as the most appropriate technology to conduct multicenter gait and balance trials in ataxia (Ilg et al., 2024). The authors recommend using three sensors, including one on the lower lumbar spine. This setup appears to strike an optimal balance between data quality and participant burden in clinical or research settings. However, it may be less practical in situations where participants are required to position the sensor themselves, such as in home-based measurements using a smartphone as the sole wearable sensor. In these cases, a front placement of the sensor or smartphone would offer practical advantages: positioning the device at the front of the body is easier for participants in terms of both vision and flexibility, and it allows for better control over sensor positioning. When not using a waist bag, the front pants pocket could also serve as an option. In general, this may improve adherence and reduce dropout rates. In our study with healthy adults, we used a smartphone as wearable sensor for collection of gait and balance outcomes and found that the data accuracy for normal gait was consistent regardless of whether the smartphone sensor was placed at the front or back of the body in a waist bag. Additionally, sensor performance was unaffected by participants' body weight, indicating that this setup provides robust data across a diverse and representative sample. Based on these findings, we chose to position the sensor in a waist bag at the front of the body for our patient group in Study 2 to simplify the process. Data from this setup are not yet analyzed and will be presented in a future publication, as the current patient study focuses exclusively on the outcomes from the force plate to streamline the scope of the corresponding manuscript. In summary, the results of Study 1 suggest that sensor placement (front of the body vs. lower back) can be selected based on what is most convenient for participants, potentially improving study adherence and reducing dropout rates.

2 Gait and Balance Characteristics

The gait and balance values reported in the two studies align closely with those in the literature. Similar or slightly better gait parameters were documented by Buckley et al. (2018) for both healthy individuals and patients with cerebellar ataxia, potentially reflecting differences in etiology of the patients, which was mixed in the studies assessed in the review. Tandem gait outcomes in healthy participants aged 47 years from Stolze et al. (2002) were consistent with the findings for healthy controls in these studies; however, tandem gait was not assessed in Study 2 due to low completion rates among patients. Notably, no published reference values for backward gait in cerebellar ataxia patients were identified, making the data from this study a valuable contribution to the field. In healthy individuals, backward gait metrics such as stride time, cadence, velocity, and step width were comparable to those reported by Gimunová et al. (2021).

The observed completion rates in stance tasks in Study 2 were highest for natural stance and feet together stance, followed by feet together stance with eyes closed, and much lower completion rates for tandem stance, and single leg stance. The is consistent with findings from Shah et al. (2024), who assessed 53 patients with hereditary cerebellar ataxias. Just in the feet-together stance with eyes closed, Shah et al. (2024) reported lower completion rates compared to the results reported here. Single leg stance was not included in the study of Shah et al. (2024), so the completion rate reported in Study 2 provides additional insights for this task. Notably, the participants in Shah et al. (2024) had greater average disease severity, likely explaining their slightly lower completion rates, particularly in more challenging tasks. They also observed that participants with greater disease severity, indicated by high SARA scores, had reduced completion rates, although some participants with moderate severity completed all tasks, and a few in early, pre-ataxic stages were unable to complete certain tasks. This variation reflects the natural diversity in physical ability, seen even in healthy populations. However, due to the rarity of SCA and smaller sample sizes, variability becomes more pronounced within this population. Interestingly, the stance width (heel-to-heel distance) observed in patients with hereditary cerebellar ataxia in Study 2 was similar to that reported for healthy adults by McIlroy and Maki (1997). This finding suggests that while certain gait parameters were affected in the sample of patients with mild to moderate cerebellar ataxia, others remained within the normal range.

Although no statistical comparison between patients with hereditary degenerative cerebellar ataxia and healthy adults was yet conducted, several observations can already be made: Regarding stance, in both natural stance and narrow stance conditions, patients displayed not only higher maximum values but also lower minimum values than healthy controls. This pattern differed for the narrow stance with eyes closed, where both minimum and maximum values were higher in patients. This suggests that, within the ataxia patient group, there may be individuals who are particularly motivated to optimize their stance, perhaps showing higher-than-average physical engagement compared to healthy controls. Conversely, others were probably unable to approach normative levels, reflecting the challenges they face in maintaining stance stability. Additionally, those overcompensation mechanisms (lower minimum values compared to healthy controls) did not seem to occur in the feet together stance with eyes closed, probably due to the increased difficulty. However, this assumption is merely a theory and cannot be classified by literature yet. Across all stance conditions, we observed that both the mean and variability values (standard deviation, SD) were higher in patients; however, the difference in variability was particularly pronounced. For instance, in the natural stance condition, patients exhibited 302 % more variability compared to healthy controls, whereas the mean was “only” 131 % higher. This highlights the considerable variability in motor control among patients, likely reflecting a wide range of compensatory capacities and motor impairments within the group, and aligns with literature, that variability measures are among the most distinguishing characteristics separating patients with cerebellar ataxia from healthy controls (Ilg et al., 2020; Seemann et al., 2024).

Given the alignment of our results with those reported in the literature, we can reasonably conclude that our samples fall within the typical range. This suggests that our findings are unlikely to be influenced by the recruitment of a particularly specific or non-representative population.

3 Training Effects

The findings of both studies suggest that regular, video-guided motor training holds the potential to foster improvements, though these were observed primarily through exploratory analyses rather than generalizable results. This section synthesizes these nuanced findings, offering insights into the shared benefits of such training approaches as well as the specific challenges encountered in different participant groups. Underlying mechanisms are discussed, potential factors influencing varied outcomes are assessed, and the practical implications for integrating video-based interventions into broader clinical or preventative care contexts are explored.

In Study 1, we first aimed to understand whether improvements after a three-week, video-based gait and balance training program at home possibly resulted from the actual training or from an unintended habituation processes, arising from the sole repetition of tasks performed in the assessments once per week. We found improvement in both groups, intervention group with training plus weekly assessments, and control group with only weekly assessments, and summarized that both the gait and balance training and the weekly repetition of assessment tasks can lead to improved gait and balance outcomes. While the specific variables showing significant improvement differed between the groups, improvements in backward and tandem gait tasks were observed across both groups, suggesting that repeated exposure and practice play a role in adaptation to these challenging tasks. However, significant changes in variables characterizing normal gait and tandem stance were only observed in the training group, indicating a potential training-specific benefit for less demanding gait patterns. A possible explanation for this pattern is that backward and tandem gait are rarely practiced in everyday life, whereas normal gait is a routine part of most people's daily activities. Consequently, backward and tandem gait may benefit more directly from repeated practice during training, while normal gait might require more targeted attention to achieve similar improvements. Apart from insights into differences between gait types and their varying demands (Donno et al., 2023; Stolze et al., 2002), there is a noticeable lack of studies exploring adaptation processes across different gait patterns. In addition, it remains unclear why no improvements were observed in tandem gait within the intervention group. While the improvement in stride time was smaller in the intervention group (0.05 s improvement vs. 0.14 s in the control group), the absolute improvement in velocity from pre- to post-intervention was similar in both groups (0.04 m/s). However, the increased variability within the intervention group, possibly due to individual differences in response to training, may have contributed to the differences in statistical significance.

In patients with hereditary degenerative cerebellar ataxia (Study 2), we found no significant changes in gait and balance outcomes from pre- to post-intervention (3-week training) dependent on groups (intervention group with 4 x 20 min training per week, intervention group with 2 x 40 min training per week or control group without weekly training), and no changes in gait and balance outcomes from pre- to post-intervention in general independent of group allocation. These findings suggest that there was no overall progression in gait and balance outcomes observed for either of the two intervention groups or the control group. In contrast, studies involving longer and more intensive training programs, conducted on-site, at home, or through a combination of both, have reported improvements in clinical scales as well as gait and balance outcomes following coordinative or balance training interventions (ranging from 4 to 30 weeks, with sessions 3-4 times per week, lasting 20-120 minutes; Ilg et al., 2010; Ilg et al., 2009; Keller & Bastian, 2014; Milne et al., 2024). Among these, only Milne et al. (2024) very recently conducted a randomized controlled trial with a substantial sample size (n = 76), though they did not assess performance-based outcomes. Other studies present mixed results. For instance, Jabri et al. (2022) reported no significant improvements after six weeks of home-based balance and coordination exercises with vibrotactile sensory augmentation, followed by six weeks without vibrotactile sensory augmentation (5 x 30 minutes per week, non-randomized). Similarly, Ayvat et al. (2022) observed limited improvement after an eight-week conventional exercise program (3 x 60 minutes per week, including participants with acquired ataxias), while Bunn et al. (2015) found minimal effects after four weeks of balance training (5 x 15 minutes per week). These discrepancies highlight the need to determine the minimum effective requirements for training duration, intensity, and specific exercises, particularly for exclusive home-based training programs. Notably, the sample size in the current study of participants who underwent training (n = 31) is significantly larger than those in most of the aforementioned studies (n = 8-17), apart from the randomized controlled trial by Milne et al. (2024). This larger sample provides a more robust basis for evaluating the presence or absence of a general training effect.

An additional exploratory analysis was conducted to evaluate changes from pre- to post-intervention within each individual group. This analysis aimed to uncover outcomes that might be particularly sensitive to training-induced changes and could serve as indicators of subtle improvements in gait and balance. By focusing on within-group differences, the approach sought to identify specific aspects of performance that may respond to targeted training, even when broader group-level improvements across all groups were not observed. Interestingly, we found significant improvements within the intervention group with longer, but less frequent training sessions (Train40, 2 x 40 min training), while no improvements were found within the intervention group receiving shorter, but more frequent training (Train20, 4 x 20 min training). A single improvement was found within in the control group (reduction in step width of normal gait). The improvements in Train40 mainly applied to normal gait outcomes (velocity, stride time and double support), as well as to one outcome of backward gait (step width). Since our control group underwent delayed-onset training with one of the two specified training frequencies, we were able to analyze these combined groups with a slightly larger sample size (Train20+C and Train40+C with n = 15/15, compared to n = 11/11/10). In this analysis, two of the improvements observed in the Train40 group were confirmed (normal gait velocity and stride time) and one additional significant improvement was found in the clinical SARA score, measuring disease severity (1.5-point reduction). This change had not reached significance in the smaller group (Train40, 1-point reduction). To put this into context, in spinocerebellar ataxias types 1, 2, 3, and 6, mean progression rates of 0.8 to 2.11 points were found per year (Jacobi et al., 2015). After training, reductions of 1.1-5.2 points were found after intensive, on-site programs (Brito et al., 2024; Ilg et al., 2009; Milne et al., 2024; Winser et al., 2022) and reductions of 0.6-1.9 points in home-based programs (Barbuto et al., 2023; Bunn et al., 2015; Jabri et al., 2022). While in many studies a 1-point reduction in the SARA score is considered meaningful (Schmitz-Hübsch et al., 2010), is has been discussed whether this actually corresponds to a meaningful change from a patients' point of view. Maas and van de Warrenburg (2021) evaluated surveys of 20 moderately affected patients with a specific subtype of hereditary cerebellar ataxia (spinocerebellar ataxia type 3, SCA3) and concluded that even a reduction of two to three points in the SARA score did not necessarily correspond to a meaningful change for a patient, if it only involved items in which the patient does not experience subjective complaints. The authors suggested to additionally use patient reported outcome measures (PROs), such as the Patient Global Impression of Change (PGIC), to evaluate meaningful changes. In Study 2, 40 % of the participants reported a 1 to 2-point improvement in both stance and gait; 56.7 % reported no change, and 3.3 % reported a 1-point worsening in the

PGIC (range -3 to 3). This alignment suggests the reported change in SARA-score may reflect real-life benefits for some patients. The improvements in gait and balance outcomes observed in the exploratory analysis are partially consistent with findings reported in the literature. Most studies, such as those by Keller and Bastian (2014) and Ilg et al. (2010), have documented enhancements in both gait and balance outcomes following coordinative/balance training. However, in our exploratory approach, improvements were observed exclusively in gait outcomes, with no significant changes detected in balance outcomes. Up to now, no direct comparisons of different training frequencies have been reported in patients with hereditary degenerative cerebellar ataxias. Milne et al. (2017) concluded in their review on rehabilitation programs in patients with genetic degenerative ataxia that the outcome measures of the studies were so heterogeneous, that the impact of training intensity or duration could not be determined. However, recommendations based on a meta-analysis of home-based exercise programs in healthy adults suggest that larger training effects are achieved with more than three sessions per week, each lasting 30 minutes or less, compared to three or fewer sessions per week with durations exceeding 30 minutes per session (Chaabene et al., 2021) and Muehlbauer et al. (2022) suggested that improvements after balance training was irrespective of training frequency (2 x 30 minutes per week or 3 x 20 minutes per week) in healthy, male adolescents.

In the following, possible reasons are discussed, why no overall training effect has been found in healthy adults and in patients with mild to moderate hereditary degenerative cerebellar ataxia:

a) Reason 1: Challenge level of the training

The participants of Study 2 rated the difficulty of all exercises they performed from 0 (not challenging) to 10 (very challenging). We found a mean perceived difficulty of 2.76 ± 1.22, indicating a rather low level of challenge. Given this information, the lack of an overall training effect in patients with mild to moderate hereditary degenerative cerebellar ataxia may be attributed to insufficient level of challenge in the training program. This aligns with findings by Keller and Bastian (2014), who concluded that the level of challenge is even more critical than the duration of exercise in achieving meaningful improvements. Without a sufficiently demanding stimulus, exercises may not effectively stimulate the neural adaptations necessary for improvements in gait and balance, particularly in populations with neurological impairments. However, this study tried to find a trade-off between exercises which can be mastered without supervision and without increased fall-risk, and sufficiently challenging exercises. In Study 1, we did not assess the perceived difficulty of the exercises, leaving it unclear whether the tasks matched the optimal challenge level for each participant. It is possible that patients required a higher intensity or variability in tasks to engage the cerebellar pathways effectively, or that the exercises were too easily mastered. Other home-based studies incorporated simple exercises (Bunn et al., 2015) or tailored exercises designed to provide a moderate level of challenge for each participant (Barbuto et al., 2023; Jabri et al., 2022). Both Barbuto et al. (2023) and Bunn et al. (2015) addressed fall risk during their interventions, reporting four falls among three participants in the former and no falls in the latter study. Thus, the risk of falls during home-based training might be influenced by the severity of the condition, but detailed information on this aspect remains limited in current studies. Further research is needed to better understand fall risk and to identify the optimal level of challenge that ensures safety while promoting effective training outcomes.

b) Reason 2: Training design

Even though the level of challenge might be more important than the total training volume or the duration of each training session (Keller & Bastian, 2014), there is no evidence that this is the primary reason for not finding an overall training effect in our study. Similarly, this could have been influenced by the total training volume (240 min), the overall training period (3 weeks) or the duration of each single training session (20 min or 40 min), and may therefore also be related to the training intensity rather than or in addition to the level of challenge. For example, the session duration of 45 min used by Bonanno et al. (2024) was comparable with the duration used in the Train40 group of the present study, i.e. the group in which the exploratory analysis found an indication for improvement. However, there are notable differences in the study designs. Bonanno et al. (2024) conducted their training in an on-site setting as an add-on to a standard rehabilitation program, using a small sample of only eight subjects with acquired, non-hereditary ataxia. Their study also employed a more controlled environment with one to two additional training sessions per week and a longer total duration of 5 weeks, resulting in a significantly higher total training volume compared to the present study, which was purely home-based. Similar, Ilg et al. (2009) used an intensive on-site coordination program in 10 patients with cerebellar degeneration and 6 patients with afferent ataxia, with slightly longer total training period (4-week vs. 3-week), higher total volume (720 minutes vs. 240 minutes) and longer single session duration (60 minutes vs. 20 or 40 minutes). They found a reduction in SARA-score, ICARS and Berg Balance scale immediately after training, as well as in gait and balance outcomes. However, the comparability to on-site studies is limited. Some studies employed similar training programs to the current one. Jabri et al. (2022) conducted a balance and coordination training program in 10 patients with hereditary cerebellar ataxia but with a longer duration (2 x 6 weeks). They assessed balance performance outcomes (PerfO) but did not evaluate gait. Their results showed improvements in disease severity (SARA) after 6 weeks of balance and coordination training with vibrotactile feedback, but no improvements were observed without the feedback, and no changes were found in balance PerfO. Keller et al. (2014) implemented a 6-week balance exercise program in 14 patients with cerebellar ataxia, with training frequencies similar or slightly higher (minimum 20 minutes per day, 4 to 6 times per week) compared to the Train20 group of Study 2. However, their performance outcomes were based on only two stance conditions and one gait condition. Both studies, however, were not randomized controlled trials, and had much smaller participant samples.

c) Task similarity and skill transfer

Another reason could be the lack of transferability of general training content to the execution of specific tasks or exercises: As noted by Burciu et al. (2013), it is important to check whether tasks included in the training intervention are also part of the clinical rating scales or belong to the tasks used for the assessment of PerfO. Some of the observed improvement could be attributed solely to practice effects, if the tasks within clinical scales or the assessment tasks are part of the training content. For example, if practicing tandem gait is part of the training and tandem gait is also assessed by the clinical scale (e.g., SARA), participants might improve on the scale simply because they practiced similar tasks (Ginis et al., 2016; Shen & Mak, 2014). This can also lead to better performance in specific tasks used to analyze PerfO: For instance, training that includes repeated backward walking may lead to greater improvements in backward gait performance (e.g., backward gait velocity used as PerfO) compared to training that focuses on other coordination exercises that do not involve backward walking.

Some potential connections and differences between the training and habituation effects observed in healthy individuals and the (lack of) training effects in patients can be noted. The two studies followed the same protocol: both assessed similar gait and stance tasks before and after a 3-week, video-based training program at home. In both studies, participants completed weekly gait and balance assessments, regardless of group allocation, while only the intervention groups engaged in the training. In both healthy participants and in ambulatory patients with hereditary degenerative cerebellar ataxia, no overall improvement was found between pre- and post-intervention, when compared between intervention and control group. A key difference between the protocols was the inclusion of a baseline week for the patient group in Study 2. This adjustment was based on findings from Study 1. Analyzing changes over time within the control group of untrained healthy subjects showed that mere repetition of the weekly assessment tasks could lead to improvements in gait and stance variables, underscoring the need for a stable baseline in the patient group to more accurately assess training effects. By including this baseline week, we aimed to reduce any initial rapid improvements due to task habituation, allowing us to focus more on training-induced changes. However, while we cannot fully rule out some degree of continued practice effect, the data suggest that its impact was limited within the control group of untrained ataxia patients. Notably, in contrast to Study 1, where the control group showed a considerable number of improvements through repetition alone, the control group in Study 2 showed only one improvement in our exploratory analysis. However, both the intervention group of Study 1, and the patient group of Study 2 with less frequent, but longer training sessions (2 x 40 min), showed improvements primarily in normal gait and, to a lesser extent, in backward gait, prompting the following hypothesis: Pure task repetition may yield quicker improvements, particularly in less familiar or more complex tasks, while structured gait and balance training might contribute more to progress in more familiar or simpler tasks. This interpretation, however, remains speculative, as our data cannot directly confirm this hypothesis, and as no overall group differences were detected, leaving this interpretation somewhat tentative.

The interaction of clinical characteristics with training success was evaluated in the patient group only. Here we aimed to analyze if clinical characteristics, such as disease severity and baseline functional status, influenced changes in gait and balance outcomes throughout the intervention phase. Several significant interactions were found, indicating that some of the initial clinical assessments could influence the extent or direction of performance improvements throughout the training period: Patients with higher initial disease severity (SARA-score) or higher impairments in activities of daily living (ADL-score) showed greater reductions in sway velocity during the feet together stance, while those with higher initial well-being (FAHW-score) experienced greater increases in gait velocity during normal gait and more pronounced reductions in stride time during backward gait. Several underlying mechanisms could potentially explain the influence of disease severity and impairments of activities of daily living on balance observed in this study. First, patients with more severe disease symptoms may have had greater room for improvement, making measurable progress more evident in this group. Conversely, patients with less severe symptoms might already have optimized their physical condition through prior attention to their health, leaving less room for further improvement. Additionally, those in a less severe state may have maintained better balance and gait due to consistent compensatory strategies, which could attenuate the observable impact of training interventions. Regarding the influence of the well-being on gait outcomes, Fonteyn et al. (2014) emphasized the importance of assessing cognitive disturbances and depressive symptoms in relation to therapy effectiveness in movement disorders, yet specific studies addressing these factors in hereditary ataxia are limited. A recent review by Karamazovova et al. (2023) highlighted that depression is a common but often underdiagnosed and undertreated symptom in hereditary ataxia. The review also noted that while depressive symptoms might lead to increased apathy, there is no direct correlation between higher motor or cognitive impairment and greater levels of depression. Lo et al. (2016) have shown that depression can significantly affect functional performance and quality of life in neurological disorders, further underscoring its potential impact on motor function. However, how depression influences motor performance or the effectiveness of training interventions remains unclear. In Study 2, baseline screening for depressive symptoms (PHQ-9) revealed clinically significant depressive symptoms in only one participant. This limited presence of depressive symptoms in our cohort provides an opportunity to explore the broader role of general well-being, distinct from clinically significant depression, as a factor influencing motor outcomes: Patients with more moderate hereditary degenerative cerebellar ataxia and with a higher well-being show potential for greater improvement after training interventions. Despite these interesting findings, the analyses conducted are not sufficient to determine whether the observed changes were induced by the training or are part of other adaptation processes. Nevertheless, it seems important to place greater emphasis on individuals' well-being, as this not only enhances quality of life but may also amplify training effects. Another aspect highlights the significance of this finding: It is well-established that physical training can improve well-being (Mikkelsen et al., 2017). Although no increase in well-being was observed from pre- to post-intervention in our study, an interesting upward spiral could emerge if both effects occur together. Specifically, training could boost well-being, which in turn could enhance the effectiveness of training.

Three main conclusions can be drawn from these findings: First, the chosen training protocol with 240 minutes over three weeks, appears insufficient to produce substantial improvements in gait and balance for both healthy participants and ambulatory patients with hereditary degenerative cerebellar ataxia. This limited training volume may not provide the intensity or challenge necessary to drive broader adaptations in motor control for these groups. Second, our data suggest that this program can yield small improvements, particularly in normal gait, indicating that some aspects of gait may be more responsive to shorter training protocols. In contrast, backward and tandem gait tasks seem to benefit primarily from repetition alone, perhaps due to their limited practice in daily life and the greater novelty effect when rehearsed. Third, in addition to disease severity, which appears to be a critical factor when designing effective training programs, future studies should place emphasis on assessing well-being as a central patient-reported outcome (next to screening instruments for depressive symptoms) ensuring that improving quality of life remains a primary goal of therapeutic strategies.

4 Challenges, Limitations, and Clinical Implications

Some limitations of the studies should be acknowledged and some challenges of the study design highlighted. Building on the limitations and challenges identified in the current two studies, several key implications emerge for future research and clinical practice.

Similar to other home-based interventions, the training compliance could only be retrieved via questionnaire. Future studies could explore alternative methods for tracking home-based assessments, such as monitoring the playback time of the training videos or regular phone checks, in addition or instead of more extensive documentation using a camera system, to improve data collection and address this limitation more effectively. While participants in the current studies were instructed to call the study supervisor if any instructions for the tasks at home or for the training at home were unclear, other studies (e.g., Cabanas-Valdés et al., 2024) offered weekly telephone or video calls with their physiotherapist if needed. This direct interaction with the therapist or coach might enhance motivation to stick to the exercises through improved personal relationship, however, it does not reflect realistic real-life situations and is therefore a trade-off between these two specific options. Possible, more realistic solutions could include interactions within the patient groups (in presence or virtual), which would enable an exchange of experiences, challenges and perception.

Second, in our studies, we were unable to verify whether the at-home tasks and training sessions were performed correctly or consistently, which is a consistent limitation among home-based study interventions (Barbuto et al., 2023; Chaabene et al., 2021). We designed a straightforward setup with minimal technical equipment and clear instructions, aiming to enhance participant adherence and minimize dropouts. This approach limited our ability to monitor the accuracy of the at-home activities, however, all participants confirmed completing the training and assessments, and in Study 1 the number of unsubmitted smartphone data entries did not differ significantly between groups. Future studies could address this limitation by incorporating methods such as tracking video playback time, conducting regular phone check-ins, or using more extensive documentation systems like cameras to improve oversight and data reliability. These approaches would increase the likelihood that the information about adherence is indeed correct, but would still not guarantee that the training was actually carried out and carried out to a high standard.

In Study 1, three different measurement systems have been evaluated for measuring gait and stance. Each measurement system offers unique advantages and limitations. For instance, force plates using capacitive pressure sensors provide very high accuracy but are confined to laboratory environments. Motion capturing systems using inertial measurement units strike a balance between accuracy and flexibility, enabling use in diverse settings, including at-home assessments, though they require sufficient space equipment. Smartphones, while less precise, excel in accessibility and ease of use, making them ideal for large-scale studies or long-term at-home monitoring to capture real-world data when cost and convenience are key considerations. However, these different operational methods of the measurement systems lead to differences in outcomes. These discrepancies align with findings from other studies comparing smartphones to camera-based systems or force plates (Karlinsky et al., 2022; Rashid et al., 2021; Reimer et al., 2022). The selection of a measurement system should align with the specific goals of the study. While combining multiple measurement systems can make the most of their individual strengths, it may compromise the simplicity and feasibility of the study. For multi-site, international trials where simplicity and consistency are most important, the use of three wearable sensors (inertial measurement units) has been recommended as a standardized approach (Ilg et al., 2024).

In both studies, a large number of statistical tests and comparisons were conducted, many of which were not entirely independent. This increases the likelihood of Type I errors, meaning there is a higher chance of falsely identifying an effect as statistically significant when no true effect exists. For example, overlapping or related variables, such as different gait or balance variables, may lead to correlated outcomes that could exaggerate the statistical significance of certain findings. Additionally, repeated testing across multiple outcomes, groups, or time points compounds the risk of detecting false results due to random chance. To address this, corrections for multiple comparisons (Bonferroni corrections) were applied to control the risk of Type I errors. However, both corrected and uncorrected values were reported as part of an exploratory approach to identify potentially relevant outcomes that could guide future research. Therefore, caution should be exercised when interpreting uncorrected results.

While in our studies different gait and balance tasks have been used in a research setting, other studies recommend to focus outcomes on real-life scenarios (e.g., real-life walking or turning, Ilg et al., 2020; Seemann et al., 2024; Thierfelder et al., 2021), or even designing exercise programs that closely relate to real-life activities (Keller & Bastian, 2014; Miyai et al., 2012). For example, balance tasks could mimic actions such as reaching for objects, navigating uneven terrain, or transitioning between different surfaces. Integrating functional, everyday tasks into training and assessment routines could not only make the exercises more engaging but also improve their relevance to daily activities, potentially enhancing participants' motivation and adherence to therapy. On the other hand, these types of tasks are not yet fully understood, which limits their comparability. Therefore, at the moment, efforts should focus on adhering to established consensus protocols to ensure greater consistency and comparability of training protocols across study sites.

Participants in both studies were instructed to maintain their standard care routines and refrain from engaging in any additional activities or practicing beyond the prescribed interventions. For patients with hereditary degenerative cerebellar ataxias, standard care primarily consisted of ongoing physiotherapy, while for healthy participants, it typically involved regular sports activities. Although this approach mirrors a realistic, real-world scenario, it may have introduced variability in treatment consistency across participants. Such variability could influence the study outcomes, as uncontrolled external factors, such as differences in physiotherapy intensity or individual adherence to exercise routines, might have affected the results. However, this approach is commonly used in research settings (Cabanas-Valdés et al., 2024) and ensures the external validity of the findings, as it closely mirrors the conditions under which patients typically receive care. If suitable devices are available, future studies could control for external activities through activity tracking, helping to isolate the specific effects of the intervention and reduce the impact of confounding variables.

Last, an important consideration when interpreting the results of Study 2 is the inclusion of participants with a variety of hereditary degenerative cerebellar ataxias. Specifically, the following genetic diagnoses were present: SCA6 (10), SCA3 (5), SCA1 (3), SCA14 (3), ADCAIII (autosomal dominant cerebellar ataxia type III, 3), SCA2 (2), SCAR10 (2), CACNA1A (2), SCA27b, ATXN2/SCA2, ATP6 mutation, and EA2. This diversity introduces an additional layer of variability, as different types of ataxia can present with varying symptoms, progression rates, and responses to interventions. This variability may have influenced the overall outcomes, making it more challenging to detect uniform effects across the group. Furthermore, the heterogeneity of the patient population emphasizes the need for personalized approaches in both clinical assessments and interventions. In an ideal scenario with a sufficient number of study participants, future research could stratify individuals by genetic subtype or symptom severity. This approach would provide deeper insights into the specific effects of training programs on various forms of ataxia, enabling the development of more tailored and potentially more effective treatment strategies. While achieving such stratification may be challenging in single-site studies, given the rarity of these conditions, it represents a promising goal for multi-site, international trials. Collaborative efforts across centers could help overcome recruitment challenges, enhance sample sizes, and facilitate more nuanced analyses of treatment effects across diverse patient subgroups.

5 Future Directions

This section explores innovative methods and approaches, discussing their potential to enhance the design, implementation, and impact of future studies.

As summarized in the section 3 “Training Effects”, and as reported in recent literature (Milne et al., 2024), it is crucial to find optimal training parameters for home-based training programs. This can include variations of frequency, intensity, level of challenge, and duration of training sessions or training program. While rehabilitation and on-site training programs are better characterized (though still not optimally), home-based programs may require a different approach. The absence of direct supervision in such settings could necessitate adjustments to other training parameters to compensate for the potentially reduced level of challenge. This might include tailoring exercises to be more engaging, increasing the frequency or intensity of sessions, or incorporating digital feedback tools to provide guidance and maintain motivation.

While our and most other studies have used gait and/or balance tasks to assess functional mobility and motor impairment in patients with cerebellar ataxia, it was shown that cerebellar clusters were larger in running than in walking or standing (Cabaraux et al., 2023). Nevertheless, using tasks that involve running seems unrealistic for patients at other than pre-ataxic stages (SARA-score <3). Transferability to real-life scenarios is very limited or even not present, as patients probably will avoid running in their daily life to prevent falls. Instead, other tasks might be used that could increase the level of challenge, and thus help induce adaptation mechanisms and improve coordination and strength, possibly in combination with the use of ceiling lifts or other kinds of safety harnesses to avoid falls.

The data of the present work further demonstrated that it seems important to focus on the well-being of patients, as this not only enhances quality of life but may also amplify training effects. Gorcenco et al. (2024) suggest to improve the well-being of the patients by providing sufficient medical information about the disease. Other strategies are suggested by the patients themselves: A high number of patients report improved symptoms and well-being when using exercise, relaxation and social interaction strategies. As a future direction, well-being emerges as a critical parameter that warrants greater attention in research involving patients with cerebellar ataxia and other chronic conditions. It should be assessed as both a baseline characteristic to understand participants' starting points and as a key outcome measure to evaluate the broader impact of interventions beyond physical performance. Importantly, enhancing patients' well-being should be prioritized as an independent goal, even outside the scope of specific interventions, as improved well-being can significantly contribute to overall quality of life.

In future, advanced methods such as machine learning and artificial intelligence will be used more and more for discrimination of patients and healthy controls, severity assessment, feature selection (e.g., Ngo et al., 2021; Tartarisco et al., 2021), and for increasing the statistical power of study outcomes (for example, see Angelopoulos et al., 2023).

6 Conclusion

This dissertation explored the impact of a three-week, video-based training program at home targeting gait and balance in individuals with hereditary degenerative cerebellar ataxia. It combined insights from a feasibility study conducted with healthy participants, and a pilot randomized controlled trial with patients. This dual approach not only evaluated the practicality of implementing such training in home environments but also provided preliminary evidence on its effectiveness. As one of the few randomized controlled trails in the field, these findings make a contribution to future research aimed at refining and optimizing at-home rehabilitation strategies for ambulatory patients with hereditary degenerative cerebellar ataxia.

Key Conclusions:

- **Sensor Placement:** As Study 1 showed comparable measurement accuracy for sensor placement on either the front or back of the body, it is recommended to use wearable sensors in one of these two positions, prioritizing the method most convenient for participants.
- **Gait and Balance outcomes:** Gait and balance outcomes measured by a force plate were comparable to literature and showed good to excellent reliability according to intraclass correlation coefficients (0.69-0.96).
- **Role of Baseline Stability:** The addition of a baseline week in the patient study, which was based on findings in Study 1, might have helped reducing practice effects, as displayed by the number of improvements within the control group.
- **Impact of Training:** While exploratory analyses suggested some improvements in gait outcomes after the 2 x 40 minutes training and no significant improvements after the 4 x 20 minutes training, no consistent overall training effects across all groups were observed, emphasizing the need to refine training protocols for more robust results. This finding might be driven by small training volume or a not adequate level of challenge for the patient sample with mild to moderate disease severity.
- **Disease severity:** Study 2 emphasized the importance of disease severity as a moderator of training effects. Patients at more advanced disease stages might benefit more substantially from targeted gait and balance training compared to those with only mild impairment.
- **Patient Well-Being:** The findings highlighted the potential role of patient well-being as both a baseline characteristic and an outcome measure, encouraging its integration into future ataxia research to optimize training effects.
- **Future Directions:** The definition of optimized training parameters remains a central task for future studies. This includes designing home-based (gait and balance) training programs that are sufficiently challenging to promote improvements in ambulatory patients with hereditary degenerative cerebellar ataxia, accommodating a wide spectrum of disease severity.

By addressing both the challenges and opportunities in home-based gait and balance training programs, this work lays a foundation for refining intervention strategies and tailoring them to individual needs. Through its combination of feasibility assessments in healthy participants and a pilot randomized controlled trial in patients, the dissertation bridges a gap between exploratory research and practical application, contributing to more robust, multi-site clinical trials in the future.

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IX. Appendix A: Affidavit

Eidesstattliche Erklärung gemäß § 5 der Promotionsordnung vom 15.06.2018 der Mathematisch-Naturwissenschaftlichen Fakultät der Heinrich-Heine-Universität Düsseldorf:

Ich versichere an Eides Statt, dass die Dissertation von mir selbständig und ohne unzulässige fremde Hilfe unter Beachtung der „Grundsätze zur Sicherung guter wissenschaftlicher Praxis an der Heinrich-Heine-Universität Düsseldorf“ erstellt worden ist.

Die Dissertation wurde in der vorliegenden oder ähnlichen Form noch bei keiner anderen Institution eingereicht. Ich habe bisher keine erfolglosen Promotionsversuche unternommen.

Düsseldorf, den ______________ ______________________

Datum Clara Rentz

X. Appendix B: Original Research Articles

Original article of Study 1:

Rentz, C., Kaiser, V., Jung, N., Turlach, B. A., Sahandi Far, M., Peterburs, J., ... & Minnerop, M. (2024). Sensor-Based Gait and Balance Assessment in Healthy Adults: Analysis of Short-Term Training and Sensor Placement Effects. Sensors, 24(17), 5598.

I was the corresponding and first author of this article. I contributed to the ethical approval, conceptualization, methodology, and development of the study design and training program. I conducted the data acquisition and subsequently analyzed and interpreted the data. I wrote the first draft of the manuscript and all authors contributed to manuscript revision, discussion and interpretation of results and approved the final version of the manuscript.

Original article of Study 2:

Rentz, C., Reinhardt, A., Jung, N., Vanchinathan, V., Peterburs, J., Jacobi, H., ... & Minnerop, M. (2024). Three-week Video- and Home-based Training Program for Ataxia Patients: A Pilot Randomized Controlled Trial (manuscript submitted for publication)

I was the corresponding and first author of this article. I contributed to the ethical approval, conceptualization, methodology, and development of the study design and training program. I conducted the data acquisition together with my co-author A.R., and subsequently analyzed and interpreted the data. I wrote the first draft of the manuscript and all authors contributed to manuscript revision, discussion and interpretation of results and approved the final version of the manuscript.

sensors

MDPI

Article

Sensor-Based Gait and Balance Assessment in Healthy Adults: Analysis of Short-Term Training and Sensor Placement Effects

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Abstract: While the analysis of gait and balance can be an important indicator of age- or disease-related changes, it remains unclear if repeated performance of gait and balance tests in healthy adults leads to habituation effects, if short-term gait and balance training can improve gait and balance performance, and whether the placement of wearable sensors influences the measurement accuracy. Healthy adults were assessed before and after performing weekly gait and balance tests over three weeks by using a force plate, motion capturing system and smartphone. The intervention group (n = 25) additionally received a home-based gait and balance training plan. Another sample of healthy adults (n = 32) was assessed once to analyze the impact of sensor placement (lower back vs. lower abdomen) on gait and balance analysis. Both the control and intervention group exhibited improvements in gait/stance. However, the trends over time were similar for both groups, suggesting that targeted training and repeated task performance equally contributed to the improvement of the measured variables. Since no significant differences were found in sensor placement, we suggest that a smartphone used as a wearable sensor could be worn both on the lower abdomen and the lower back in gait and balance analyses.

Keywords: gait; balance; training; habituation effects; motion capturing; smartphone; IMU; wearables; sensor placement; home-based

1. Introduction

Gait disorders affect about 32% of the elderly population and are associated not only with lower quality of life and increased fall risk but also with cognitive decline and depression [1,2]. Since gait is an important marker of health, observational gait and stance analysis is common practice in neurology with standardized rating scales for general and disease-specific applications. A clear understanding of a patient's gait and its change over time is essential for optimized patient care and disease management [3]. Gait analysis is used to monitor the response to a variety of different interventions [4,5]. Although standardized rating scales help to guide clinical assessments by structuring the observations, they may have major drawbacks regarding interrater reliability, sensitivity, and specificity necessary for defining disease state or progression [6–11].

Quantitative gait analysis tools offer the ability to detect nuanced changes in gait by measuring spatiotemporal, kinetic, and kinematic gait characteristics [12,13]. These may include stride time, cadence, step width, joint angles, and time spent in each phase of the gait cycle [3]. For example, decreased stride length, decreased cadence, and increased gait variability have been observed in Parkinson's disease as one of the most frequent neurological movement disorders [12,14].

When evaluating participants over time, and especially when assessing an intervention, it is important to distinguish the effects of the intervention from the habituation effects of performing a test multiple times. While such "practice effects" or habituation effects are well known in neuropsychological tests [15,16], less knowledge is available on motor tasks, and specifically gait and balance. Meyer et al. [17] assessed the habituation effect in patients with multiple sclerosis for various standardized rating scales, including Timed Up and Go test, 2-Minute Walk Test, and Timed 25-Foot Walk Test. After performing these tests on three consecutive days, they found improvements due to habituation effects of up to 50% of the clinically meaningful detectable change and recommended that training tests should be performed before the actual assessment to mitigate the practice effect. Similarly, Keklicek et al. [18] investigated the habituation effect on balance in healthy participants using the Bertec balance test. Participants' stability improved between the first and second trial and was subsequently maintained (one attempt right after the other). This indicates a stabilization of the habituation effect after the third trial and supports the need for training tests prior to observation in stance tasks. However, Salthouse et al. [19], after analyzing six different cognitive tasks, reported that it might take up to seven years until no retest effect can be found. In a previous feasibility study, we compared a smartphone app to gold standard methods for assessing the effect of a three-week exercise intervention on gait and balance in a sample of healthy adults [20]. Participants improved their motor performance, but our study lacked a comparison to a control cohort not undergoing the exercise program (but performing the weekly gait and balance tests, including three gait tasks and four stance tasks). Here, we now present a group of participants that did not receive the training but completed the gait and balance tests to assess the practice/habituation effect induced only by the gait and balance tests per se and contextualize our previous findings.

Despite clear advantages, quantitative gait analysis methods are rarely used in clinical practice. This is partly due to the high cost and low ecological validity of the most commonly used systems [21–23]. Motion capture systems, while highly accurate, require trained personnel and a controlled laboratory environment [24]. Force plates are expensive and due to their limited length measurements are restricted to short distances and thus limit the ability to study gait variability over long distances [25,26]. Small, portable, and less expensive inertial measurement units (IMUs) address many of the aforementioned issues, but full-body IMU systems require that a sensor is placed on each body segment, which might impede the use of this technology for daily monitoring [25]. Therefore, wearable measurement systems with fewer IMU sensors and the use of IMU-equipped smartphones have recently become of great interest [27–32]. IMUs use an accelerometer, a gyroscope, and a magnetometer, which are now standard sensors in modern smartphones [33]. As of 2018, 78% of German adults own a smartphone, making this gait analysis method highly accessible in a person's daily life [34]. Additionally, smartphone-based measurement systems are inexpensive, allow for the monitoring of everyday gait and postural patterns, and incorporate familiar technology for users.

In systematic reviews [8,35], pelvis, shank, and feet have been named as the preferred segments for wearable sensor placement. Those studies using the pelvis mostly placed the wearable sensor or smartphone at the lower back (for review, see Hubble et al. [36] or Ilg et al. [31]), since it is close to the center of mass and movement there reflects the movement of the rest of the body [27,30,37]. Likewise, standard gait measurement systems like Mobility Lab [38–40] or other motion capturing systems like Xsens (Xsens Technologies B.V., Enschede, The Netherlands, https://www.movella.com/products/motion-capture, accessed on 24 July 2024) use one of their sensors at the lower back by default (L5 region). Differences in sensor placement have been assessed in several studies, but those studies only compared sensor placement on different segments of the body (e.g., pelvis vs. feet), not different placements on one specific segment (e.g., lower back or lower abdomen used as the "pelvis segment") [41–43]. In everyday life or during study participation requiring frequent interaction with the phone, a person may prefer to carry their phone on the front of their body as it is easier to reach and to handle [28]. This is particularly important for older people and patients with movement disorders, whose fine motor skills are often impaired in addition to their gait and already find it difficult to use a telephone. Improving the user-friendliness of a smartphone-based measurement system would facilitate the implementation of the technology in clinical trials with multiple study sites and frequent follow-up visits and would even allow remote recording of gait and stance in patient's everyday life. Therefore, it is necessary to understand if placing the device at the front or back of the body affects the results of the gait analysis. Even though a few studies used the wearable sensor or smartphone in a waist bag or belt [44], they did not define where the bag was placed [45] or left it open to the participants where to place the waist bag [46]. No comparison to "gold standard placement" at the lower back was performed and no explanation for a deviation from the standard was given. The present study therefore investigates a comparison of gait variables using a smartphone placed on the front vs. on the back of the trunk and compares those to standard laboratory methods using force plates.

This study builds on previous research by analyzing and distinguishing between training and habituation effects in healthy adults. This distinction is crucial not only for interpreting the outcomes of motor performance assessments but also for applying these findings to patient populations, where distinguishing between genuine intervention effects and practice effects is vital for disease management and the development of intervention strategies. Furthermore, we assessed whether the more convenient front placement of a smartphone sensor has any drawbacks compared to the traditional back placement, which is commonly used in gait analysis. This will help determine whether the more patient-friendly front placement can be used for gait and balance analyses in patient studies without compromising accuracy or whether the back placement is necessary for more precise measurements. If both placements prove equally accurate, the patient-friendly front placement could be recommended for future patient studies as it simplifies the feasibility of gait and balance assessments.

2. Materials and Methods

This study consists of three parts:

a. Analysis of habituation effects in healthy adults performing weekly gait and balance tests over three weeks,
b. Re-analysis of previously reported training effects [20] in healthy adults by comparing an intervention group (four times 20 min gait and balance training per week, plus weekly gait and balance tests at home) with a matched control group (only weekly gait and balance tests at home),
c. Comparative analysis of the results of gait and balance analysis obtained with sensor placement on the lower back (gold standard) vs. on lower abdomen (easier positioning into a waist bag).

2.1. Participants

All participants needed to be able to walk safely without a walking aid, have no joint problems (e.g., osteoarthritis, endoprostheses), or other neurological, muscular, or other medical problems affecting gait (e.g., falls, deep brain stimulation).

For the analysis of habituation effects, 26 participants were recruited to perform weekly gait and balance tests. For the re-analysis of training effects, this sample was compared to 25 participants from a previous feasibility study [20], receiving home-based video training in addition to the weekly gait and balance tests. For analyzing the impact of sensor placement on gait and balance analysis, 32 participants were recruited.

All participants gave their written informed consent in agreement with the Declaration of Helsinki, and the study protocol was approved by the ethics committee of the Faculty of Psychology of the Heinrich Heine University Düsseldorf, Germany (DU01-2021-01).

2.2. Tasks and Questionnaires

Participants had two study visits (T1 and T2) in Düsseldorf, Germany. At the study site, participants of the habituation vs. training effects cohort performed gait and balance tests, consisting of three different gait tasks (normal, backward, and tandem gait) and four different stance tasks (narrow, tandem, single leg stance, and narrow stance with eyes closed) on a force plate. Data were additionally measured by a motion capturing system (Mocap System) and individual smartphones of the participants. Participants were instructed to walk at a normal pace for the gait tasks and move as little as possible for the stance tasks. The maximum duration for a stance task was set to 30 s, but time was stopped if the participant held onto something or changed their foot position. During the three-week period at home, both groups repeated the seven gait and balance tests once a week at home. The intervention group additionally performed four trainings per week, 20 min each, containing mobility, strength, and coordination exercises [20]. By questionnaire, the participants' age, gender, height, weight, and years of education were retrieved, as well as depression and anxiety scores ([47], German version: HADS-D [48]), self-efficacy, optimism and pessimism (SWOP-K9 [49]), and general habitual well-being (FAHW [50]). Their self-efficacy in relation to falls was assessed via the (modified) German version of the Activities-Specific Balance Confidence scale (ABC-D [51]). Scale ranges and definitions can be found in Rentz et al. [20]. At the second study visit, participants again performed the gait and balance tests and completed the FAHW, SWOP-K9 and ABC-D questionnaires.

In the separate sample to test sensor placement, participants had only one study visit and performed a normal walk across the force plate (about 4 m each way) at their normal pace. They performed this task twice for two minutes each, once with the waist bag at the lower back and once with the waist bag in front on the lower abdomen.

2.3. Measurement Systems

A zebris FDM force plate (4.24 m, zebris Medical GmbH, Isny, Germany, https://www.zebris.de/en/medical/stand-analysis-roll-analysis-and-gait-analysis-for-the-practice, accessed on 27 August 2024), an Xsens motion capturing system (Xsens Technologies B.V., Enschede, Netherlands, https://www.xsens.com/motion-capture, accessed on 27 August 2024), and individual smartphones of the participants with the app JTrack Social installed [52] were used to measure gait and stance tasks of the participants. The force plate uses capacitive pressure sensors to capture the pressure distribution during the task. No preprocessing was performed on the force and pressure data, which were recorded with a frequency of 100 Hz. Gait or balance reports were created automatically by the Noraxon myoPressure™ software (Noraxon U.S.A., Inc., Scottsdale, AZ, USA, https://www.noraxon.com/our-products/myopressure/, accessed on 28 August 2024). The Mocap System uses 17 IMUs to record angular velocity, acceleration, atmospheric pressure, and the Earth's magnetic field. A calibration process (neutral pose, walk, turn, walk back) was performed as described in the MVN User Manual, i.e., to calculate the orientations of the sensors with respect to the corresponding segments. The data were recorded with the Xsens MVN 2020.2 software and stored in the mvnx format after reprocessing in HD. The participants' smartphones, which recorded accelerometer and gyroscope data, were placed in waist bags at the lower abdomen. Only in the group to test sensor placement was the waist bag placed at the lower back and lower abdomen successively. The gait and balance measurement systems, variable definitions, and feature extraction process have been described in detail by Rentz et al. [20]. It should be noted that the use of various smartphones introduces variability in the gait and balance measurements due to differences in hardware and sensor accuracy.

2.4. Statistical Analyses

An a priori calculation for the required sample size (G*Power 3.1.9.7 [53]) indicated a minimum number of 19 participants for one group to determine differences over time (matched pairs). A one-tailed significance level with $\alpha = 0.05$, $1 - \beta = 0.95$ and a calculated effect size of 0.8 (according to the results of gait velocity and cadence in Miyai et al. [54]) was used.

Chi-squared tests were used to analyze differences in distribution for gender and handedness. *T*-tests were used to test for differences in age, height, weight, years of education, anxiety and depression scores. A Mann–Whitney test was conducted to compare time spans between the two study visits and the number of missing data collection points at home.

Paired *t*-tests were conducted for both questionnaire scores and gait and balance variables to allow direct comparison to the previous results of the training group [20], as well as to compare mean differences between sensor placement at the front vs. back. Following the previous publication, Bonferroni correction for multiple comparisons with *p*-values of less than 0.013 (force plate, mocap system) and 0.017 (smartphone) were used for gait, and $p = 0.025$ for balance tasks. For all other statistical analyses, a *p*-value of less than 0.05 was considered significant. Spearman's rank correlation was calculated to examine the relationship between sensor placement (difference between front and back) and body weight of the participants. The Minimal Detectable Change (MDC) was calculated ($MDC_{90} = 1.64 * SEM * \sqrt{2}$ and $MDC_{95} = 1.96 * SEM * \sqrt{2}$) at the 90% and 95% confidence levels (SEM = standard error of measurement). The reliability of measurements was assessed using the intraclass-correlation coefficients (ICCs) with two-way random effects models.

Boxplots of all gait and balance variables were examined, and extreme outliers, defined as values greater than 3 times the interquartile range above the third quartile, were excluded.

For group comparison, we chose linear models with fixed and random effects as the statistical approach. A linear model using generalized least squares [55,56] was applied to describe three-way interaction effects between questionnaire scores, group (intervention or control), and measurement time (study visit 1, T1, or study visit 2, T2). Four-way interaction effects between gait or balance variable (cadence, stride time, and velocity for gait; sway area, and velocity for balance), group, measurement time, and measurement system used (force plate, Mocap System or smartphone) were investigated by using a linear mixed-effects model [57]. The same model was used separately for the different gait and balance tasks (e.g., backward gait, tandem stance) to decrease model difficulty. Pairwise comparisons were used to display patterns of interaction; however, they may not capture all nuances of the interaction between factors.

With a generalized least squares fitted linear model, the three-way interactions between the variable, the measurement system, and the placement of the waist bag (front, back) were described. For all linear models, stepwise backward elimination was used to select the most significant predictors and refine the model's explanatory power.

3. Results

3.1. Demographic Characteristics

The control group (n = 26) and intervention group (n = 25) did not differ significantly in the distribution of handedness (21 right-handed and 23 right-handed, respectively, $p = 0.663$), and gender (12 female and 13 female, respectively, $p = 0.891$). No statistical differences in age ($p = 0.253$), height ($p = 0.841$), weight ($p = 0.318$), years of education ($p = 0.345$), HADS anxiety score ($p = 0.264$), or depression score ($p = 0.347$) were found (see Table 1 for values). The number of tests actually carried out at home could not be checked. Only the number of smartphone recordings transmitted was available. No difference in the number of missing recordings was found ($p = 0.331$, 0.5 ± 0.8 missing recordings in the control group, 1.0 ± 1.2 in the intervention group, both in the range of 0 to 3). All participants confirmed that they had completed the requested measurements and training completely. Incomplete execution would not have led to any disadvantages regarding reimbursement.

Table 1. Demographic and anthropometric data for control and intervention groups.

Variable	Mean ± SD (Range Min.–Max.)	
	Control (n = 26)	**Intervention (n = 25)**
Age [years]	38.3 ± 17.4 (21–75)	44.1 ± 18.4 (20–71)
Body Height [cm]	172.8 ± 8.8 (155–185)	172.3 ± 9.9 (154–193)
Body Weight [kg]	72.32 ± 10.64 (57–90) [2]	67.83 ± 13.83 (43–97) [1]
Education [years]	14.5 ± 1.9 (12–20)	15.2 ± 3.2 (10–25)
HADS Anxiety [score]	4.3 ± 3.4 (0–14)	3.3 ± 2.8 (0–9)
HADS Depression [score]	2.0 ± 2.2 (0–7)	2.6 ± 2.6 (0–10)

[1] n = 18; [2] n = 19. HADS = Hospital Anxiety and Depression Scale; SD = standard deviation.

3.2. Group Comparison: Questionnaire Scores

No statistically significant three-way interaction effect between questionnaire scores, group, and measurement time was found ($p = 0.867$). After removing the three-way interaction from the model, no significant two-way interactions were found (p-values between 0.634 and 0.946). Eventually, in the resulting main-effects only model, neither the effect of the factor "group" ($p = 0.867$) nor of the factor "measurement time" ($p = 0.398$) was significant—only the factor "questionnaire scores" ($p < 0.0001$), indicating that single questionnaire scores differed from each other in general. Additional paired t-tests revealed no statistical difference for the single questionnaire scores over time (p-values between 0.091 and 0.880; for mean values of both groups, see Table 2).

Table 2. Questionnaire scores at first and second study visit for both groups.

Questionnaire [Score]	Control Group		Intervention Group	
	Mean ± SD (Min.–Max.)		**Mean ± SD (Min.–Max.)**	
	T1 (n = 26)	**T2 (n = 23)**	**T1 (n = 25)**	**T2 (n = 21)**
SWOP-SE	3.02 ± 0.53 (1.2–4.0)	3.03 ± 0.54 (2.0–4.0)	3.08 ± 0.49 (2.0–3.8)	3.23 ± 0.45 (2.2–4.0)
SWOP-OP	3.23 ± 0.71 (2.0–4.0)	3.33 ± 0.68 (2.0–4.0)	3.24 ± 0.63 (2.0–4.0)	3.12 ± 0.79 (1.5–4.0)
SWOP-PS	1.63 ± 0.61 (1.0–3.0)	1.67 ± 0.65 (1.0–3.0)	1.74 ± 0.61 (1.0–3.0)	1.67 ± 0.71 (1.0–3.0)
ABC-D	18.1 ± 3.11 [1] (16–28)	18.7 ± 4.85 (16–33)	18.0 ± 2.57 (16–28)	17.8 ± 2.34 (16–24)
FAHW	56.5 ± 20.7 [1] (1–89)	56.3 ± 23.1 (8–86)	59.1 ± 16.8 (21–83)	54.6 ± 25.3 [2] (−5–86)

[1] n = 25; [2] n = 20. ABC-D = Activities-Specific Balance Confidence scale, German version; FAHW = questionnaire for general habitual well-being; SD = standard deviation; SWOP = questionnaire for self-efficacy (SE), optimism (OP) and pessimism (PS); T1 = study visit one; T2 = study visit two.

3.3. Group Comparison: Gait and Balance Scores

To compare the control group without training to the previously published results of the intervention group, paired t-tests were conducted. These revealed a significant improvement between study visit 1 and study visit 2 for five variables in the control group: backward gait (BG) stride time ($p = 0.004$) and cadence ($p = 0.005$), as well as tandem gait (TG) stride time, cadence and velocity (all $p = 0.003$), all measured by the force plate. In comparison, the previous results of the intervention group revealed eleven variables with a significant improvement, including measurements from both the force plate and motion capturing system (see Table 3). For example, mean velocity in the normal gait (NG, measured by the force plate) increased non-significantly from 0.96 m/s to 1.00 m/s in the control group ($p = 0.361$) and significantly from 0.98 m/s to 1.09 m/s in the intervention group ($p = 0.002$). On the other hand, mean velocity in tandem gait (measured by the force plate) increased significantly from 0.41 m/s to 0.45 m/s in the control group ($p = 0.003$). The effect did not reach significance in the intervention group with mean velocity increasing from 0.45 m/s to 0.49 m/s ($p = 0.065$). To contextualize these findings, the Minimal Detectable Change (MDC) was calculated and is indicated in Table 3. For example, for mean velocity in the normal gait measured by the force plate, an MDC of 0.26 m/s (at a 95% confidence level, or 0.22 m/s at a 90% confidence level) was found for both groups. This indicates that both changes (0.11 m/s improvement in the intervention group and 0.04 m/s in the control group) did not exceed measurement error and variability. MDC values can be found in Table 3 for variables with significant changes, and all remaining values are shown in Appendix A (Table A1).

For the stance tasks, a single significant difference (surviving Bonferroni correction) between T1 and T2 was found in the control group: sway velocity in the single leg stance (SS), measured with the smartphone ($p = 0.013$), and one difference for the intervention group: sway velocity in the tandem stance (TS), measured with the force plate ($p = 0.006$).

Secondly, an advanced statistical model (linear model) was used to gain more profound insight into the interaction of the groups, measurement systems, study visits, and variables. Three significant four-way interactions were found, two within the narrow stance (NS, p-values 0.016 and 0.044) and one for the narrow stance with eyes closed (NSEc, $p = 0.003$). No statistically significant four-way interaction effect between gait or balance variables, group, measurement time and used measurement system was found for normal gait (NG, p-values between 0.620 and 0.973), backward gait (BG, p-values between 0.506 and 0.960), tandem gait (TG, p-values between 0.054 and 0.822), tandem stance (TS, p-values 0.067 and 0.119) and single leg stance (SS, p-values 0.215 and 0.848). The interactions are described in detail below.

For normal gait, stepwise backward elimination terminated at a model that included overall two two-way interactions: one between the variable and measurement time and one between the variable and measurement system used. The individually listed contrasts revealed a difference in step width between force plate and Mocap System (higher step width for force plate, $p = 0.002$) and in step width between T1 and T2 in general, not depending on the group or measurement system (lower step width at T2, $p = 0.002$).

For backward gait and tandem gait, stepwise backward elimination terminated at a model that included a three-way interaction between the variable, group, and measurement system used (p-values < 0.0001 to 0.007), but none of the significant interactions included the measurement time (T1, T2). In backward gait, the individually listed contrasts revealed a difference in the step width between the two groups when measured with the Mocap System (lower step width for intervention group, $p = 0.0005$) and a difference in step width between the force plate and the Mocap System in general (higher step width for the force plate, $p < 0.0001$). In tandem gait, individually listed contrasts showed a difference in step width between the two groups (lower step width for intervention group, $p < 0.0001$, measured with the Mocap System) and a difference in cadence between the two groups (higher cadence in the intervention group, $p = 0.024$, measured with the smartphone), as well as a difference in step width between the force plate and the Mocap System in general (higher step width for the Mocap System, $p = 0.002$ for the intervention group, $p < 0.0001$ for the control group).

Table 3. Side-by-side presentation of intervention group and control group at the first and second study visit.

Measurement System	Variable	Control Group Mean ± SD (Min.–Max.) T1	Control Group Mean ± SD (Min.–Max.) T2	Control Group Sign./ MDC95	Control Group ICC	Intervention Group Mean ± SD (Min.–Max.) T1	Intervention Group Mean ± SD (Min.–Max.) T2	Intervention Group Sign./ MDC95	Intervention Group ICC
Force Plate	NG stride time	1.20 ± 0.10 s (1.02–1.40)	1.16 ± 0.07 s (1.01–1.31)	p = 0.053 0.17	0.52	**1.20 ± 0.13 s** **(0.97–1.55)**	**1.13 ± 0.10 s** **(0.91–1.29)**	**p = 0.003** 0.18	0.71
	NG cadence	1.69 ± 0.14 s^{-1} (1.43–1.95)	1.73 ± 0.10 s^{-1} (1.53–1.98)	p = 0.077 0.23	0.53	**1.70 ± 0.17 s^{-1}** **(1.30–2.08)**	**1.80 ± 0.18 s^{-1}** **(1.55–2.20)**	**p = 0.002** 0.22	0.80
	NG velocity	0.96 ± 0.16 m/s (0.58–1.28)	1.00 ± 0.10 m/s (0.81–1.19)	p = 0.361 0.26	0.51	**0.98 ± 0.14 m/s** **(0.64–1.28)**	**1.09 ± 0.12 m/s** **(0.92–1.42)**	**p = 0.002** 0.26	0.59
	NG step width	11.1 ± 2.1 cm (8–16)	10.6 ± 2.5 cm (6–16)	p = 0.266 3.68	0.66	**11.6 ± 2.6 cm** **(7–16)**	**10.7 ± 2.5 cm** **(8–15)**	**p = 0.004** 2.18	0.91
	BG stride time	**1.24 ± 0.13 s** **(0.99–1.64)**	**1.17 ± 0.12 s** **(0.98–1.38)**	**p = 0.004** 0.22	0.60	*1.22 ± 0.13 s* *(1.04–1.56)*	*1.18 ± 0.12 s* *(0.94–1.37)*	*p = 0.027* 0.20	0.68
	BG cadence	**1.64 ± 0.16 s^{-1}** **(1.23–2.02)**	**1.73 ± 0.17 s^{-1}** **(1.45–2.03)**	**p = 0.005** 0.29	0.61	*1.66 ± 0.16 s^{-1}* *(1.32–1.92)*	*1.72 ± 0.18 s^{-1}* *(1.47–2.12)*	*p = 0.028* 0.27	0.68
	BG velocity	*0.63 ± 0.12 m/s* *(0.33–0.78)*	*0.70 ± 0.11 m/s* *(0.50–0.89)*	*p = 0.013* 0.22	0.55	**0.69 ± 0.09 m/s** **(0.53–0.86)**	**0.76 ± 0.09 m/s** **(0.61–0.92)**	**p = 0.005** 0.16	0.65
	TG stride time	**1.83 ± 0.34 s** **(1.33–2.57)**	**1.69 ± 0.31 s** **(1.25–2.43)**	**p = 0.003** 0.49	0.72	1.66 ± 0.31 s (1.19–2.44)	1.61 ± 0.35 s (1.00–2.44)	p = 0.180 0.65	0.49
	TG cadence	**1.14 ± 0.22 s^{-1}** **(0.78–1.52)**	**1.24 ± 0.22 s^{-1}** **(0.83–1.62)**	**p = 0.003** 0.30	0.76	*1.23 ± 0.24 s^{-1}* *(0.68–1.68)*	*1.33 ± 0.26 s^{-1}* *(0.85–2.02)*	*p = 0.019* 0.32	0.79
	TG velocity	**0.41 ± 0.09 m/s** **(0.25–0.58)**	**0.45 ± 0.10 m/s** **(0.28–0.64)**	**p = 0.003** 0.15	0.67	0.45 ± 0.12 m/s (0.22–0.72)	0.49 ± 0.13 m/s (0.25–0.83)	p = 0.065 0.14	0.84
	TS sway velocity	43.3 ± 17.2 mm/s (26–99)	41.7 ± 20.9 mm/s (13–103)	p = 0.419 24.92	0.77	**52.3 ± 17.9mm/s** **(28–107)**	**45.7 ± 22.7 mm/s** **(22–113)**	**p = 0.006** 28.64	0.74
Mocap System	NG stride time	1.18 ± 0.13 s (0.99–1.36)	1.15 ± 0.10 s (0.98–1.27)	p = 0.104 0.15	0.59	**1.18 ± 0.13 s** **(0.94–1.51)**	**1.11 ± 0.10 s** **(0.93–1.28)**	**p = 0.002** 0.19	0.67
	NG cadence	1.70 ± 0.14 s^{-1} (1.47–2.02)	1.75 ± 0.11 s^{-1} (1.58–2.05)	p = 0.137 0.22	0.62	**1.71 ± 0.18 s^{-1}** **(1.33–2.13)**	**1.82 ± 0.17 s^{-1}** **(1.56–2.14)**	**p = 0.001** 0.24	0.77
	BG velocity	0.63 ± 0.12 m/s (0.34–0.78)	0.64 ± 0.14 m/s (0.25–0.89)	p = 0.131 0.21	0.67	**0.66 ± 0.12 m/s** **(0.31–0.84)**	**0.75 ± 0.10 m/s** **(0.58–0.89)**	**p = 0.007** 0.26	0.34

Table 3. *Cont.*

Measurement System	Variable	Control Group				Intervention Group			
		Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC	Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC
		T1	T2			T1	T2		
Mocap System	TG stride time	1.93 ± 0.59 s (1.24–3.76)	1.73 ± 0.37 s (1.20–2.51)	*p* = 0.069 0.69	0.75	**1.76 ± 0.42 s (1.17–3.11)**	**1.49 ± 0.23 s (1.00–1.96)**	***p* = 0.003** 0.64	0.61
	TG cadence	1.12 ± 0.28 s^{-1} (0.53–1.61)	1.21 ± 0.24 s^{-1} (0.80–1.66)	*p* = 0.106 0.31	0.83	**1.19 ± 0.25 s^{-1} (0.64–1.70)**	**1.35 ± 0.18 s^{-1} (1.02–1.69)**	***p* = 0.001** 0.38	0.65
Smart-phone	SS sway velocity	**30.5 ± 8.9 mm/s (10.9–57.4)**	**44.6 ± 4.4 mm/s (18.5–107.5)**	***p* = 0.013** 46.7	0.36	16.9 ± 8.9 mm/s (0.9–32.6)	17.8 ± 4.4 mm/s (8.1–22.9)	*p* = 0.439 12.4	0.62

p-values highlighted in bold represent significant values after Bonferroni correction (<0.013 for gait tasks, <0.025 for balance tasks), *p*-values in italics represent significant values before Bonferroni correction (<0.05). The Minimal Detectable Change (MDC) for a 95% confidence interval is indicated for both the intervention and control groups. BG = backward gait, ICC = Intraclass Correlation Coefficient, Interv. = intervention group, NG = normal gait, Sign. = significance, SS = single leg stance, TG = tandem gait, TS = tandem stance, T1 = study visit one, T2 = study visit two.

ference in step width between the two groups (lower step width for intervention group, $p < 0.0001$, measured with the Mocap System) and a difference in cadence between the two groups (higher cadence in the intervention group, $p = 0.024$, measured with the smartphone), as well as a difference in step width between the force plate and the Mocap System in general (higher step width for the Mocap System, $p = 0.002$ for the intervention group, $p < 0.0001$ for the control group).

For tandem stance and single leg stance, stepwise backward elimination terminated at a model that included a three-way interaction between the variable, group and measurement system used (*p*-values < 0.0001 to 0.002), as well as a three-way interaction between the variable, measurement system and stance ($p = 0.043$). As for tandem stance, this included a difference between the intervention and control group when measured by smartphone (higher sway area in the intervention group) or Mocap System (higher sway area in the control group), as well as a difference between the measurement systems for sway area in both groups (higher sway area for Mocap System compared to smartphone and force plate, and for force plate compared to smartphone); no differences were found for sway velocity. In single leg stance, differences in sway area were found between intervention and control group at T1 and an even greater difference at T2 (higher sway area in the control group, $p < 0.0001$, measured with the Mocap System).

A four-way interaction was present in the narrow stance with eyes closed (see Figure 1 for raw data), indicating a complex interaction of all factors for this task. Individual contrasts showed an increase in sway area between T1 and T2 for the intervention group, measured with the smartphone ($p = 0.038$), and for the control group, measured with the Mocap System ($p < 0.0001$). Another difference was found in sway area between the intervention group and control group at T2, measured with the smartphone (higher sway area in the intervention group, $p = 0.027$) and with the Mocap System (higher sway area in the control group, $p < 0.0001$). Another significant four-way interaction was found in the narrow stance (see Figure 1 for raw data), where individual contrasts revealed a difference in sway area between T1 and T2 for the intervention group (higher sway area at T2, $p = 0.0002$, measured with the smartphone); as well as between intervention group and control group at T1 (higher sway area in the control group, $p = 0.0003$, measured with the Mocap System) and at T2 (higher sway area in the intervention group, $p = 0.0001$, measured with the smartphone; and higher in the control group, $p < 0.0001$, measured with the Mocap System).

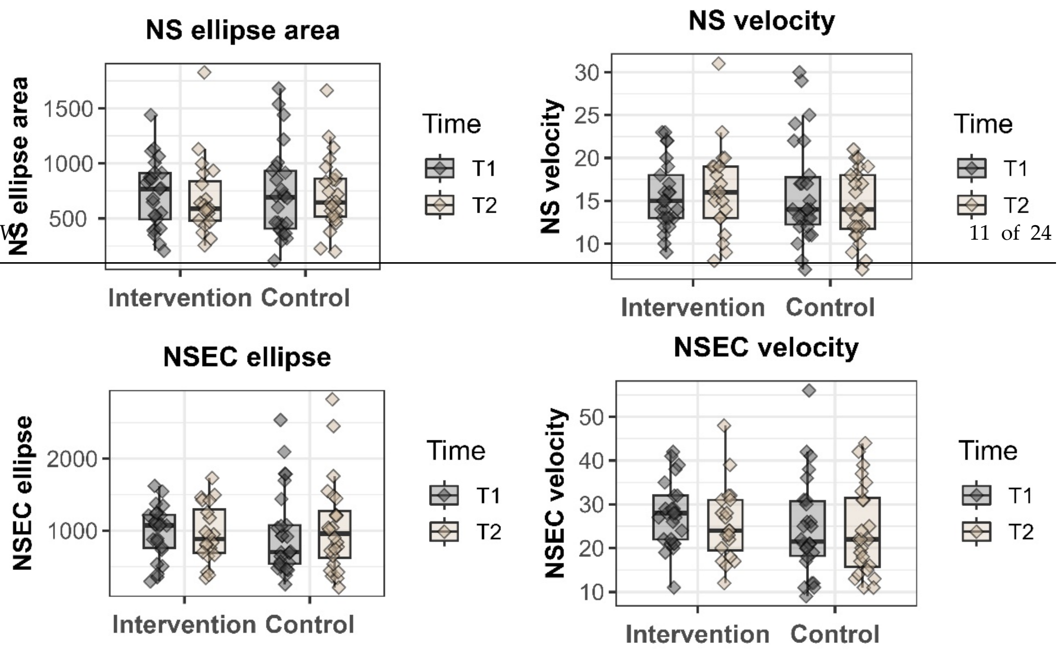

Figure 1. Narrow stance with eyes open (NS) and with eyes closed (NSEc) variables, as the tasks showing the only four-way interaction in the linear models, displayed for the control group and intervention group at both study visits, measured with the force plate.

3.4. Sensor Placement

In the sensor placement group, 32 middle-aged adults took part in the study (37.1 ± 15.7 years old, 171.5 ± 6.4 cm body height, 72.9 ± 14.9 kg body weight, body mass index 24.7 ± 4.3).

The interaction model indicated no statistically significant interaction for the three-way interactions of variable, measurement system and sensor placement (*p*-values 0.237 to 0.396). Significant two-way interactions were only found between the variable and measurement system ($p < 0.005$).

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Additionally, we checked whether the mean differences between smartphone and force plate values (same task, same variable) were different, depending on the sensor placement (front vs. back). No statistically significant difference was found for any of the variables (p-values 0.116 to 0.192, see Table 4).

Table 4. Comparison of normal gait variables for sensor placement at the front or back.

Variable	Smartphone		Force Plate		
	Mean ± SD Front (Min.–Max.)	**Mean ± SD Back (Min.–Max.)**	**Mean ± SD Front (Min.–Max.)**	**Mean ± SD Back (Min.–Max.)**	**Sign.**
velocity	0.66 ± 0.17 m/s (0.35–1.06)	0.63 ± 0.15 m/s (0.37–1.10)	1.05 ± 0.15 m/s (0.83–1.42)	1.07 ± 0.14 m/s (0.83–1.36)	$p = 0.118$
str. time	1.31 ± 0.24 s (1.03–2.09)	1.45 ± 0.64 s (0.53–3.38)	1.20 ± 0.10 s (1.03–1.37)	1.19 ± 0.10 s (1.00–1.42)	$p = 0.192$
cadence	1.56 ± 0.26 s^{-1} (0.93–2.00)	1.51 ± 0.41 s^{-1} (0.48–1.99)	1.68 ± 0.14 s^{-1} (1.47–1.95)	1.70 ± 0.14 s^{-1} (1.42–2.00)	$p = 0.116$

p-values refer to the mean difference between front and back placement, comparing the difference of differences between the two measurement systems. Str. = stride. Differences between the two measurement systems are likely attributable to the way they operate (accelerometry vs. capacitive sensors).

To test whether the difference between front and back, measured with the smartphone, was dependent on body weight, we calculated the linear correlation between the individual differences and body weights. The weak correlation of 0.21 did not reach statistical significance ($p = 0.317$).

4. Discussion

This study applied three different measurement systems to analyze in healthy adults (a) the impact of habituation effects on an improvement of gait and balance variables before (T1) and after (T2) performing a gait and balance training, and (b) the effect of sensor (smartphone) placement on the body on gait variables in comparison to values obtained with a force plate as the gold standard.

4.1. Training Effect vs. Habituation Effect

Clear and significant training effects are typically anticipated in subjects with age- or disease-related limitations [5,54,58–60]. However, healthy control subjects frequently serve as a comparison group in training studies targeting these populations. Therefore, it is crucial to understand whether unintended habituation or training effects in the control group could obscure a potential group-specific effect in the actual target population (patients, older adults) within the study setting.

When using paired t-tests within each group to compare mean differences of the first and second study visit, we found significant improvements in both the control group and—as reported earlier—the intervention group [20], mainly in gait and only in two stance variables. Remarkably, there was no overlap regarding the involved variables between both groups. Thus, none of the variables with a significant change at the second study visit in the control group showed significant changes in the intervention group and vice versa. In the control group, participants performed better at follow-up after three weeks in variables related to the more difficult gait tasks (backward and tandem gait), while they performed worse at the second study visit in the single leg stance. Participants of the intervention group also performed better in (a different set of) variables related to backward and tandem gait, but also in normal gait and tandem stance (Table 3). Interestingly, although the significant variables of the control and intervention group did not match, in the backward gait measured with the force plate, all corresponding variables in the respective other group were close to significance (significant before Bonferroni correction, p-values between 0.013 and 0.028). This was not the case for normal gait, only for one variable in the tandem gait, and not for the other two measurement systems, indicating a tendency for habituation effects in the backward gait, i.e., participants might show improvements in backward gait after repeating the tasks three times (once weekly) at home. Given that the number of gait and stance tasks as well as the respective variables with significant improvements (across all measurement systems) was higher in our intervention group (eleven improvements in four tasks) compared to our control group (five improvements in two tasks), this could be interpreted cautiously as indicator of (a) a habituation effect for the more difficult tandem gait tasks and especially backward gait, and (b) a training effect of a short-term training of three weeks, which is stronger than the habituation effect, relevant for normal gait and the tandem stance task.

A potential habituation effect indicated by the comparison of the control group and intervention group is partly in line with Meyer et al. [17] and Keklicek et al. [18], who found improvements between the first and second trial in a gait (patients with multiple sclerosis and healthy adults, respectively) or balance task (healthy adults) at much shorter intervals (three repetitions in three days, or seven repetitions in one day, respectively). Probably because of these short intervals, Keklicek et al. [18] found an improvement between the first and second trial but a stabilization afterwards, while our participants had weekly tests and were only assessed in their first and fifth trial (three trials at home), indicating a potential habituation effect after the fifth trial. Of note, in our study, it was not possible to check whether and to what quality the measurements (corresponding to trials 2–4) and training were carried out at home. Our intention was to keep the study setup and instructions for the video-based training and gait and balance tests at home as simple as possible to facilitate the implementation (little technical equipment, clear instructions) and thus maintain the adherence of the participants to the training and reduce the risk of dropouts. Even though this setup limited our ability to comprehensively monitor the correct performance of the training and tests at home, all participants confirmed that training and measurements had been carried out in full, and the number of unsubmitted smartphone data showed no statistical difference between the two groups. However, future studies could explore alternative methods for tracking home-based assessments, such as monitoring the playback time of the training videos or regular phone checks, in addition or instead of more extensive documentation using a camera system, to improve data collection and address this limitation more effectively.

While the studies mentioned above assessed habituation effects, other studies addressed gait and balance training effects in subjects of different age groups or with various diseases using different periods of training and different statistical approaches, mostly repeated measures ANOVA. Applying a three-week balance training program, as in our study, significant improvements in step widths and step width variability were found in healthy older adults [58], or improvements in gait velocity, cadence, and stride length in patients with stroke [59]. Other studies used slightly longer time periods, and Mak et al. [60] recommended a minimum of four weeks of training for gait training and eight weeks for balance training in their review of patients with Parkinson's disease. A longer time period may lead to higher training effectiveness [61,62], in particular, if exactly those tasks are trained that are also assessed [63,64], but this may also result in a drop in compliance [65]. However, Li et al. [66] compared Tai Chi training to conventional training in their meta-analysis and found that, among the included studies, only Tai Chi training with shorter time periods (<20 weeks) and shorter total duration (<24 h) showed greater improvement compared to conventional training. Chaabene et al. [67] found in their meta-analysis small positive effects of home-based strength and balance training in healthy older adults, but no overall influence of training duration, frequency or session duration. These results demonstrate that there is still no clear consensus on detailed, optimal training designs.

When considering the calculated MDC in our samples, this indicates that the changes observed within each group applying paired *t*-tests were not large enough to exceed measurement error and variability.

Since comparing first and second study visit within each group does not allow statistically sound statements regarding group differences, we additionally applied a linear mixed effect model to investigate four-way interaction effects between gait or balance variable, group, measurement time and measurement system. By using this statistically more sophisticated approach, only one interaction hinting towards a potential habituation effect was found: in normal gait step, widths were lower at T2 in general, indicating that participants were able to improve their gait stability between the first and second study visit, independent of group affiliation. With respect to training effects, most gait and balance tasks (five out of seven) revealed no significant different trends over time in our control group vs. intervention group, arguing against a training effect. There are several possible explanations for why both training and habituation effects resulted in significant improvements in gait and balance. The most obvious is that practicing the tasks may have been more challenging than the training itself, leading to improvements through repetition. Alternatively, the initial performance may have been low, so any form of practice—whether through training or habituation—would naturally lead to improvements. Other less likely explanations could involve different underlying mechanisms of improvement, such as increased motivation to perform better with each subsequent attempt. The narrow stance with eyes closed and eyes open were the only two tasks where an interaction between all four factors of interest was found, indicating a group difference over time. However, according to pairwise contrast calculations, these group differences were surprisingly caused by an increase in sway area (worse performance) over time for the intervention group (smartphone) and the control group (Mocap System), arguing against a training effect for these two stance tasks as well. The observed decline was contrary to the literature [68]. Of interest, Uematsu et al. [69] found an effect of a dual-task balance training on dynamic and static balance in a small healthy older adults' cohort, but similar to our study, their control group without training decreased in their standing time in the single leg stance. We observed a similar decline in performance for two stance tasks in our control and in our intervention group (healthy subjects). Possible reasons could be that by being familiar with the task, participants underestimated it, paid less attention or lost their focus, as it was no longer a challenging new task.

Our approach also revealed some methodological issues. Compared to the control group, participants of the intervention group had lower step widths in backward and tandem gait plus higher cadence in tandem gait as well as lower sway area in narrow stance at both visits, which might hint towards an overall better gait performance of the intervention group, independent of measurement time. Possible reasons for this are unclear since both groups did not differ regarding age or anthropometric data. However, if the intervention group should have had an overall better gait performance, this would have increased the likelihood of depicting significant group differences compared to our control group—which was not the case. This further strengthens our assumption, that there was no relevant training effect in our intervention group. The linear models indicated that step widths measured with the force plate were in general different compared to step widths measured with the Mocap System. These differences are likely attributable to the way these two measurement systems operate—while the former uses pressure capacitive sensors with precise distance information, the latter is prone to imprecision in the calibration process which is used to create an avatar based on biomechanical models. The different measurement systems, mocap system and smartphone, led to contradictory results in three out of four stance tasks (tandem stance, narrow stance with eyes open/closed): using the smartphone, sway area was larger in the intervention group, but using the Mocap System, sway area was larger in the control group. This indicates that, at least for stance tasks, these two measurement systems are not yet highly comparable. Differences in accuracy are known from other studies using smartphones vs. camera-based systems [70,71], or smartphones vs. force plate [72], and should be minimized in the future. In general, the ways of operating and different advantages/disadvantages of the three measurement systems should be considered depending on the study setup and the tasks analyzed: while the force plate, which is considered the gold standard, shows an excellent accuracy but is limited to laboratory environments, Mocap Systems offer a balance between accuracy and flexibility, making them suitable for a broader range of settings, including assessments at home, although with some restrictions regarding space and maximum possible time interval. Smartphones, on the other hand, are less precise but provide the greatest accessibility and ease of use, making them ideal for large-scale studies or at-home monitoring over longer time periods (e.g., to capture real-world data) where cost and convenience are prioritized. Considering that the measuring systems all work in different ways, not only the four-way but also the three-way interactions between gait or balance variable, group and measurement time only would have been of interest for detecting training effects, but no interaction of that kind was found.

Summing up, both the three-week gait and balance training in the intervention group and just repeating gait and balance tests once per week in the control group led to improvements in the tested gait and stance tasks, but these improvements did not differ and were below measurement error and variability according to the MDC calculation. The additional gait and balance training therefore did not generate a measurable additional benefit in healthy controls. Our future research efforts will focus on examining patient data to build on the insights gained from this study and to explore the implications of our findings in a clinical context. Understanding how certain effects manifest in healthy subjects is crucial for accurately interpreting patient outcomes (particularly when compared with healthy control subjects) and ensuring the relevance of our findings in a clinical setting. Our findings can help to understand how much of the observed improvement might be due to specific training versus general familiarity with the tasks. While we cannot directly infer how these improvements would differ in patients, establishing this baseline in healthy subjects is a critical step toward interpreting studies comparing patient data to a control group more accurately.

4.2. Sensor Placement

While previous studies have assessed differences in sensor placement, addressing the placement at different body segments [35,41–43,73], our study addresses differences between specific sensor (smartphone) placement at the pelvis (lower back vs. lower abdomen). The lower abdomen might be the most convenient place to put a sensor since, e.g., smartphones used as a sensor device could easily be put into a waist bag or pants pocket [74].

Of note, our results did not reveal a statistically significant interaction between the variable, measurement system, and sensor placement, suggesting that the placement of the sensor (front vs. back) does not have an overall influence on the outcome variable. The only significant two-way interaction found was an interaction between the measurement system and variable, indicating that, not surprisingly, the measurement system used (force plate, Mocap System or smartphone) did have an influence on the value of the outcome variable. Any interaction including sensor placement did not reach statistical significance (p-values between 0.145 and 0.396). Additionally, calculated differences between the values for each variable obtained with the force plate (gold standard measurement system) and the smartphone did not differ between front vs. back placement of the smartphone. Furthermore, the differences between front and back placement were not dependent on body weight. While the effect of obesity on gait kinematics in general (e.g., shorter step length, longer stance phase) is well known [75], only few studies assessed the influence of BMI on gait analyses with wearable sensors [76,77], but they did not compare their results to a gait analysis system that did not use body-worn sensors. Our sample included healthy adults with on average normal body weight but included both an underweight adult (n = 1, BMI < 18.5) and adults with obesity (n = 3, BMI of 30 or greater), suggesting the generalizability of these findings to a diverse and representative population.

While previous studies have used wearable sensors mostly at the lower back [31,36], the results of the present study support the use of wearable sensors in a manner (front of body) that is most convenient for participants, which could ideally lead to greater study adherence and lower drop-out rates. Additionally, this increases comparability to other studies which might have used a sensor placement at the lower back. Nevertheless, further studies should address whether our results obtained in a sample of healthy adults with a broad age and weight range can be generalized to patient samples or samples with a more restricted age range.

5. Conclusions

In our previous analysis, which was restricted to the intervention group [20], a three-week gait and balance training was able to induce small changes in a group of healthy adults. The here performed comparison with a control group addressed habituation effects and applied more advanced statistical models to compare both groups. Both the training and habituation effects resulted in significant improvements in gait and balance after a three-week period of either weekly tests alone or a combination of training and weekly tests. However, these improvements remained below the calculated measurement error and variability. While three weeks of gait and balance training in healthy adults did not significantly enhance gait and stance patterns beyond the small improvements already achieved through weekly tests alone, the overall positive impact on motor function is promising. This indicates that even minimal interventions could possibly lead to detectable changes in gait and balance in healthy adults and that more intensive training may be necessary to produce distinct training effects. These insights are important for contextualizing patient data, as they provide a baseline for understanding how different types of interventions might influence outcomes in a clinical setting. Based on the results and limitations of the current study, for future investigations, we recommend addressing video-based training at home to implement monitoring of tasks performed at home (e.g., tracking, regular calls) and at least one baseline measure to reduce habituation effects. In addition, our analysis of the sensor placement (lower abdomen vs. lower back) showed comparable values in healthy adults, which leads to the conclusion that a smartphone as a wearable sensor could also be worn in the position on the lower abdomen, which is probably more comfortable and easier to access for study participants.

Future studies should explore the effects of varying training frequencies, durations and intensities to clarify when the training and habituation effects stabilize and to gain a better understanding of how these factors and effects influence outcomes.

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Informed Consent Statement: Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: The sensor data presented in this study are openly available in the pedestrian dynamics data archive at https://doi.org/10.34735/ped.2022.7.

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Conflicts of Interest: The authors declare no conflicts of interest.

Appendix A

Table A1. Comparison of *t*-test results of the intervention group and control group for all variables.

Measurement System	Variable	Control Group				Intervention Group			
		Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC	Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC
		T1	T2			T1	T2		
Force Plate	NG stride time	1.20 ± 0.10 s (1.02–1.40)	1.16 ± 0.07 s (1.01–1.31)	*p* = 0.053 0.17	0.52	**1.20 ± 0.13 s (0.97–1.55)**	**1.13 ± 0.10 s (0.91–1.29)**	***p* = 0.003** 0.18	0.71
	NG cadence	1.69 ± 0.14 s^{-1} (1.43–1.95)	1.73 ± 0.10 s^{-1} (1.53–1.98)	*p* = 0.077 0.23	0.53	**1.70 ± 0.17 s^{-1} (1.30–2.08)**	**1.80 ± 0.18 s^{-1} (1.55–2.20)**	***p* = 0.002** 0.22	0.80
	NG velocity	0.96 ± 0.16 m/s (0.58–1.28)	1.00 ± 0.10 m/s (0.81–1.19)	*p* = 0.361 0.26	0.51	**0.98 ± 0.14 m/s (0.64–1.28)**	**1.09 ± 0.12 m/s (0.92–1.42)**	***p* = 0.002** 0.26	0.59
	NG step width	11.1 ± 2.1 cm (8–16)	10.6 ± 2.5 cm (6–16)	*p* = 0.266 3.68	0.66	**11.6 ± 2.6 cm (7–16)**	**10.7 ± 2.5 cm (8–15)**	***p* = 0.004** 2.18	0.91
	BG stride time	**1.24 ± 0.13 s (0.99–1.64)**	**1.17 ± 0.12 s (0.98–1.38)**	***p* = 0.004** 0.22	0.60	*1.22 ± 0.13 s (1.04–1.56)*	*1.18 ± 0.12 s (0.94–1.37)*	*p = 0.027* 0.20	0.68
	BG cadence	**1.64 ± 0.16 s^{-1} (1.23–2.02)**	**1.73 ± 0.17 s^{-1} (1.45–2.03)**	***p* = 0.005** 0.29	0.61	*1.66 ± 0.16 s^{-1} (1.32–1.92)*	*1.72 ± 0.18 s^{-1} (1.47–2.12)*	*p = 0.028* 0.27	0.68
	BG velocity	*0.63 ± 0.12 m/s (0.33–0.78)*	*0.70 ± 0.11 m/s (0.50–0.89)*	*p = 0.013* 0.22	0.55	**0.69 ± 0.09 m/s (0.53–0.86)**	**0.76 ± 0.09 m/s (0.61–0.92)**	***p* = 0.005** 0.16	0.65
	BG step width	17.7 ± 3.7 cm (13–23)	17.0 ± 3.7 cm (9–23)	*p* = 0.167 4.28	0.81	18.1 ± 3.2 cm (10–24)	17.5 ± 3.2 cm (12–24)	*p* = 0.203 3.77	0.82
	TG stride time	**1.83 ± 0.34 s (1.33–2.57)**	**1.69 ± 0.31 s (1.25–2.43)**	***p* = 0.003** 0.49	0.72	1.66 ± 0.31 s (1.19–2.44)	1.61 ± 0.35 s (1.00–2.44)	*p* = 0.180 0.65	0.49
	TG cadence	**1.14 ± 0.22 s^{-1} (0.78–1.52)**	**1.24 ± 0.22 s^{-1} (0.83–1.62)**	***p* = 0.003** 0.30	0.76	*1.23 ± 0.24 s^{-1} (0.68–1.68)*	*1.33 ± 0.26 s^{-1} (0.85–2.02)*	*p = 0.019* 0.32	0.79
	TG velocity	**0.41 ± 0.09 m/s (0.25–0.58)**	**0.45 ± 0.10 m/s (0.28–0.64)**	***p* = 0.003** 0.15	0.67	0.45 ± 0.12 m/s (0.22–0.72)	0.49 ± 0.13 m/s (0.25–0.83)	*p* = 0.065 0.14	0.84
	TG step width	2.3 ± 0.9 cm (1–4)	2.2 ± 1.0 cm (1–4)	*p* = 1.000 2.11	0.31	2.2 ± 1.0 cm (1–5)	2.0 ± 0.9 cm (1–4)	*p* = 0.549 2.26	0.32
	NS sway area	724 ± 403 mm^2 (118–1680)	721 ± 332 mm^2 (199–1663)	*p* = 0.992 807	0.37	720 ± 308 mm^2 (206–1439)	688 ± 353 mm^2 (256–1826)	*p* = 0.492 891	0.02
	NS sway velocity	16.0 ± 6.0 mm/s (7–30)	14.3 ± 4.1 mm/s (7–21)	*p* = 0.556 9.48	0.57	15.6 ± 4.0 mm/s (9–23)	16.3 ± 5.3 mm/s (8–31)	*p* = 0.744 8.76	0.53
	TS sway area	1053 ± 547 mm^2 (328–2217)	1147 ± 745 mm^2 (204–2819)	*p* = 0.193 1221	0.53	1430 ± 853 mm^2 (336–3348)	1075 ± 595 mm^2 (227–2314)	*p* = 0.180 1849	0.24

Table A1. *Cont.*

Measurement System	Variable	Control Group Mean ± SD (Min.–Max.) T1	Control Group Mean ± SD (Min.–Max.) T2	Sign./MDC95	ICC	Intervention Group Mean ± SD (Min.–Max.) T1	Intervention Group Mean ± SD (Min.–Max.) T2	Sign./MDC95	ICC
Force Plate	TS sway velocity	43.3 ± 17.2 mm/s (26–99)	41.7 ± 20.9 mm/s (13–103)	p = 0.419 24.92	0.77	**52.3 ± 17.9 mm/s (28–107)**	**45.7 ± 22.7 mm/s (22–113)**	***p* = 0.006** 28.64	0.74
	NSEc sway area	959 ± 586 mm^2 (256–2536)	1051 ± 642 mm^2 (212–2823)	p = 0.392 1004	0.65	981 ± 367 mm^2 (296–1622)	960 ± 400 mm^2 (345–1730)	p = 0.630 703	0.55
	NSEc sway velocity	24.7 ± 11.2 mm/s (9–56)	23.9 ± 10.2 mm/s (11–44)	p = 0.522 12.63	0.82	27.6 ± 7.5 mm/s (11–42)	25.6 ± 8.5 mm/s (12–48)	p = 0.094 12.49	0.68
	SS sway area	1017 ± 438 mm^2 (473–2017)	1079 ± 426 mm^2 (413–2092)	p = 0.414 804	0.54	878 ± 221 mm^2 (439–1255)	978 ± 447 mm^2 (394–2345)	p = 0.807 629	0.58
	SS sway velocity	44.9 ± 16.5 mm/s (28–95)	46.0 ± 19.7 mm/s (25–98)	p = 0.517 14.30	0.92	53.6 ± 26.5 mm/s (24–111)	47.9 ± 21.8 mm/s (22–109)	p = 0.073 30.39	0.80
Mocap System	NG stride time	1.18 ± 0.13 s (0.99–1.36)	1.15 ± 0.10 s (0.98–1.27)	p = 0.104 0.15	0.59	**1.18 ± 0.13 s (0.94–1.51)**	**1.11 ± 0.10 s (0.93–1.28)**	***p* = 0.002** 0.19	0.67
	NG cadence	1.70 ± 0.14 s^{-1} (1.47–2.02)	1.75 ± 0.11 s^{-1} (1.58–2.05)	p = 0.137 0.22	0.62	**1.71 ± 0.18 s^{-1} (1.33–2.13)**	**1.82 ± 0.17 s^{-1} (1.56–2.14)**	***p* = 0.001** 0.24	0.77
	NG velocity	0.96 ± 0.16 m/s (0.66–1.31)	0.94 ± 0.18 m/s (0.58–1.24)	p = 0.380 0.27	0.67	0.97 ± 0.15 m/s (0.59–1.27)	1.03 ± 0.17 m/s (0.65–1.39)	p = 0.071 0.26	0.67
	NG step width	10.4 ± 3.6 cm (4–17)	10.1 ± 3.2 cm (4–17)	p = 0.902 8.06	0.24	10.6 ± 3.4 cm (5–16)	9.3 ± 3.5 cm (2–17)	p = 0.266 7.63	0.37
	BG stride time	1.27 ± 0.14 s (1.09–1.63)	1.25 ± 0.15 s (1.01–1.53)	p = 0.191 0.23	0.67	1.21 ± 0.11 s (1.03–1.46)	1.16 ± 0.11 s (0.94–1.35)	p = 0.073 0.26	0.37
	BG cadence	1.56 ± 0.21 s^{-1} (0.91–1.83)	1.63 ± 0.18 s^{-1} (1.31–1.97)	p = 0.117 0.32	0.66	1.66 ± 0.15 s^{-1} (1.37–1.95)	1.74 ± 0.18 s^{-1} (1.48–2.14)	p = 0.074 0.37	0.36
	BG velocity	0.63 ± 0.12 m/s (0.34–0.78)	0.64 ± 0.14 m/s (0.25–0.89)	p = 0.131 0.21	0.67	**0.66 ± 0.12 m/s (0.31–0.84)**	**0.75 ± 0.10 m/s (0.58–0.89)**	***p* = 0.007** 0.26	0.34
	BG step width	12.8 ± 4.3 cm (6–23)	13.2 ± 3.7 cm (5–19)	p = 0.625 7.46	0.54	11.9 ± 3.4 cm (6–20)	11.5 ± 3.7 cm (2–18)	p = 0.676 9.01	0.14
	TG stride time	1.93 ± 0.59 s (1.24–3.76)	1.73 ± 0.37 s (1.20–2.51)	p = 0.069 0.69	0.75	**1.76 ± 0.42 s (1.17–3.11)**	**1.49 ± 0.23 s (1.00–1.96)**	***p* = 0.003** 0.64	0.61
	TG cadence	1.12 ± 0.28 s^{-1} (0.53–1.61)	1.21 ± 0.24 s^{-1} (0.80–1.66)	p = 0.106 0.31	0.83	**1.19 ± 0.25 s^{-1} (0.64–1.70)**	**1.35 ± 0.18 s^{-1} (1.02–1.69)**	***p* = 0.001** 0.38	0.65
	TG velocity	0.42 ± 0.12 m/s (0.20–0.75)	0.44 ± 0.14 m/s (0.03–0.72)	p = 0.568 0.20	0.67	*0.38 ± 0.12 m/s (0.15–0.66)*	*0.44 ± 0.13 m/s (0.19–0.80)*	*p = 0.044* 0.22	0.61

Table A1. *Cont.*

Measurement System	Variable	Control Group Mean ± SD (Min.–Max.) T1	Control Group Mean ± SD (Min.–Max.) T2	Sign./MDC95	ICC	Intervention Group Mean ± SD (Min.–Max.) T1	Intervention Group Mean ± SD (Min.–Max.) T2	Sign./MDC95	ICC
	TG step width	5.2 ± 2.9 cm (1–12)	4.5 ± 1.7 cm (1–7)	*p* = 0.171 6.15	0.15	2.4 ± 1.1 cm (1–6)	2.8 ± 1.7 cm (1–7)	*p* = 0.393 3.82	0.06
Mocap System	NS sway area	2032 ± 1157 mm^2 (210–4631)	2075 ± 1158 mm^2 (691–5824)	*p* = 0.982 2388	0.43	1522 ± 772 mm^2 (312–3629)	1359 ± 727 mm^2 (522–3528)	*p* = 0.263 1923	0.14
	NS sway velocity	7.2 ± 2.2 mm/s (3.3–11.8)	6.9 ± 2.0 mm/s (4.2–11.6)	*p* = 0.978 5.05	0.24	6.6 ± 1.5 mm/s (4.8–10.5)	6.4 ± 1.5 mm/s (3.7–10.1)	*p* = 0.192 2.19	0.72
	TS sway area	2230 ± 1070 mm^2 (750–4492)	2431 ± 1720 mm^2 (391–7005)	*p* = 0.942 3440	0.25	1515 ± 948 mm^2 (264–4095)	1398 ± 681 mm^2 (376–2609)	*p* = 0.732 2014	0.23
	TS sway velocity	9.3 ± 2.4 mm/s (5.9–15.8)	8.8 ± 3.3 mm/s (4.4–18.1)	*p* = 0.687 4.85	0.62	8.6 ± 1.8 mm/s (5.1–11.6)	9.3 ± 2.4 mm/s (4.4–19.3)	*p* = 0.737 6.21	0.41
	NSEc sway area	*1929 ± 941 mm^2 (579–4294)*	*2631 ± 1690 mm^2 (623–6926)*	*p = 0.039* 3460	0.20	1731 ± 656 mm^2 (754–3138)	1543 ± 829 mm^2 (529–3467)	*p* = 0.201 1046	0.74
	NSEc sway velocity	8.2 ± 2.5 mm/s (4.2–13.2)	8.2 ± 1.9 mm/s (5.1–12.4)	*p* = 0.551 4.76	0.39	8.7 ± 2.4 mm/s (5.5–16.4)	7.8 ± 2.0 mm/s (3.9–11.4)	*p* = 0.075 3.60	0.67
	SS sway area	12019 ± 17118 mm^2 (954–75252)	5721 ± 4243 mm^2 (1153–18136)	*p* = 0.906 29140	0.36	3860 ± 3863 mm^2 (466–15835)	2710 ± 2321 mm^2 (435–10074)	*p* = 0.750 4922	0.70
	SS sway velocity	12.3 ± 4.8 mm/s (7.2–28.4)	12.9 ± 5.6 mm/s (6.8–28.0)	*p* = 0.164 6.09	0.82	13.1 ± 6.4 mm/s (6.7–28.9)	11.8 ± 4.2 mm/s (6.4–21.9)	*p* = 0.497 14.40	0.08
Smartphone	NG stride time	*1.34 ± 0.15 s^{-1} (1.16–1.82)*	*1.28 ± 0.11 s^{-1} (1.13–1.51)*	*p = 0.036* 0.20	0.70	1.23 ± 0.11 s (1.01–1.51)	1.19 ± 0.13 s (0.97–1.51)	*p* = 0.105 0.18	0.70
	NG cadence	*1.39 ± 0.29 s^{-1} (0.65–1.70)*	*1.53 ± 0.20 s^{-1} (0.86–1.78)*	*p = 0.013* 0.40	0.70	*1.63 ± 0.16 s^{-1} (1.31–1.92)*	*1.72 ± 0.18 s^{-1} (1.34–2.08)*	*p = 0.028* 0.25	0.71
	NG velocity	0.57 ± 0.18 m/s (0.34–1.12)	0.59 ± 0.15 m/s (0.29–0.92)	*p* = 0.896 0.32	0.50	0.63 ± 0.09 m/s (0.48–0.80)	0.67 ± 0.08 m/s (0.54–0.82)	*p* = 0.113 0.12	0.74
	BG stride time	*1.34 ± 0.13 s (1.13–1.62)*	*1.25 ± 0.10 s (1.06–1.45)*	*p = 0.039* 0.27	0.39	1.22 ± 0.06 s (1.09–1.32)	1.24 ± 0.14 s (1.05–1.52)	*p* = 0.516 0.23	0.28
	BG cadence	*1.49 ± 0.15 s^{-1} (1.22–1.77)*	*1.57 ± 0.18 s^{-1} (0.95–1.82)*	*p = 0.015* 0.37	0.39	1.65 ± 0.08 s^{-1} (1.52–1.81)	1.63 ± 0.18 s^{-1} (1.33–1.92)	*p* = 0.607 0.31	0.28
	BG velocity	0.53 ± 0.14 m/s (0.35–0.83)	0.56 ± 0.14 m/s (0.26–0.88)	*p* = 0.616 0.26	0.57	0.60 ± 0.08 m/s (0.44–0.74)	0.61 ± 0.12 m/s (0.30–0.82)	*p* = 0.716 0.28	−0.08

Table A1. *Cont.*

Measurement System	Variable	Control Group				Intervention Group			
		Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC	Mean ± SD (Min.–Max.)		Sign./ MDC95	ICC
		T1	T2			T1	T2		
Smartphone	TG stride time	*1.86 ± 0.42 s (1.33–3.40)*	*1.58 ± 0.22 s (1.28–2.02)*	*p = 0.023* 0.98	0.04	1.42 ± 0.31 s (1.08–2.47)	1.37 ± 0.23 s (1.10–1.99)	*p* = 0.938 0.47	0.61
	TG cadence	1.02 ± 0.31 s^{-1} (0.31–1.53)	1.21 ± 0.30 s^{-1} (0.44–1.56)	*p* = 0.051 0.74	0.29	1.47 ± 0.24 s^{-1} (0.82–1.78)	1.51 ± 0.23 s^{-1} (1.00–1.87)	*p* = 0.923 0.45	0.53
	TG velocity	*0.29 ± 0.08 m/s (0.12–0.47)*	*0.33 ± 0.10 m/s (0.16–0.57)*	*p = 0.040* 0.18	0.45	0.30 ± 0.07 m/s (0.14–0.46)	0.32 ± 0.08 m/s (0.22–0.56)	*p* = 0.293 0.16	0.37
	NS sway area	151 ± 428 mm^3 (0–2039)	34 ± 118 mm^3 (0–533)	*p* = 0.764 955	−0.10	98 ± 120 mm^3 (0–416)	785 ± 1225 mm^3 (0–3510)	*p* = 0.383 2206	0.10
	NS sway velocity	38.1 ± 25.5 mm/s (7.0–110.9)	24.4 ± 10.4 mm/s (10.9–44.9)	*p* = 0.221 68.9	−0.40	*16.3 ± 6.2 mm/s (3.2–24.8)*	*15.5 ± 6.3 mm/s (5.9–24.0)*	*p = 0.047* 8.8	0.74
	TS sway area	316 ± 957 mm^3 (0–4220)	61 ± 171 mm^3 (0–764)	*p* = 0.381 2025	−0.03	967 ± 1345 mm^3 (1–4403)	165 ± 147 mm^3 (16–393)	*p* = 0.065 3413	−0.07
	TS sway velocity	28.0 ± 12.3 mm/s (9.0–52.4)	30.8 ± 11.5 mm/s (10.6–49.1)	*p* = 0.465 27.8	0.28	17.0 ± 6.0 mm/s (1.0–24.7)	20.3 ± 11.0 mm/s (1.5–41.1)	*p* = 0.339 24.2	−0.04
	NSEc sway area	10 ± 20 mm^3 (0–94)	16 ± 27 mm^3 (0–90)	*p* = 0.460 70	−0.11	49 ± 43 mm^3 (0–156)	501 ± 715 mm^3 (24–1989)	*p* = 0.180 1283	0.03
	NSEc sway velocity	22.9 ± 12.1 mm/s (9.1–51.6)	31.6 ± 17.4 mm/s (10.1–70.6)	*p* = 0.169 46.7	−0.18	16.9 ± 4.5 mm/s (9.7–24.3)	16.9 ± 5.1 mm/s (7.7–24.0)	*p* = 0.894 7.5	0.67
	SS sway area	511 ± 1427 mm^3 (0–6080)	65 ± 133 mm^3 (1–466)	*p* = 0.268 2894	0.03	384 ± 495 mm^3 (16–1819)	592 ± 725 mm^3 (11–1743)	*p* = 0.202 1561	0.06
	SS sway velocity	**30.5 ± 8.9 mm/s (10.9–57.4)**	**44.6 ± 4.4 mm/s (18.5–107.5)**	***p* = 0.013** 46.7	0.36	16.9 ± 8.9 mm/s (0.9–32.6)	17.8 ± 4.4 mm/s (8.1–22.9)	*p* = 0.439 12.4	0.62

p-values highlighted in bold represent significant values after Bonferroni correction (<0.013 for gait tasks, <0.025 for balance tasks), *p*-values in italics represent significant values before Bonferroni correction (<0.05). The Minimal Detectable Change (MDC) for a 95% confidence interval is indicated for both the intervention and control groups. BG = backward gait, ICC = Intraclass Correlation Coefficient, Interv. = intervention group, NG = normal gait, NS = narrow stance, NSEc = narrow stance with eyes closed, Sign. = significance, SS = single leg stance, TG = tandem gait, TS = tandem stance, T1 = study visit one, T2 = study visit two.

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Three-week Video- and Home-based Training Program for Ataxia Patients: A Pilot Randomized Controlled Trial

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Abstract

Three-week Video- and Home-based Training Program for Ataxia Patients: A Pilot Randomized Controlled Trial

Background:

Gait and balance impairment is a disabling clinical feature in patients with degenerative cerebellar ataxia.

Objectives:

We performed a rater-blinded, parallel 3-arm randomized controlled trial with delayed-start-design (exploratory proof-of-concept study) to assess whether patients with mild/moderate hereditary ataxia benefit from additional video-based training using different training protocols, and how clinical characteristics interact with training success.

Methods:

Digital gait/stance measures were assessed before and after a three-week video-based training program at home (Train20: 4x20min/week, n=11; Train40: 2x40min/week, n=11; control: standard medical care, n=10). Group differences at baseline and changes over time were assessed using ANOVA. Linear mixed models were conducted to examine the influence of clinical variables on outcomes over time. Further exploratory analyses were performed using paired t-tests within each group.

Results:

All variables showed good to excellent test-retest reliability (intraclass correlation coefficient ≥ 0.69). No significant interactions between group and measurement time were found for clinical or gait/stance variables ($p \geq 0.338$). However, patients with higher initial disease severity (SARA-score), greater impairment in activities of daily living (ADL-score), and better well-being (FAHW-score) showed significant improvements in feet-together stance, normal, and backward gait ($p<0.05$). Exploratory analyses showed improvement only in Train40.

Conclusions:

Although the protocol did not lead to general improvements across all participants, irrespective of training frequency, those with higher initial SARA- and ADL-scores and better mental well-being showed significant benefits. Greater attention should be given to the impact of well-being to enhance motor training outcomes. Longer, less frequent sessions may offer greater potential for improvement in patients with mild/moderate ataxia.

Key Words: ataxia; training; rehabilitation; video-based; home-based; RCT

Introduction

Progressive impairments in gait and balance are the main challenges for patients with hereditary cerebellar ataxia in everyday life. According to patients' reports, exercise and physiotherapy are among the most effective supportive measures that are currently available[1]. Targeted and intense training programs lasting one to six months, including gait and balance training, have shown potential to improve functional mobility, reduce fall risk, and improve well-being[2,3]. However, these in-person approaches are only suitable for a subset of patients, inciting the need for effective training and monitoring solutions that require little or no physical presence at the study center[4,5]. Shorter or home-based training regimens led to improvements in clinical disease severity scores and quantitative gait and stance parameters, e.g., after four weeks of coordinative training in patients with cerebellar and afferent ataxias in the short term[6], and for cerebellar ataxia patients even in the long term[7]. However, insights into remote training interventions are limited. A systematic review on rehabilitation programs in patients with genetic degenerative ataxia[8] summarized that only four out of 17 studies included home-based training, and only two were randomized controlled trials. Except for one very recent publication (n=76)[9], other training studies in patients with cerebellar ataxia had comparably low sample sizes (n=8-17)[10-13]. A recent study reported improvements in balance confidence, quality of life (mobility, self-care, usual activities), health status, gait speed and fall rate after a five-week home-based core stability exercises in patients with hereditary ataxias, but no change in clinically rated disease severity[14]. Quantitative gait and balance parameters are considered as more sensitive methods to depict functional improvements[15,16].

Defining training parameters (frequency, duration, intensity) is crucial for optimizing rehabilitation outcomes[9]. Standardized guidelines for hereditary cerebellar ataxia are lacking, and further randomized controlled trials are needed to optimize home-based training programs.

Following current guidance documents[17] and consensus recommendations for quantitative gait and balance outcomes and the use of smartphone sensors[18,19], we integrated clinician-reported outcomes (ClinRO) with patient-reported outcomes (PRO), and quantitative performance outcomes (PerfO). Here, we present an exploratory proof-of-concept randomized controlled trial (RCT) with comparably high sample size on the impact of home-based, video-based training on gait and stance performance of patients with hereditary degenerative cerebellar ataxia using digital motor biomarkers as PerfO in combination with ClinRO and PRO. We further analyzed whether the distribution of training sessions across the week, with consistent weekly training time and content, affects the training effect; and how clinical characteristics interact with training success.

We hypothesized that (a) video-based training at home results in significant improvements in gait and stance abilities, (b) shorter, more frequent training sessions lead to greater improvements compared to longer, less frequent training sessions, and (c) clinical characteristics, such as disease severity and baseline functional status, would be key determinants of individual training success.

Methods

Participants

Participants with confirmed hereditary ataxia – indicated by genetic diagnosis, positive family history, or early-onset symptoms – were recruited at the University Hospitals Düsseldorf, Essen, and Heidelberg, via the German Heredo-Ataxia Society (Deutsche Heredo-Ataxie-Gesellschaft e.V.), and via social media between January 2023 and April 2024. Participants were excluded if they were unable to walk without walking aids for at least 2 minutes or had any signs of secondary CNS disease. Written informed consent was obtained in agreement with the Declaration of Helsinki, and the study protocol was approved by the ethics committee of the Medical Faculty of the Heinrich Heine University Düsseldorf, Germany (2022-1994). The study was preregistered at ClinicalTrials.gov (NCT06617884).

Study design / Interventions

The study comprised at least three visits: T0 (screening), T1 (baseline), and T2 (post-training, see Figure 1). All patients participated in a one-week baseline phase without training (T0 to T1). They were then randomly assigned to one of two three-week video-based training protocols or a control group with standard medical care only (Train20, Train40, Control) in a 1:1:1 ratio using a simple, computer-generated random allocation sequence (R software, version 4.3.1). After T2, participants in the control group were randomly reassigned to one of the two original training protocols and completed a fourth study visit (T3, post-control-training, after week 7). To increase statistical power, data was subsequently merged with their respective training groups from the first phase, forming two larger groups (Train20+C, Train40+C).

Training

Participants followed uniform, pre-recorded videos for training. Both training protocols had identical content and total weekly duration but differed in session frequency and length: Train20 performed 4 x 20-minute sessions per week, and Train40 2 x 40-minute sessions. The control group followed their standard medical care without additional training. Exercises, designed with an ataxia physiotherapy expert (D.B.), included easy-to-perform coordination, strength, and mobility exercises (see Supplementary Material) to avoid an increased risk of falling during the unsupervised home-based setting. The total training duration and session length were modeled after standard physiotherapy practices, which typically involve 6-12 sessions of approximately 20 minutes each, and based on literature, which suggests a drop in study compliance after three weeks[20]. All participants maintained their standard medical care routine, including physiotherapy, prescribed medications, and other exercises.

Assessments

ClinRO: Cognitive impairment was assessed for descriptive purposes at T0 using the Montreal Cognitive Assessment Test (MoCA[21,22]). Four dependent variables were assessed longitudinally at T0 and T2 (and T3): Severity of ataxia (SARA-score, scale for the assessment and rating of ataxia[23]), presence or absence of non-ataxia symptoms (INAS-score, inventory of non-ataxia signs[24]), functional mobility (Timed Up and Go test, TUG[25]), and impairment of daily life activities (activities of daily living section of the Friedreich's ataxia rating scale, FARS-ADL[26]). A.R., who assessed the ClinRO, was blinded to group allocation.

PRO: Baseline demographics and variables were collected via questionnaire at T0: medical history, handedness, physical/sport activity (amount per week/day), amount of physiotherapy, occupational therapy and speech therapy per week, estimated number of (almost) falls (past six months and one week), and years of education (school plus further education). Depressive and anxiety symptoms were retrieved with the depression module of the Patient Health Questionnaire (PHQ-9[27]). After the training, perceived change in gait and stance was retrieved via a Patient Global Impression of Change (PGIC) questionnaire. Longitudinally assessed dependent variables included questionnaires on habitual well-being (FAHW[28]), and fall-related self-efficacy (ABC-D[29]), at T1 and T2 (and T3). ABC-D scores range from 0% (no confidence) to 100% (full confidence), while lower FAHW-scores indicate less well-being, and higher scores indicate greater well-being (details in Supplementary Material).

PerfO: Longitudinal performance outcomes were derived from three gait and five stance tasks at each study visit: Normal gait (NG), backward gait (BG), tandem gait (TG), natural stance (NS), feet-together stance (FTS), tandem stance (TS), FTS with eyes closed (FTSec), and single-leg stance (SS), recorded with a force plate (zebris Medical GmbH, Isny, Germany)[30]. NG was conducted for 2 minutes, BG and TG for 4 lanes (each 4.24m), and each stance task was attempted for 30 seconds without support, with values under 30 seconds excluded from longitudinal analyses. We analyzed only tasks completed by at least 75% of participants[31] (≥30s for stance tasks, gait without support). Outcomes included the dependent variables stride time [s], double support proportion [%], mean velocity [m/s], external rotation of the feet [°], step width [cm], and step width SD [cm] for each of the gait tasks, and sway area [mm^2] and sway velocity [mm/s] for each of the stance tasks (for details see Supplementary Material). The primary outcome was NG velocity.

Statistical methods

Based on reported effect size and SD in gait velocity[2], we estimated a sample size of 17 participants per group to achieve 80% power for detecting pre- to post-training changes.

Statistical analyses were performed using R software (version 4.3.1) and IBM SPSS Statistics (version 27). We report significance levels as exact *p*-values, distinguishing between uncorrected (p-unc$\leq$0.05), and Bonferroni-corrected values for multiple comparisons (p-corr$\leq$0.05/n, number of analyzed features). Missing values were excluded, while outliers were retained, as they reflect the natural variability in this population.

Reliability (whole sample). For all PerfO, intraclass-correlation coefficients (ICCs) with two-way random effects models were calculated to confirm stability and reliability of the gait and stance measures (PerfO) between T0 and T1 (screening and baseline visit). The minimal detectable change (MDC) of PerfO was calculated between T0 and T1 ($MDC = 1.96 * SEM * \sqrt{2}$) at the 95% confidence level (SEM = standard error of measurement) and changes within the whole group in PerfO between T0 and T1 were identified using dependent samples t-tests (p-corr$\leq$0.05/20).

Baseline comparisons. Baseline comparisons of PRO and ClinRO between groups used independent t-tests (Analysis 1, two groups) or a univariate ANOVA (Analysis 2, three groups; p-corr$\leq$0.05/17). Categorical variables were analyzed with chi-square tests.

Analysis of the training effect. To investigate group differences in PerfO, ClinRO, and PRO across the intervention phase, a series of 2 × 3 ANOVAs was performed (Analysis 3). These included the within-subjects factor 'time point' (pre, post), and the between-subjects factor 'group' (Train20, Train40, Control). Each dependent variable was analyzed separately (n=18 for PerfO; n=5 for ClinRO/PRO, p-corr$\leq$0.05/18 or p-corr$\leq$0.05/5), testing for main effects of group and time point, as well as their interaction. Similarly, a series of 2 × 2 ANOVAs was conducted for comparisons between the larger training groups (Analysis 4, Train20+C, Train40+C) across time (pre, post). For the primary outcome gait velocity, independent contrasts of improvement were calculated between the groups (independent t-tests) and are reported in the Supplementary Material. An exploratory analysis compared pre- and post-training values within each group using dependent samples t-tests.

Interaction of ClinRO/PRO and PerfO. For all participants who had completed training (Train20+C plus Train40+C, n=31), a linear mixed model was used to assess whether baseline values of ClinROs and PROs influenced changes in PerfO across the intervention phase (Analysis 5, the sample size of n=31 does not apply to FTS/FTSec, as not all participants were able to complete this task). The model included fixed effects for ClinRO/PRO, time point (T1, T2), and their interaction to examine their influence on change of performance outcomes over time. To account for the repeated measures design, a random intercept for individual subjects was included, capturing individual variability in baseline levels. This model was applied separately for all PerfOs (p-corr≤0.05/18). For those models that revealed a significant interaction effect, further analyses were conducted to resolve the interactions. Hence, estimated marginal means for gait or stance at each time point were calculated, specifically examining the effects at higher and lower levels of the clinical scores (one SD above and below the mean). Pairwise contrasts were conducted to further explore the differences between the estimated marginal means at T1 and T2 (p-corr≤0.05/2).

Results:

Of the 80 participants assessed for eligibility, 34 participants completed the first two study visits, and 31 participants completed the training (see Figure 1). All participants had mild to moderate cerebellar ataxia (SARA-score of 8.4±3.5) and a mean disease duration of 9.2±8.3 years (see Table 1 and Supplementary Table 1). TS, SS, and TG had completion rates of <75% and were not evaluated.

Reliability (whole sample). Most variables demonstrated good to excellent reliability (ICCs 0.69-0.96, 0.94 for primary outcome NG velocity), indicating consistent measurement across the two time points. No significant difference was found between T0 and T1 according to pairwise t-tests (all p≥0.051). ICC and MDC values are reported in Supplementary Table 4.

Baseline comparisons. In Analysis 1, Train20, Train40 and control group did not differ significantly in the distribution of age, sex, number of pure cerebellar ataxias (hereditary ataxias commonly regarded as "pure" cerebellar ataxias (e.g., SCA6, SCA14)), disease duration, age at disease onset (univariate ANOVA, all p≥0.098), or other baseline variables (see Table 1 for variables used for descriptive purposes). The groups did further not differ in ClinRO and PRO scores at baseline (p≥0.139). In Analysis 2, including the two larger training groups, a higher balance confidence (t-test, p-unc=0.050), and a higher educational level (p-unc=0.004) were observed in Train40+C compared to Train20+C (see Supplementary Material).

Analysis of the training effect. Mean descriptive values for dependent variables assessed longitudinally (ClinRO, PRO, and PerfO, pre- and post-training) can be found in Table 2. For each dependent variable, separate ANOVAs were conducted in Analysis 3, to determine whether there were changes over time (before and after training), dependent on groups (Train20, Train40, control). No significant interaction effects of 'time x group' was found for the primary outcome NG velocity (p=0.880) or for any other of the dependent variables (all p≥0.602, see Table 2). More detailed analyses for the primary outcome gait velocity are reported in the Supplementary Material. A significant main effect of group was found for the ABC-D score, indicating generally lower balance confidence in Train20 compared to Train40 (*p*-unc=0.043) and to control group (*p*-corr=0.008), and a generally lower step width in NG in the control group compared to Train20 (*p*-unc=0.029). No significant main effects of time were found (all *p*≥0.244). In the PGIC (n=30, range -3 to 3), 40% of the participants reported a 1 to 2-point improvement in both stance and gait; 56.7% reported no change, and 3.3% reported a 1-point worsening.

In Analysis 4, comparing Train20+C and Train40+C, no significant difference was found across measurement times for any of the dependent variables (all *p*≥0.338, see Supplementary Table 5), as well as no main effects of time (all *p*≥0.434). Similar to the smaller groups, a generally lower balance confidence was found in group Train20+C (*p*-corr=0.004).

In an exploratory approach, pre- and post-training values were compared within each group. While no significant changes occurred in Train20, Train40 showed improvements in the primary outcome NG velocity (*p*-unc=0.030), and in stride time (*p*-unc=0.050), double support (*p*-unc=0.033), and BG step width (*p*-unc=0.011). The control group showed an improvement in NG step width (*p*-unc=0.045, see bold values in Table 2). Within the two larger training groups, only Train40+C showed improvements in NG velocity (*p*-unc=0.025) and stride time (*p*-unc=0.027), and in the SARA-score (1.5-point reduction, *p*-unc=0.020, see Supplementary Table 5).

Interaction of ClinRO/PRO and PerfO. To assess the impact of baseline ClinRO/PRO scores on changes in PerfO (T1 to T2) among all participants who underwent training (n=31), a linear mixed model was used (Analysis 5). Significant 'ClinRO/PRO × time' interactions were further analyzed, as this interaction suggests that initial clinical assessments may influence performance changes, aiding in identifying subgroups that respond differently to interventions. Significant interactions (see Figure 2) were found between:

- SARA-score and time, for sway velocity of FTS (*p*-unc=0.037*),
- ADL-score and time, for sway velocity of FTS (*p*-unc=0.040*),
- FAHW-score and time, for velocity of NG (*p*-unc=0.013*),
- FAHW-score and time, for stride time of BG (*p*-unc=0.028*).

All other interactions did not reach statistical significance (all *p*≥0.079). Several main effects for time and main effects for dependent ClinROs/PROs were found (Supplementary Table 6).

Estimated marginal means for PerfO at T1 and T2 explored the effects of ClinRO/PRO scores one standard deviation above and below the mean, illustrating how score levels influenced gait or stance at both time points (see Figure 2, right panel). Pairwise contrasts revealed significant reductions in FTS sway velocity between T1 and T2 for those half of the participants with higher SARA-scores (mean score = 12.14, 14.8mm/s reduction, *p*-corr=0.011) compared to those with lower scores (5.02, 3.0mm/s increase, *p*=0.700); for participants with higher ADL-scores (mean score = 12.38, 14.1mm/s reduction, *p*-corr=0.012) versus lower scores (3.97, 1.6mm/s increase, *p*=0.750); and significant increase in the primary outcome NG velocity and decrease in BG stride time between T1 and T2 for participants with higher FAHW-scores (mean score = 51.60, 0.07m/s increase and 0.07s decrease, *p*-corr=0.001/0.005) versus lower scores (9.24, no change, *p*=0.837/0.858).

Discussion:

The present study aimed to evaluate the effectiveness of video-based training at home in improving gait and balance in patients with mild to moderate hereditary cerebellar ataxia, the influence of training session distribution on outcomes, and the role of baseline clinical characteristics in determining training success. Our findings partially support our hypotheses and highlight considerations for optimizing rehabilitation strategies.

Although our data collection preceded the AGI gait and balance consensus publication[18], our study aligns with many of the recommended criteria and contributes to the ongoing effort of standardizing study protocols in clinical ataxia research. We were able to show good to excellent reliability of all analyzed gait and stance variables and provided values for a minimal detectable change. This does not necessarily correspond to the minimal clinically important difference (MID), but currently there are no reference values available for MIDs, except for the SARA-score[32].

Contrary to our expectations and independent of the distribution of training sessions, our results revealed no significant effects of the three-week video-based training at home on gait and balance across groups. Nevertheless, including ClinRO (SARA and ADL) as continuous predictors revealed that participants with varying levels of impairment experienced different outcomes, though only reaching uncorrected levels of significance. Both scores affected the feet together stance: Participants with higher clinical scores showed a significant improvement (decrease) in sway velocity after training, likely due to the increased challenge the task posed for them, offering greater potential for progress. As this analysis assessed all participants together without control group comparison, it remains unclear if the effect stems solely from the training. Notably, the more challenging tandem and single-leg stance were not included in the analysis due to insufficient completion rates. The effects could have been particularly interesting, even though rarely included in training studies involving patients with cerebellar ataxia[18]. Similarly, only participants who could maintain a 30-second stance were analyzed. Although nearly all patients reported no depressive symptoms above the clinical cut-off (with one exception scoring 19), those with higher baseline well-being scores (FAHW) demonstrated significant improvements in gait velocity and stride time during normal and backward gait. Mental well-being seemingly not only enhances quality of life but may also be a critical factor in determining the effectiveness of interventions, such as physical training or practice, in improving motor function. The results are consistent with a current study on Parkinson's Disease patients, which classified high responders and non-responders of training and reported that high responders had the worst balance, most frequent falls, slowest gait velocity, and lowest self-perceived walking ability but also the highest balance confidence[33].

We also explored training effects per group, although they should be interpreted with caution since they are lacking a direct comparison with a control group. We found that longer, less frequent training sessions may be more effective than shorter, more frequent sessions (2 x 40-minute vs. 4 x 20-minute). Improvements (uncorrected level of significance) in NG variables, including gait velocity as primary outcome, were found in Train40 only, supported by similar effects in Train40+C. A significant improvement was found in Train40+C for SARA-score (1.5-point reduction), similar to other, more intensive home-based programs[11,12,14]. This change did not reach significance in the smaller Train40 group (1-point reduction). Mean progression rates in SCAs are 0.8-2.1 points/year[34], and a change of 1 SARA-point can already be considered as meaningful[32], although it has been challenged whether the delta SARA-score is an appropriate outcome from a patients' perspective[35]. Our data hints that it may be worth exploring longer training sessions performed less frequently in patients with mild/moderate degenerative hereditary cerebellar ataxia for designing physical training and prescribing physiotherapy (standard unit in Germany 20min).

Previous intensive training programs with smaller sample sizes reported significant improvements after four or five weeks of training[6,14]. In contrast, findings in our study, one of the few RCTs in the field of home-based training in hereditary cerebellar ataxia, indicate that a three-week training with a total volume of 240 minutes may not offer a sufficient volume to achieve comparable outcomes, particularly for participants with mild/moderate ataxia in whom a more intensive training might be required. This distinction further highlights the need to identify the minimal effective training protocol (duration, intensity) necessary to generate substantial improvements. By clarifying the limitations of the chosen protocol, our study yields valuable insights toward the broader goal of defining effective yet feasible training protocols. Notably, other interventions may have incorporated tasks in their training that resemble those assessed in the ClinRO and PerfO. In our training program, we used general coordination, mobility, and strength exercises without including any of the specific tasks assessed on-site, to avoid any bias by a sole practice effect. The mean perceived difficulty of exercises in this study was rated as 2.76±1.22 out of 10, possibly indicating that the exercises were not challenging enough[36] to provoke substantial improvements. However, when conducting home-based training without supervision, it is crucial to select exercises that do not increase the risk of falling for patients, leading to a more conservative exercise selection. While on-site studies can explore solutions that allow to safely perform more challenging exercises, such as the use of ceiling lifts or other assistive devices, comparable solutions for home use are lacking.

Limitations

The sample size has limited the statistical power of the study, potentially masking smaller but relevant effects, even though it was relatively high in comparison to similar training studies in patients with cerebellar ataxia[11-13]. Some other limitations should be acknowledged. First, study participants were instructed to adhere to their standard medical care routines, including physiotherapy, which may have introduced variability in treatment consistency and affected the overall outcomes. Second, we only measured gait at preferred speed. Current research recommends incorporating different gait speeds to provide a greater challenge to cerebellar gait control[18,37]. Additionally, the large number of statistical tests and comparisons, which were not entirely independent, should be considered, as this could increase the likelihood of Type I errors. Last, we were unable to control how often or with what quality the training was performed, as this information was based solely on self-reports from participants.

Conclusions

This RCT offers important insights into the effects of a 3-week video-based gait and balance training program at home. Although the training did not lead to general improvements across all participants, those with higher disease severity and better mental well-being experienced significant benefits, suggesting that these factors may influence the effectiveness of interventions, practice or adaptation processes. While our study found no significant overall effect of training volume distribution (2 x 40-minute vs. 4 x 20-minute), our data hint that it may be worth exploring the benefits of longer, less frequent training sessions in patients with mild to moderate hereditary cerebellar ataxias.

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Authors' Roles

C.R. and M.M. planned the project. M.M. supervised the project. J.P., H.J., D.T., A.T., D.B., C.B, A.S., K.A., and M.M. provided the resources for the study, including funding, facilities, equipment, expert guidance, and patient recruitment. C.R. and A.R. performed the investigation. N.J. and V.V. prepared data for analysis. C.R. performed the data analysis and wrote the first draft of the manuscript. All authors contributed to manuscript revision and discussion and interpretation of results. All authors approved the final version of the manuscript.

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The authors declare that there are no conflicts of interest regarding the publication of this paper and that they have no relevant financial or non-financial interests to disclose.

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<u>Data Availability Statement</u>

Anonymized data may be shared upon request to the corresponding or senior author from a qualified investigator for noncommercial use, subject to restrictions according to participant consent and data protection legislation.

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<u>Figures</u>

Figure 1: Flow of participants through the trial (CONSORT flow diagram), including group assignments for analysis

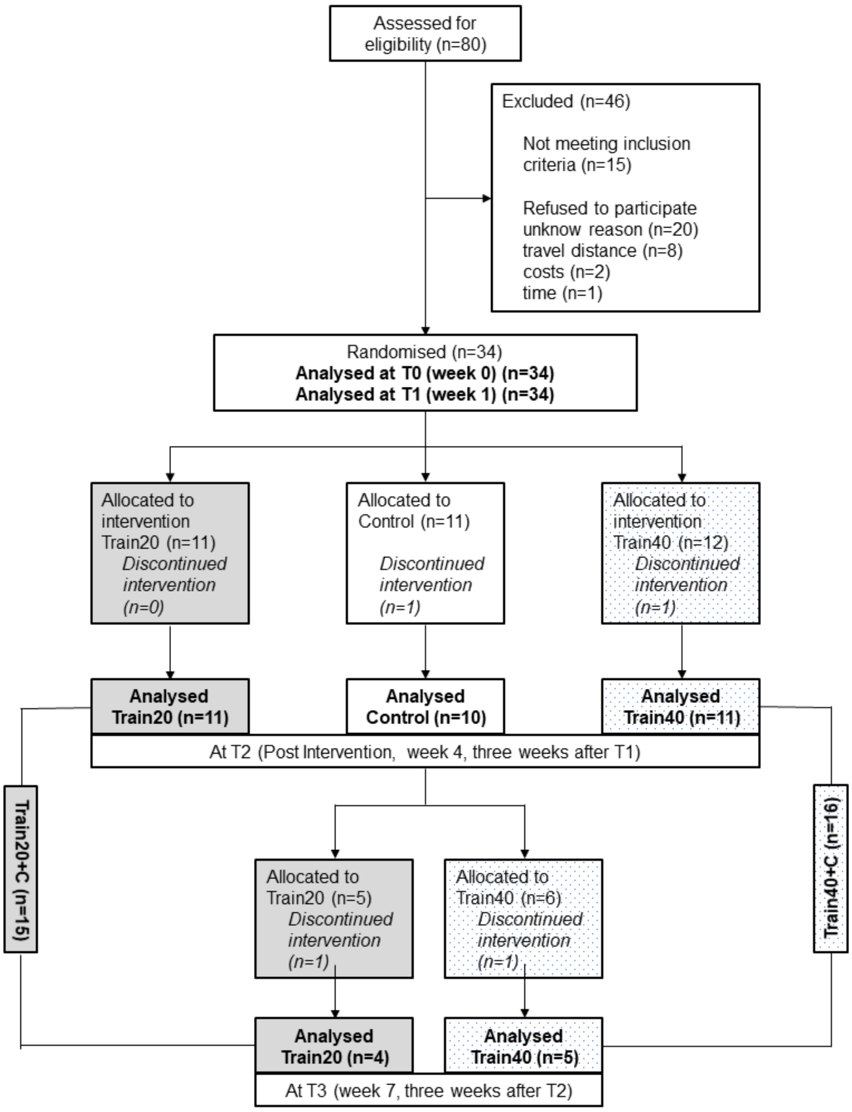
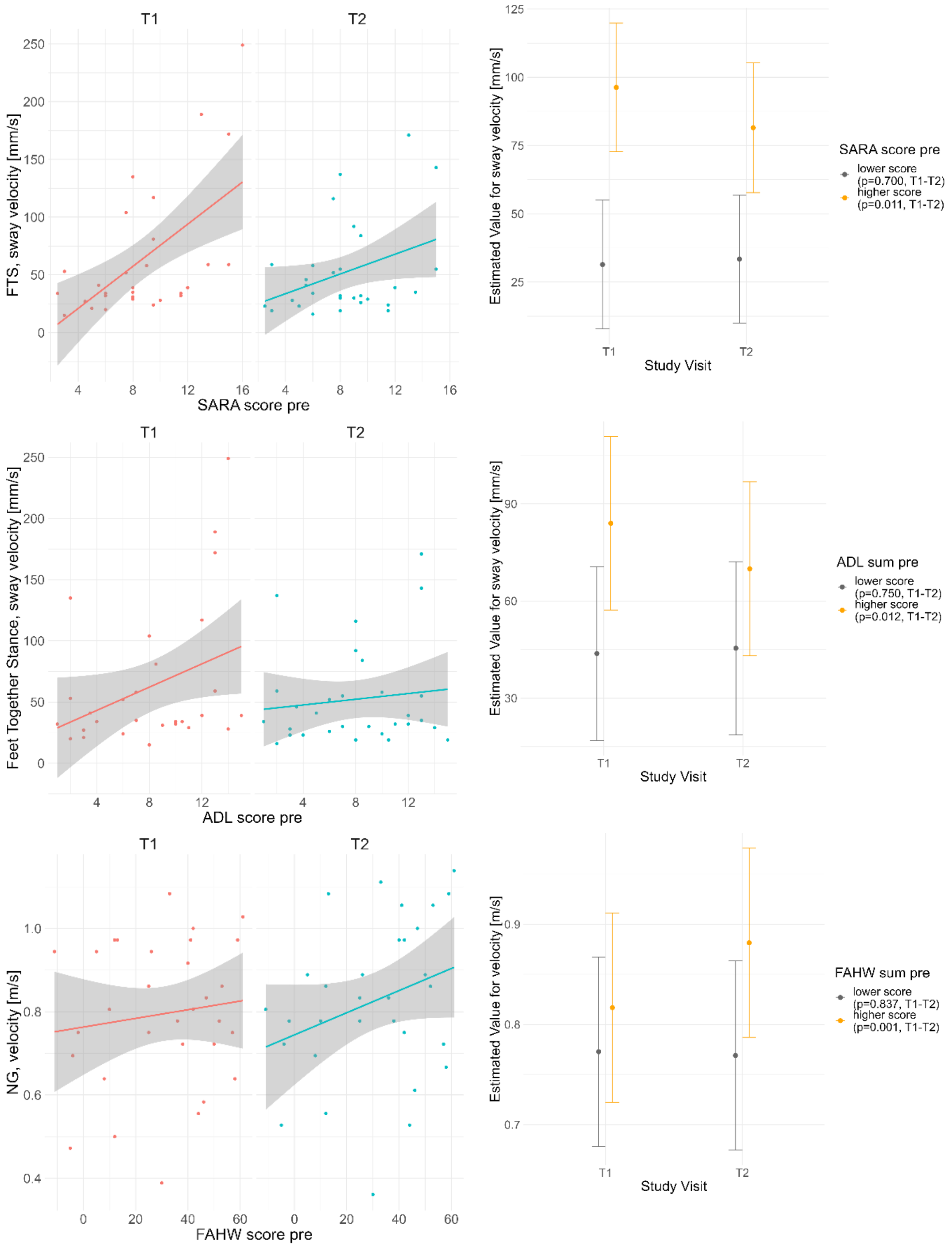
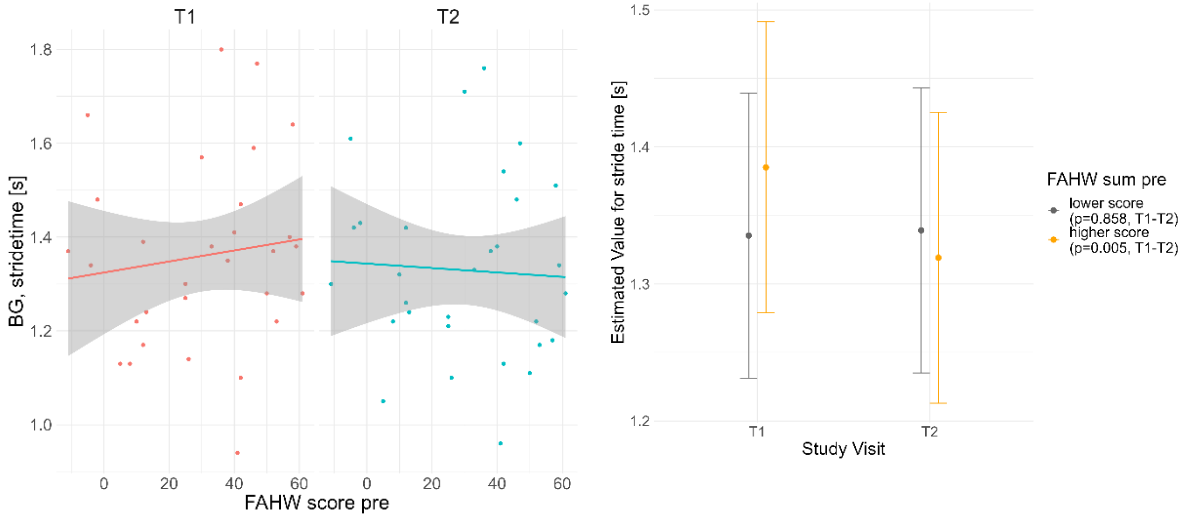


Figure 2: Interaction effect of baseline clinical scores and study visit on gait and stance PerfO for the variables for which interactions were found, and estimated marginal means with 95% confidence intervals for PerfO across study visits (T1 and T2) for lower and higher ClinRO/PRO scores.





Left panel: Linear relationship between baseline ClinRO/PRO (x-axis) and PerfO scores pre- and post-training (y-axis). **Right panel:** Estimated mean PerfO values, categorized by high and low ClinRO/PRO groups (orange and grey), shown for both pre- and post-training.

Tables

Table 1: Baseline information for the whole group, the two training groups and the Control group, with comparisons between the three smaller groups using univariate ANOVAs.

	Whole Group	**Train20**	**Train40**	**Control**	**ANOVA**
Sex [n female]	16 (n=34)	6 (n=11)	6 (n=11)	2 (n=10)	
Handedness [n left-handed]	1 n=34	0 n=11	1 n=11	0 n=10	
Number of pure cerebellar ataxias	21 n=34	7 n=11	5 n=11	9 n=10	
Age [years]	54.8 ± 11.5 (27 - 73) n=34	52.8 ± 12.7 (32 - 66) n=11	56.6 ± 8.6 (40 - 67) n=11	57.9 ± 12.8 (27 - 73) n=10	*p* = 0.573
Height [cm]	173.1 ± 8.1 (157 – 190) n=34	172.3 ± 9.0 (157 – 185) n=11	174.6 ± 6.9 (163 – 187) n=11	173.4 ± 9.5 (162 – 190) n=10	*p* = 0.822
Weight [kg]	73.1 ± 14.5 (50 – 108) n=29	69.3 ± 16.3 (50 – 94) n=10	69.8 ± 8.3 (58 – 83) n=9	82.4 ± 14.5 (65 – 108) n=9	*p* = 0.083
Disease duration [years]	9.2 ± 8.3 (0 – 36) n=32	10.1 ± 8.2 (0 – 25) n=11	7.0 ± 6.2 (1 – 21) n=9	11.7 ± 10.7 (1 – 36) n=10	*p* = 0.441
Age at disease onset [years]	45.6 ± 14.4 (12 – 68) n=34	42.7 ± 14.5 (18 – 60) n=11	49.6 ± 11.1 (34 – 65) n=11	46.2 ± 18.5 (12 – 68) n=10	*p* = 0.560
Education [years]	15.5 ± 2.9 (11 - 23) n=34	13.9 ± 2.0 (11 - 18) n=11	16.9 ± 2.8 (12 - 22) n=11	15.7 ± 3.5 (13 - 23) n=10	*p* = 0.055
PHQ score [/27]	6.8 ± 4.0 (1 - 19) n=34	6.5 ± 3.2 (2 - 11) n=11	4.9 ± 3.6 (1 - 12) n=11	9.0 ± 4.4 (4 - 19) n=10	*p* = 0.057
MOCA score [/30]	25.0 ± 3.9 (11 – 30) n=34	25.0 ± 3.1 (19 - 30) n=11	26.0 ± 2.4 (21 - 29) n=11	25.6 ± 3.8 (18 - 29) n=10	*p* = 0.753
Sport per week [days]	4.2 ± 2.2 (0 - 7) n=34	4.2 ± 1.6 (2 - 7) n=11	4.0 ± 2.6 (0 - 7) n=11	4.4 ± 2.8 (0 - 7) n=10	*p* = 0.926

Sport per day [hours]	1.6 ± 1.2 (0 - 6) n=33	2.3 ± 1.6 (1 - 6) n=11	1.2 ± 0.7 (0 – 2.5) n=11	1.3 ± 1.1 (0 - 3) n=9	*p* = 0.064
Physiotherapy per week [amount]	1.4 ± 0.8 (0 - 3) n=34	1.6 ± 0.8 (0 - 3) n=11	1.1 ± 0.8 (0 - 2 n=11	1.4 ± 0.8 (0 - 2) n=10	*p* = 0.435
Occupational therapy per week [amount]	0.4 ± 0.6 (0 - 2) n=34	0.5 ± 0.7 (0 - 2) n=11	0.2 ± 0.4 (0 - 1) n=11	0.4 ± 0.7 (0 - 2) n=10	*p* = 0.459
Speech therapy per week [amount]	0.4 ± 0.8 (0 - 3) n=34	0.5 ± 0.9 (0 - 3) n=11	0.2 ± 0.4 (0 - 1) n=11	0.2 ± 0.4 (0 - 1) n=10	*p* = 0.447
Falls within 6 months [amount]	3.4 ± 7.8 (0 - 40) n=30	3.2 ± 5.4 (0 - 18) n=10	1.8 ± 2.2 (0 - 6) n=11	6.7 ± 14.8 (0 - 40) n=7	*p* = 0.461
Almost falls within 6 months [amount]	19.0 ± 66.1 (0 - 365) n=30	44.2 ± 113.5 (0 - 365) n=10	7.3 ± 8.5 (0 - 25) n=11	6.9 ± 8.9 (0 - 24) n=7	*p* = 0.402
Falls within 1 week [amount]	0.5 ± 1.9 (0 - 10) n=31	0.4 ± 0.9 (0 - 3) n=11	0.1 ± 0.3 (0 - 1) n=10	1.3 ± 3.5 (0 - 10) n=8	*p* = 0.441
Almost falls within 1 week [amount]	1.9 ± 5.0 (0 - 20) n=31	2.3 ± 5.6 (0 - 18) n=11	2.0 ± 6.3 (0 - 20) n=10	1.6 ± 2.9 (0 - 8) n=8	*p* = 0.966

Pure cerebellar ataxias = hereditary ataxias commonly regarded as “pure” cerebellar ataxias (e.g., SCA6, SCA14 etc.); Disease duration = Years since disease onset; Education = Educational level measured in years of Education; Sport per week/day = Amount of physical/sport activity perceived as demanding, per week or per day; PHQ = depression module of the Patient Health Questionnaire; MOCA = cognitive impairment according to the Montreal Cognitive Assessment Test

Table 2: Descriptive statistics of the longitudinal ClinRO and PRO variables (neurological examinations, questionnaires) and of the PerfO gait and stance variables, with comparisons between the three smaller groups using two-way ANOVAs.

Variable	**Mean ± SD (Min.–Max.)**			**Interaction Effect (G*T) Main Effect Group (G) Main Effect Time (T)**
	Control n=10	**Train20 n=11**	**Train40 n=11**	
SARA score pre	8.2 ± 3.3 (5–16)	9.6 ± 3.5 (3–15)	7.9 ± 3.8 (2.5–15)	G*T: *p* = 0.976 G: *p* = 0.170 T: *p* = 0.434
SARA score post	7.5 ± 5.1 (0.5–17.5)	9.1 ± 2.4 (5.5–13.5)	6.9 ± 2.8 (2.5–11.5)	
ADL score pre	7.5 ± 5.3 (1–15)	8.9 ± 3.8 (2–13)	8.5 ± 3.8 (3–14)	G*T: *p* = 0.999 G: *p* = 0.601 T: *p* = 0.460
ADL score post	6.8 ± 4.7 (0–15)	8.0 ± 4.3 (1–14)	7.7 ± 3.6 (4–15)	
TUG time pre	11.4 ± 3.7s (7.5–18.2)	13.1 ± 5.7s (6.2–26.5)	10.7 ± 3.4s (4.7–15.2)	G*T: *p* = 0.835 G: *p* = 0.063 T: *p* = 0.956
TUG time post	11.2 ± 4.3s (5.9–17.5)	14.0 ± 5.2s (7.9–24.3)	10.1 ± 3.4s (4.5–17.1)	
ABC-D score pre	68.63 ± 16.07 (45.0-89.1)	54.29 ± 15.04 (31.6-76.3)	67.68 ± 18.51 (30.0-86.3)	G*T: *p* = 0.982 **G: *p* = 0.007**** T: *p* = 0.803
ABC-D score post	67.31 ± 13.24 (49.0-81.0)	52.71 ± 10.99 (34.0-66.0)	64.72 ± 15.34 (36.0-86.0)	
FAHW score pre	28.40 ± 20.23 (-5-61)	29.91 ± 25.28 (-11-58)	32.45 ± 18.79 (5-59)	G*T: *p* = 0.910 G: *p* = 0.623 T: *p* = 0.855
FAHW score post[1]	25.90 ± 22.39	26.60 ± 30.61	34.82 ± 19.78	

	(2-73)	(-15-73)	(5-64)	
NG stride time pre	1.22 ± 0.10 s (1.09–1.37)	1.18 ± 0.15 s (0.95–1.51)	**1.18 ± 0.11 s (1.01–1.30)**	G*T: *p* = 0.960 G: *p* = 0.457 T: *p* = 0.455
NG stride time post	1.20 ± 0.12 s (1.06–1.41)	1.17 ± 0.13 s (0.92–1.40)	**1.14 ± 0.11 s (0.99–1.32)**	
NG double supp. pre	34.34 ± 6.59 % (26.8–48.4)	35.61 ± 6.12 % (26.8–49.1)	**32.98 ± 2.48 % (29.5–36.9)**	G*T: *p* = 0.942 G: *p* = 0.209 T: *p* = 0.726
NG double supp. post	33.77 ± 7.48 % (27.4–52.3)	35.74 ± 8.43 % (26.1–57.0)	**31.84 ± 2.76 % (27.6–36.0)**	
NG velocity pre	0.79 ± 0.14 m/s (0.53–1.00)	0.74 ± 0.20 m/s (0.39–1.08)	**0.83 ± 0.15 m/s (0.50–0.97)**	G*T: *p* = 0.880 G: *p* = 0.079 T: *p* = 0.411
NG velocity post	0.83 ± 0.18 m/s (0.47–1.03)	0.75 ± 0.22 m/s (0.36–1.11)	**0.89 ± 0.17 m/s (0.56–1.08)**	
NG foot rot. pre	15.6 ± 6.5 ° (5.1–25.5)	11.3 ± 7.1 ° (3.2–23.6)	11.5 ± 4.0 ° (4.0–18.0)	G*T: *p* = 0.990 G: *p* = 0.055 T: *p* = 0.932
NG foot rot. post	15.5 ± 6.3 ° (4.6–24.1)	11.70 ± 7.4 ° (2.3–24.9)	11.6 ± 4.3 ° (5.6–18.4)	
NG step width pre	**15.80 ± 2.70 cm (12–21)**	17.82 ± 3.82 cm (11–23)	17.36 ± 4.39 cm (12–26)	G*T: *p* = 0.602 **G: *p* = 0.038*** T: *p* = 0.631
NG step width post	**15.10 ± 2.18 cm (13–20)**	18.55 ± 2.98 cm (13–23)	16.09 ± 3.51 cm (12–25)	
NG step width SD pre	3.70 ± 1.25 cm (2–6)	3.45 ± 1.37 cm (2–7)	4.09 ± 1.04 cm (3–6)	G*T: *p* = 0.737 G: *p* = 0.290 T: *p* = 0.918
NG step width SD post	4.00 ± 1.05 cm (3–6)	3.36 ± 1.12 cm (2–6)	3.82 ± 1.33 cm (2–6)	
BG stride time pre	1.42 ± 0.36 s (1.14–2.39)	1.42 ± 0.14 s (1.22–1.64)	1.33 ± 0.21 s (0.94–1.77)	G*T: *p* = 0.918 G: *p* = 0.450 T: *p* = 0.388
BG stride time post	1.33 ± 0.23 s (1.10–1.80)	1.38 ± 0.17 s (1.17–1.71)	1.30 ± 0.20 s (0.96–1.60)	
BG double supp. pre	51.91 ± 11.29 % (36.6–68.2)	49.93 ± 10.99 % (38.0–74.8)	44.49 ± 7.73 % (30.3–52.7)	G*T: *p* = 0.911 G: *p* = 0.085 T: *p* = 0.704
BG double supp. post	49.40 ± 10.94 % (35.8–69.9)	49.75 ± 10.92 % (39.5–75.6)	44.25 ± 6.39 % (32.5–51.9)	
BG velocity pre	0.39 ± 0.12 m/s (0.25–0.64)	0.33 ± 0.14 m/s (0.11–0.50)	0.40 ± 0.15 m/s (0.19–0.64)	G*T: *p* = 0.962 G: *p* = 0.173 T: *p* = 0.451
BG velocity post	0.44 ± 0.15 m/s (0.19–0.69)	0.35 ± 0.15 m/s (0.11–0.56)	0.42 ± 0.15 m/s (0.22–0.75)	
BG foot rot. pre	6.0 ± 6.5 ° (-1.4–17.4)	3.9 ± 4.3 ° (-3.1–11.4)	5.0 ± 6.0 ° (-5.5–14.8)	G*T: *p* = 0.991 G: *p* = 0.480 T: *p* = 0.985
BG foot rot. post	5.8 ± 4.3 ° (-1.2–12.7)	4.0 ± 4.6 ° (-3.9–10.2)	5.2 ± 5.4 ° (-4.1–14.2)	
BG step width pre	25.30 ± 5.14 cm (15–33)	24.90 ± 4.25 cm (18–30)	**25.55 ± 4.34 cm (19–35)**	G*T: *p* = 0.993 G: *p* = 0.927 T: *p* = 0.604
BG step width post	24.60 ± 3.69 cm (17–31)	24.50 ± 4.45 cm (18–31)	**24.91 ± 4.28 cm (18–34)**	
BG step width SD pre	3.40 ± 1.58 cm (2–7)	2.70 ± 0.67 cm (2–4)	2.82 ± 1.47 cm (1–6)	G*T: *p* = 0.926 G: *p* = 0.163 T: *p* = 0.619
BG step width SD post	3.60 ± 1.51 cm (2–6)	3.00 ± 1.05 cm (2–5)	2.82 ± 1.08 cm (1–5)	
NS sway area pre	1212 ± 1409 mm^2 (77–4045)	820 ± 696 mm^2 (208–2394)	837 ± 911 mm^2 (190–3036)	G*T: *p* = 0.753 G: *p* = 0.463 T: *p* = 0.244
NS sway area post	797 ± 804 mm^2 (86–2854)	788 ± 805 mm^2 (252–3093)	495 ± 393 mm^2 (134–1275)	

NS sway velocity pre	35.6 ± 45.4 mm/s (6–156)	22.8 ± 13.1 mm/s (6–46)	20.6 ± 13.2 mm/s (7–56)	G*T: p = 0.636 G: p = 0.362 T: p = 0.248
NS sway velocity post	21.6 ± 17.4 mm/s (7–58)	19.4 ± 7.4 mm/s (11–35)	18.4 ± 14.5 mm/s (7–59)	
FTS sway area pre[2]	3862 ± 3222 mm^2 (603–9871)	2583 ± 1427 mm^2 (668–5015)	2328± 1765 mm^2 (608–6113)	G*T: p = 0.694 G: p = 0.228 T: p = 0.578
FTS sway area post[2]	2940 ± 2072 mm^2 (796–7201)	2556 ± 1585 mm^2 (1174–6812)	2386 ± 1572 mm^2 (865–4792)	
FTS sway velocity pre[2]	84.1 ± 121.9 mm/s (18–413)	65.9 ± 50.6 mm/s (24–189)	57.0 ± 48.8 mm/s (15–172)	G*T: p = 0.907 G: p = 0.552 T: p = 0.635
FTS sway velocity post[2]	72.5 ± 73.2 mm/s (20–249)	50.3 ± 42.1 mm/s (19–171)	59.2 ± 42.5 mm/s (19–143)	
FTSec sway area pre[3]	3138 ± 3211 mm^2 (718–10114)	3797 ± 2479 mm^2 (1359–8491)	3294 ± 2187 mm^2 (1594–8413)	G*T: p = 0.567 G: p = 0.740 T: p = 0.850
FTSec sway area post[3]	3262 ± 2584 mm^2 (1047–8714)	2844 ± 1872 mm^2 (816–6122)	4625 ± 4925 mm^2 (1267–17036)	
FTSec sway velocity pre[3]	59.3 ± 40.4 mm/s (22–138)	112.9 ± 77.5 mm/s (29–256)	92.6 ± 67.9 mm/s (37–211)	G*T: p = 0.686 G: p = 0.170 T: p = 0.682
FTSec sway velocity post[3]	61.4 ± 40.9 mm/s (24–137)	84.8 ± 46.6 mm/s (28–175)	98.3 ± 73.2 mm/s (28–254)	

p-values highlighted in bold with asterisk represent significant ANOVA values with * uncorrected $p<0.05$, ** Bonferroni-corrected $p<0.05/n$. Values highlighted in bold without asterisk represent significant changes between pre- and post-training within one group (according to dependent samples t-tests, p-values reported in the Results section). G*T = interaction effect between group and time; G = main effect of group; T = main effect of time. TUG = Timed Up and Go test; ADL = Activities of Daily Living; SARA = Scale for the Assessment and Rating of Ataxia; ABC-D = fall-related self-efficacy; FAHW = general habitual well-being; NG = Normal Gait; BG = Backward Gait; NS = Natural Stance; FTS = Feet-together Stance; FTSec = Feet-together Stance with Eyes Closed; [1]n=10 in group Train20 (one missing value); [2]n=10 in group Train40 pre-training, [3]n=7 in control group pre- and post-training, n=9/n=8 in group Train20 pre- and post-training and n=8/n=9 in group Train40 pre- and post-training