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Telehealth delivery of a high-intensity motor priming intervention in cerebellar ataxia: a single-case experimental design

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Abstract

Background: Hereditary Cerebellar Ataxias (HCA) cause symptoms that affect balance, gait, and motor learning. Balance training (BT) and aerobic exercise (AE) improve motor function in HCA. Motor-priming is a non-conscious process of learning, where exposure to one stimulus will alter response to another. Studies in Parkinson Disease have used AE before BT as motor priming to enhance motor learning. This study describes a novel application of motor priming in HCA.

Methods: Single-case experimental design with repeated measures. Participants (n=4) completed 16, 45-minute Telehealth-sessions of AE before BT, twice-weekly for 8-weeks. Outcomes evaluated at baseline, mid- and post-intervention, and included: Cerebellar Cognitive Affective Syndrome Scale (CCAS), modified Scale for Assessment and Rating of Ataxia (mSARA), Static Postural Sway (SPS), feasibility metrics.

Results: Participants' mean (SD) age was 58.5(4.4) yrs; 3M/1F with early-mid progression of spinocerebellar ataxia type 2, 3, 6, and cerebellar ataxia. All participants had 100% adherence to intervention without adverse events and improved on the CCAS (range 1-11 pt), mSARA (range 1-3 pt), SPS Neutral Stance (range 0.005-0.009 m/s^2).

Conclusions: Impaired motor learning in HCA likely impacts sustained benefits following rehabilitation. Motor priming has potential to improve disease-specific measures and may enhance motor learning for functional gain

Keywords: Cerebellar Ataxia, Balance, Aerobic Exercise, Motor Priming, Motor Learning, Physical Therapy, Neurorehabilitation, Telehealth

Introduction

Hereditary Cerebellar Ataxia (HCA) is a group of rare degenerative neurogenetic disorders characterized by progressive symptoms of ataxia that impact balance and gait [1]. The cerebellum is the most affected brain region in HCA, and progressive cerebellar dysfunction leads to impairments in motor control, resulting in long-term disability, and reduced quality of life [1,2]. Currently, no disease-modifying medications exist, however, rehabilitation interventions have been effective in improving motor skills and functional independence [2].

Rehabilitation for individuals with ataxia has focused on balance training (BT), with more recent investigation into aerobic exercise (AE). Balance training and AE may activate different mechanisms of neural recovery and plasticity [3,4]. Functionally, BT has been shown to improve both steady state balance and gait [5], while mechanistically, BT has been shown to increase cortical thickness and excitability [4,6]. Moderate to vigorous intensity AE has been shown to improve levels of fitness [7], muscle co-contraction and coordination [8], and at least 1 measure of ataxia on scales of disease-specific motor function

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in clinical studies [2]. Mechanistically, AE has been shown to improve neuroplasticity by inducing a cascade of events including increased blood flow, oxygenation, receptor activity, and release of neurotropic factors [3]. As such, a combination of AE and BT interventions may produce greater benefits than either intervention alone.

Motor priming is defined as a non-conscious process which is associated with learning, whereby exposure of one stimulus will alter the response of a separate stimulus [9]. Studies in stroke [10] and Parkinson disease [11] have evaluated AE prior to BT as a way to "prime" the brain and enhance motor learning [9]. The concept of motor priming is based on the assumption that AE upregulates neurotrophins (e.g., brain-derived neurotrophic factor) and increases blood flow and oxygenation to the brain [3]. This upregulation has been shown to improve motor learning and control when completed immediately prior to task-specific training [9]. Motor priming has not yet been explored in individuals with HCA.

While the benefits of in-person rehabilitation are well understood, HCAs are rare diseases, and accessing in-person therapy can be challenging for individuals with neurodegenerative diseases. Common barriers include fatigue, impaired balance and gait, fear of falling, financial burden, access to transportation, and lack of care-partner support [12]. Such barriers lead to discontinuous care and poor disease management outcomes [2]. Telehealth is an effective method of rehabilitation delivery and addresses some of these barriers, however remote exercise interventions in HCA remain understudied.

The purpose of this case series was to describe delivery of a novel motor priming intervention via telehealth for 4 individuals with HCA. The intervention consisted of high-intensity interval training (HIIT) followed by BT over 45-minute sessions. We choose HIIT as the AE motor priming method because HIIT has been recognized as an effective approach to obtaining the benefits of sustained high-intensity AE in those with neurodegenerative diseases [13]. We chose BT as the task for this intervention as it has been shown to improve gait and balance in ataxia [5].

Methods

Design

The PRIME-Ataxia pilot study was an unblinded, double baseline, repeated measures design of a telehealth-delivered motor priming intervention in a single cohort of four individuals with HCA. Potential participants were referred by neurologists, and a phone screening process was used to determine interest and eligibility. Participants were eligible for inclusion if they were between the ages of 18 and 85 years, had a neurologist-confirmed diagnosis of cerebellar ataxia, Scale for Assessment and Rating of Ataxia (SARA) score between 8-25/40 noting mild to moderate disease, ability to walk with or without assistive device, had care-partner availability for assessments and intervention, and successfully completed the Physical Activity Readiness Questionnaire (PAR-Q) [14] or received medical clearance from a physician. If participants did not pass the PAR-Q, they were referred to their physician for clearance prior to intervention. Participants were excluded from this study if they presented with severe non-ataxic motor symptoms such as dystonia, tremor, or Parkinsonism, measured by Inventory of Non-Ataxia Signs (INAS) [15], had coexisting neurologic, musculoskeletal, or cardiopulmonary comorbidities that would prevent participation in an exercise program. They were also excluded if they currently engaged in moderate to vigorous aerobic exercise or balance training more than 3 days per week. This pilot study was approved by the Institutional Review Boards of Teachers College, Columbia University, and Columbia University Irving Medical Center. All participants signed informed consent prior to participation. Funders played no role in the design, conduct, or reporting of this study.

Participants

Participant 1 (P1)

History and Systems Review. P1 was a 54-year-old male who racially identifies as white, with a past medical history (PMHx) of high cholesterol controlled with atorvastatin (see **Table 1** for all case demographics). He was diagnosed with Spinocerebellar Ataxia (SCA) Type 2 in 2020 based on clinical presentation and extensive family history of SCA2 with family members having genetic confirmation. Symptoms of ataxia and imbalance began in 2019. P1 lived with his wife (care-partner) and adult son. He worked full-time as a systems engineer. Prior to diagnosis, he attended the gym 2-3x/week, and engaged in resistance training and AE. Despite continued home exercise for 30-minutes, 2x/week, he noted disease progression, making him fearful to engage in activities that challenged balance. After his baseline assessment, P1 was diagnosed with COVID-19, and his start date was delayed 2-months. P1 was given medical clearance by his physician. Baseline measures were re-tested and were similar to pre-COVID scores. P1 reported mild residual post-COVID fatigue, which was monitored throughout the intervention. His primary goal was to improve exercise tolerance and balance confidence to continue working.

Clinical Impression and Examination. **Table 2** provides a review of baseline outcomes for P1. The mSARA score for P1 denotes early disease, however, progressive symptoms of imbalance and ataxia have led to decreased physical activity. As P1 contracted COVID-19 prior to study start, he was progressing through the final stages of recovery when he began the intervention. With gradual decline in physical function, from both disease progression and COVID-19, we were concerned for his overall exercise tolerance. Further, extended use of Atorvastatin has been linked to reduced exercise tolerance in males [16]. Balance testing revealed impairments in steady state and proactive balance with difficulty integrating sensory organization (proprioceptive and vestibular cues). This contributed to instability in gait and

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Table 1. Baseline Characteristics.

Participants n=4	P1	P2	P3	P4
Sex	M	M	M	F
Age	54	56	64	60
Race	White	White	White	Other
Ethnicity	not Hispanic or Latinx	not Hispanic or Latinx	not Hispanic or Latinx	Indian
Dx	SCA2	SCA6	HCA	SCA3
Dx Date	2020	2005	2019	2019
Comorbidities	High cholesterol	CAD HTN High cholesterol Sleep apnea Obesity Chronic LBP	HTN Spasticity	Neuropathic pain, RLE
Comorbidities management	Atorvastatin	Amlodipine Metoprolol Losartan CPAP at night	Losartan Tizanidine	Gabapentin
BMI	32.8	40	25.2	21.7
Education	College	College	College	College
Work Status	Working full-time	Working full-time	Retired	Not currently working
# Falls in the past year	0	1	1	0

Abbreviations: M, Male, F, Female, Dx, Diagnosis, SCA, Spinocerebellar ataxia, HCA, Hereditary Cerebellar Ataxia, CAD, coronary artery disease, HTN, hypertension, LBP, low back pain, RLE, right lower extremity

decreased functional independence negotiating crowded community settings and uneven terrain.

Participant 2 (P2)

History and Systems Review. P2 was a 56-year-old male who racially identifies as white, with a PMHx of coronary artery disease controlled with amlodipine, hypertension (HTN) controlled with metoprolol and losartan, high cholesterol, sleep apnea managed with nightly continuous positive airway pressure therapy, obesity, and chronic low back pain. On screening, P2 failed the PAR-Q due to cardiac history and was referred to his physician for medical clearance. P2 was diagnosed with ataxia in 2005 through clinical examination. P2 had multiple family members with progressive ataxia, and 1 brother having SCA6 identified through genetic testing. P2 is undergoing genetic testing for SCA6. Symptoms began in his early twenties with blurred vision and diplopia. He resided with his wife (care-partner) and two young children and worked full time as a technology consultant. Prior to diagnosis P2 was an avid exerciser, routinely engaging in weight training and AE. As symptoms progressed, exercise engagement declined due to imbalance and fear of falling. At baseline assessment, P2 reported little physical activity outside activities of daily living. P2's main goals were to improve exercise tolerance, balance, and balance confidence to return to the gym and play sports with his children. P2 was enrolled in the intervention and received 7 sessions, however injured his back outside of the study (gardening). He was referred to his physician, and the intervention was placed on hold. P2 did not seek rehabilitation services, however, pain was managed with diclofenac. P2 was given medical clearance by his physician and re-enrolled after 2-months. P2 was reassessed, and new baseline scores were used for outcomes, and he received an additional 16 sessions.

Clinical Impression and Examination. **Table 2** provides a review of baseline scores for P2. The mSARA score for P2 denotes early disease. P2 led a sedentary lifestyle and was on multiple cardiac medications, including a beta blocker, known to blunt heart rate response to exercise and limit exercise tolerance [**17**]. Balance testing revealed impairments in steady state and proactive balance, with difficulty integrating sensory organization (vestibular more than proprioceptive). Balance impairments led to instability in gait and decreased functional independence for participation in sporting activities with his children.

Participant 3 (P3)

History and Systems Review. P3 was a 54-year-old male who racially identifies as white, had a PMHx of HTN controlled with losartan, and spasticity managed with tizanidine. He was

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Table 2. Clinical Outcomes for Participants 1-4 at baseline, mid-intervention, post-intervention.

Clinical Participant Outcomes					
Outcome Group	**Measure**	**ID**	**Baseline**	**Mid-Intervention**	**Post-Intervention**
Disease Specific Measure	mSARA (#/24)	P1	5	4	5
		P2	3	2	1
		P3	9	7	6
		P4	4	3	2
	CCAS Raw Score (#/120)	P1	91	98	101
		P2	110	110	111
		P3	69	74	71
		P4	89	96	100
Functional and Digital Measures of Balance	TUG Test Total Time (sec)	P1	11.51	10.89	10.03
		P2	11.58	11.48	12.59
		P3	47.91	38.86	40.39
		P4	14.89	17.06	20.04
	Neutral Stance Average YZ Direction $(m/s)^2$	P1	0.0062	0.0045	0.0056
		P2	0.1420	0.0680	0.0277
		P3	0.0300	0.0080	0.0079
		P4	0.0310	0.0115	0.0095
	Romberg Eyes Open Average YZ Direction $(m/s)^2$	P1	0.0092	0.0114	0.0143
		P2	0.0123	0.0145	0.0077
		P3	0.1170	0.0210	0.0180
		P4	0.0129	0.0125	0.0122
	Romberg Eyes Closed Average YZ Direction $(m/s)^2$	P1	0.0240*	0.0234	0.0346*
		P2	0.0114	0.0090	0.0059
		P3	0.0445	0.0320	0.0195
		P4	0.0152*	0.0208	0.0223
Patient Reported Outcome	ABC (%)	P1	72.5	80.0	78.1
		P2	90.0	90.0	91.0
		P3	55.0	54.0	53.8
		P4	58.8	63.8	72.5
Reliance on Care-Partner During Intervention	Aerobic Exercise (%)	P1	50	25	0
		P2	25	0	0
		P3	75	50	50
		P4	25	0	0
	Balance Training (%)	P1	50	25	0
		P2	25	25	0
		P3	75	50	50
		P4	50	25	0

*Indicates need for intermittent external support
Abbreviations: SARA, Scale for Assessment and Rating of Ataxia, CCAS, Cerebellar Cognitive Affective Syndrome Scale, TUG, Timed Up and GO test, ABC, Activities Specific Balance Confidence Scale.

diagnosed with HCA in 2019 through clinical examination, without genetic testing. He had a family history of progressive ataxia, and differential diagnoses (e.g., amyotrophic lateral sclerosis, toxicity-induced ataxia) were ruled out. Symptoms began in 2018 with mild gait imbalance followed by increasing spasticity and cerebellar signs in 2019. He resided with his wife and adult daughter (care-partners) and was a retired ferry boat captain who was an avid exerciser prior to diagnosis. He continued to exercise 5 times per week with treadmill walking (15-minutes, 1.0 mph) and seated tai chi. P4's primary goal was to improve balance and balance confidence so he could continue to exercise and delay disease progression.

Clinical Impression and Examination. **Table 2** provides a review of baseline scores for P3. The mSARA score for P3 denotes mid-disease. Spasticity, imbalance, and lack of motor control, as identified on the mSARA and Timed Up and Go Test (TUG), contribute to heightened fear of falling, limiting activity tolerance and safe mobility. P3 was on medication for mild HTN and spasticity, both of which have heart rate blunting effects with exercise [**18**]. Balance testing revealed greater impairments in proactive over steady state balance with challenges in sensory organization (proprioceptive more than vestibular). Balance impairment and impaired motor control contributed to gait instability and decreased functional independence with daily tasks such as yardwork, housework, and community ambulation.

Participant 4 (P4)

History and Systems Review. P4 was a 60-year-old female who racially identifies as other, with a PMHx of neuropathic pain

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in the right lower extremity, managed with Gabapentin. She was diagnosed with HCA in 2019 through clinical examination. Genetic testing confirmed SCA3. Symptoms began in 2018 with mild imbalance on stair negotiation and gait, and progressed to include loss of balance, dizziness, nystagmus, and diplopia. P4 resided with her husband and lived close to her sister (care-partner), and was a retired librarian who, prior to diagnosis, was active, walking most days of the week. P4 continued to exercise 2-3 times per week on a recumbent stationary cycle ergometer for 10-15 minutes, followed by seated Theraband™ exercises. P4's primary goal was to walk more comfortably in household and community environments, and to be able to play with her grandchildren.

Clinical Impression and Examination. **Table 2** provides a review of baseline scores for P4. The mSARA score for P4 denotes early disease. P4's spasticity, imbalance, and lack of motor control, as identified on the mSARA and TUG Test, contribute to fear of falling, limiting activity tolerance and safe mobility. Balance testing revealed greater impairments in proactive over steady state balance with challenges in sensory organization (proprioceptive more than vestibular). Impaired motor control and imbalance contributed to significant gait instability and decreased functional independence with household chores, community ambulation, and playtime with grandchildren.

Context

This study was conducted over telehealth in each participant's home, or outside on their property.

Measures and Materials

Participants were evaluated at baseline 1 (week 0), baseline 2 (week 1), mid-intervention (week 4), and post-intervention (week 8) on a range of outcome measures including disease specific measures of Cerebellar Cognitive Affective Scale (CCAS) [**19**], and the first four items of the Scale for Assessment and Rating of Ataxia (mSARA) [**20**], measures of balance and balance confidence including the Activities Specific Balance Scale (ABC) [**21**], as well as Static Postural Sway (SPS), and the Timed Up and Go Test (TUG) [**22**] which were assessed using the Encephalog Balance Assessment System via smartphone. Care-partner involvement was summed in quarter increments (0-24.9, 25-49.9, 50-74.9, 75-100) of percent time involved per session throughout the intervention, to offer insight into participant functional independence, and confidence. At the time of data collection, the SARA had not yet been validated for remote use, and we decided to reduce the scale to measures that could be adapted for telehealth: Speech, Sitting, Stance, and Walking (mSARA). The Mon4t Encephalog system is a smartphone application that uses integral sensors embedded within the smartphone which provides accelerometry data on total sway to enhance standard neurological and balance assessments [**23**]. It is reliable and valid in other neurodegenerative diseases like Parkinson disease, however has yet to be tested in HCA [**23**]. The Mon4t Encephalog Balance Assessment includes six balance tests (Neutral Stance, Romberg eyes open and closed, Tandem Stance, Single Leg Stance right and left). Participants were evaluated on tests only if they were able to stand without assistance for 10 seconds. Order of assessments was consistent between participants. Assessments and interventions were conducted by a licensed physical therapist (CM).

A post-intervention questionnaire was used to measure intervention fidelity and was administered by a research assistant (MK) via phone interview. Participants were asked closed-ended questions on a 5-point Likert scale, followed by open-ended questions about study involvement (see Supplemental Digital Content). The method of qualitative data analysis was phone interview and transcription, as this approach was most feasible for participants.

Intervention

Prior to the intervention participants and care-partners completed one 30-minute training session on guarding techniques and establishment of safe home environment. Participants were mailed a Fitbit Charge HR 4 device for heart rate (HR) monitoring, gait belt for safety during BT, and chest strap for the Mon4t Encephalog Balance Assessment. Participants and care-partners were instructed on manual and digital (Fitbit Charge HR4) vital sign monitoring and medical safety. Training handouts were provided as reference.

The intervention was delivered via telehealth using Zoom for Healthcare. The intervention consisted of 25-minutes of HIIT prior to 20-minutes of intensive BT twice-weekly, 45-minutes per session, for 8-weeks (16 sessions). Intervention fidelity was maintained by having the intervention by delivered by the same therapist over time, and by having the therapist follow procedural guidelines for intervention delivery. Additionally, HR and Rating of Perceived Exertion (RPE) were routinely recorded to ensure that participants were achieving required intervention intensity.

Aerobic Exercise: The HIIT protocol was based in part on previous protocols used for HCA and other neurodegenerative diseases [**7**,**24**]. Participants were instructed in a 5-minute warm-up, 15-minutes of HIIT, and a 5-minute cool-down. The HIIT consisted of 5 sets of 3-minute segments, divided into 2-minutes of moderate-intensity exercise (50-64% Heart Rate Reserve (HRR); RPE on Category Ratio-10 (CR-10) Scale 4-6), followed by 1-minute of high-intensity exercise (65-85% HRR; corresponding RPE 7-9 on CR-10). The RPE and HR (using Fitbit) were documented at each intensity change. Participants were provided with individualized ramp HIIT protocols using available home equipment. P1 and P2 underwent walking programs, P3 underwent a bodyweight training program, and P4 used a recumbent stationary cycle ergometer (**Table 3**).

Balance Training: The BT was conducted immediately following completion of AE [**25**]. The BT protocol was based in part on previous protocols used for HCA and other neurodegenerative diseases [**26**]. Exercises were individualized based

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Table 3. Protocol Details of Aerobic Exercise and Balance Training Intervention.

High-Intensity Interval Training (HIIT) Protocol	**High-Intensity Balance Training Protocol**	
HIIT Program Details	***Balance Exercises***	***Balance Progressions***
Frequency 2x/week for 8 weeks	**Static Standing** With progressions	**Manipulation of Physical Support** Bilateral upper extremity support Unilateral upper extremity support No upper extremity supports
Intensity High intensity: 65-85% Heart Rate Reserve Moderate intensity: 50-65% Heart Rate Reserve **Individualized, based off Karvonen Formula, or Brawner Beta Blocker Formula*	**Dynamic Standing** Sit-to-stand Partial squats Ball Toss/Catch Reaching outside base of support (upper or lower extremity) Forward, backward, and lateral toe-taps High-Low Reaching with upper extremity	**Manipulation of Base of Support** Wide stance Neutral stance Narrow stance Semi-tandem stance Tandem stance Single-leg stance
Time Warm-up: 5-minutes HIIT protocol: 15-minutes · 5 x 3-minute intervals · Intervals: 1-minute high-intensity + 2-minutes moderate intensity Cool-down: 5-minutes	**Walking Balance** Forward walking Forward to backward walking Forward tandem walking Zig-zag walking Running/hopping in place Side-stepping	**Manipulation of Visual Input** Eyes open Eyes closed Dim lit environment Head Turn/Nod
Type The types of exercise used varied based on equipment availability: Walking (P1, P2) Recumbent cycle ergometer (P4) Bodyweight exercises (P1, 3) ·Examples: Step-ups and lunges Resistance training exercises (P1, P3) ·Examples: Dumbbell renegade rows and Dumbbell high pulls	**Vestibular Integration Exercises** Optokinetic exercises Vestibulo-ocular reflex x1	**Manipulation of Proprioceptive Input** Firm surface Pliable surface **Manipulation of Vestibular Input** Stationary head Horizontal head movement Vertical head movement
Materials/Equipment Used: Outdoor Walking/ Walking Trail, Treadmill, Recumbent Bicycle, Dumbbells, Elastic Resistance Bands, Stairs/Steps	Materials/Equipment Used: Folded Blankets/Towels, Pillows, Foam Seat Cushions, Yoga Mats, Variable Terrain (Pebbles, Grass, Mulch, Sand), Sunglasses (simulation of dim-lit environment), Small vs. Large ball (tennis ball, basketball), Cue cards with large font letters.	

on HCA severity. Fitting with the Challenge Point Hypothesis, BT exercises focused on the skill, learner, and difficulty of tasks to be learned [27]. To optimize motor learning, BT exercises were individualized, variable, progressive, and included active problem solving. The role of vision, proprioception, and vestibular senses were integrated within a range of tasks that challenged proactive, reactive and steady state balance [5]. BT exercises and progressions are listed in **Table 3**. Care-partners for P1, P2, and P4 assisted with set up and distant-supervision for BT only. Care-partners for P3 provided the most interaction with assistance for set up and close-supervision for AE and BT.

Analysis

Descriptive statistics were performed on participant characteristics, measures of exercise intensity (HR, RPE), as well as pre-post outcome assessments. Rates of recruitment and retention were calculated as percentages, and average scores were calculated per domain on the post-intervention questionnaire.

Results

All participants completed 16/16 sessions within 8-weeks. One participant (P2) had initially begun the study, however, was placed on hold due to back pain, unrelated to study participation. P2 restarted the intervention after 2-months of no exercise or rehabilitation and completed the intervention without incidence. There were no adverse events. Clinical outcomes are shown in **Table 2**.

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Heart rate response to exercise was blunted due to medication in P1, P2 and P3. Due to underlying medical conditions and medication side effects, HR response to exercise was found to be a potentially unreliable estimate of exercise intensity. For this reason, RPE was used in conjunction with HRR to assess and guide exercise intensity [25]. Averaging RPE across sessions, all participants achieved moderate intensity exercise (RPE 4-6 on CR-10) during each session of HIIT, however, the total percentage of time spent at moderate intensity differed per participant (range: 21.9%-91.2%). Similarly, according to RPE, participants 1, 3, and 4 achieved high-intensity exercise (RPE 7-9 on CR-10) during each session of HIIT, however, total percentage of time spent at high-intensity differed per participant (range: 23.53-92.31%). Inconsistencies between HRR and RPE were observed during the intervention. For example, during high-intensity intervals, P2 reported an RPE range of 3-5, but according to HRR, achieved high-intensity exercise during 72.73% of high-intensity intervals. In this situation, physical signs of exertion (shortness of breath, sweating, fatigue) were used to objectify RPE and HRR. In participants 1, 3, and 4 HRR was inconsistent, however RPE combined with physical signs of exertion provided an accurate depiction of intensity. Results for HRR and RPE are listed in **Table 4**.

All participants improved on disease-specific measures of cognition on the CCAS (range 1-11 pt) and motor scores on the mSARA (range 1-3 points) (**Figures 1A** and **1B** respectively). All participants improved on digital biomarkers of Static Postural Sway (SPS) Neutral Stance (range 0.005-0.009 m/s^2 total sway) (**Figure 1C**), Romberg Eyes Open (range 0.005-0.03 m/s^2), Romberg Eyes Closed (range 0.006-0.03 m/s^2). Two participants (P1, P2) improved on time to complete the TUG test (range 1.48-7.52 sec) (**Figure 1D**). The ABC score improved in P3 and P4 (range 7.5-13.75%); P1 and P2 were unchanged. All participants decreased in-session reliance on care-partner for AE and BT throughout intervention (**Table 2**). By the end of the intervention, 3 out of 4 participants (P1, P2, P4) required no care-partner assistance for either AE or BT.

Themes generated from patient responses on the post-intervention questionnaire included perceived benefits of exercise to improve physical abilities and decreased fear of falling (see Supplemental Digital Content). Motivation for participation included maintaining independence and a desire to slow disease progression through exercise. Two out of four participants also expressed favoring telehealth over face-to-face intervention for purposes of time management, travel, cost, and comfort.

Discussion

This case series describes a motor priming intervention delivered via telehealth for four individuals with HCA. The intervention had high adherence, no adverse events, and all participants had improvements in disease-specific measures of motor (mSARA) and cognitive function (CCAS). Natural history data for individuals with HCA have shown phenotype-specific annual declines in motor and cognitive function [29]. Annual increases in total SARA score for people with SCA2, 3 and 6 range from 0.65-0.87 points [1]. In this case series, all participants improved mSARA scores by 2-3 points, which is equivalent to regaining 2-3 years of natural disease progression [1]. The CCAS is a new measure of cognitive function and does not have established natural history data for comparison. Nonetheless, improvement on CCAS was observed in all participants, showing enhanced cognitive function with reduced disease impact.

The current public health environment has facilitated a shift not only in healthcare delivery, but also in the approach to human research and clinical trials. Remote exercise interventions have the potential to reach a greater number of individuals and to promote disease self-management. Work by Barbuto et al., [7] determined feasibility of a remote vigorous-intensity stationary cycling program, while Keller et al., [5] showed safety and efficacy of an intensive remote balance program to improve function in cerebellar ataxia. Both trials employed participant supervision for outcome assessment only, not intervention. Despite improvements, both trials reported that participants self-restricted intensity and frequency of

Table 4. Exercise Intensity and Target Heart Rate.

ID	Moderate Intensity: Calculated Target HR (50-64% HRR)	Moderate Intensity: Average HR Mean ± SD (Range)	Moderate Intensity: Average RPE Mean ± SD (Range)	High Intensity: Calculated Target HR (65-85% HRR)	High Intensity: Average HR Mean ± SD (Range)	High Intensity: Average RPE Mean ± SD (Range)
1*	120-133	108.52 ± 7.40 (Range: 88.00-124.00)	6.79 ± 0.68 (Range: 5-9)	134-152	109.24 ± 7.94 (Range: 96.00-128.30)	7.35 ± 0.61 (Range: 6-8)
2*	100-105	108.47 ± 6.12 (Range: 92.18-120.10)	3.93 ± 0.52 (Range: 3-5)	106-117	110.75 ± 5.33 (Range: 100.44-121.40)	3.98 ± 0.57 (Range: 3-5)
3*	108-121	87.23 ± 8.42 (Range: 68.00-104.00)	7.31 ± 0.90 (Range: 5-8)	122-142	94.21 ± 9.62 (Range: 74.00-113.00)	7.38 ± 0.65 (Range: 6-8)
4	118-130	113.23 ± 5.79 (Range: 99.00-122.00)	5.06 ± 1.13 (Range: 3-8)	131-147	117.30 ± 8.16 (Range: 96.00-130.30)	5.74 ± 1.26 (Range: 3-8)

*Indicates use of beta blocker formula was used
Abbreviations: ID, Participant Identification, HR, Heart Rate, HRR, Heart Rate Reserve, RPE, Rating of Perceived Exertion

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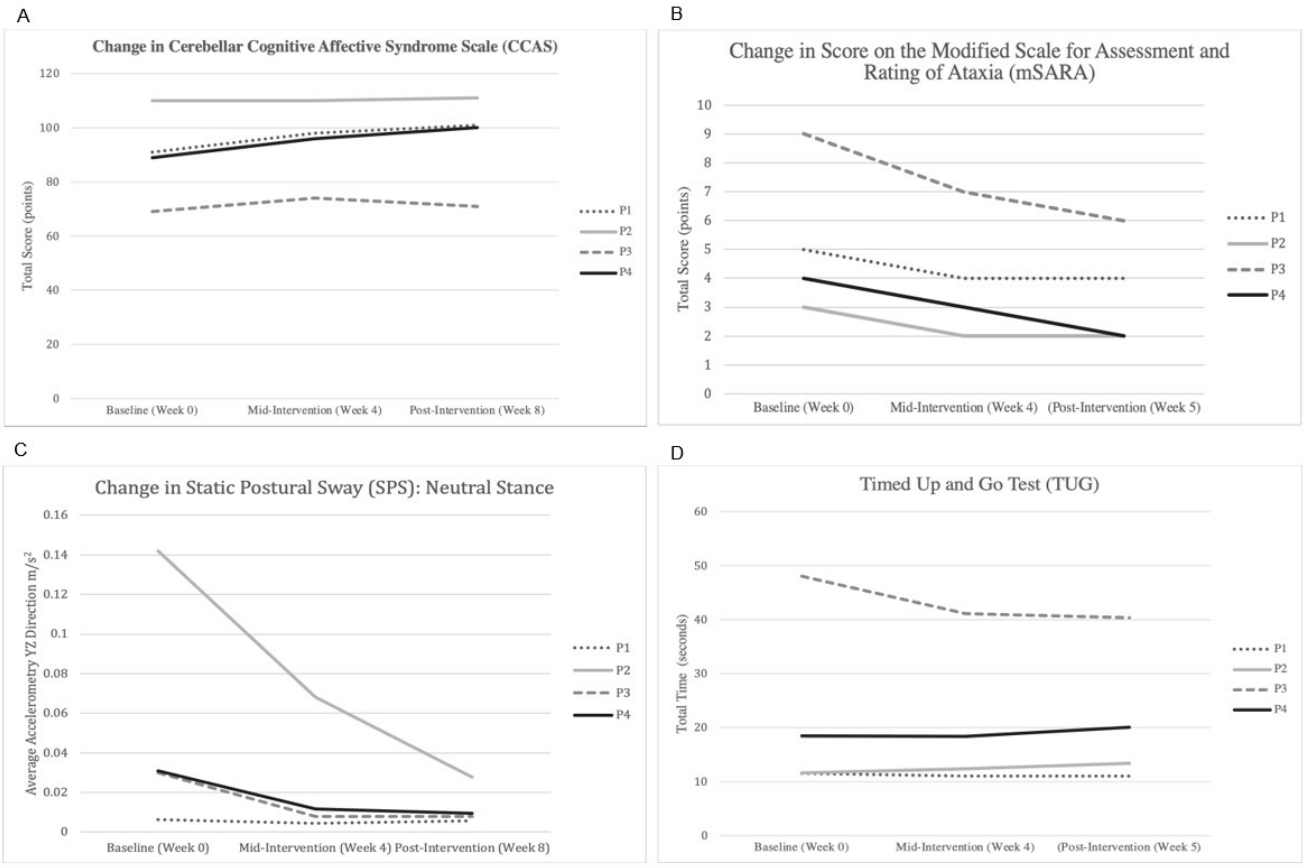

Figure 1. (**A**) depicts the change in total score achieved on the Cerebellar Cognitive Affective Syndrome Scale (CCAS) per participant throughout the course of this intervention. (**B**) depicts the change in score on the Modified Scale for Assessment and Rating of Ataxia (mSARA) throughout intervention. (**C**) depicts the change in Static Postural Sway (SPS) in Neutral Stance per participant throughout the course of this intervention. (**D**) depicts the change in total time to complete the Timed Up and Go Test (TUG) per participant throughout the course of this intervention.

engagement for prescribed protocols, which could impact efficacy. Building from these studies, this case series was the first to employ direct supervision with care-partner training to ensure safety while remotely reaching high intensities of exercise.

We measured exercise intensity using HR monitoring via Fitbit wearable devices and participant reported RPE levels. Due to the HR-blunting effect of medications, HR may have been an unreliable estimate of exercise intensity for participants in this study. For these reasons, RPE was used concomitantly with HR to assess intensity, however, RPE reliability and validity have not yet been assessed in HCA. Studies examining the reliability and validity of RPE in other neurological populations have found that RPE is a valid and reliable method for assessing exercise intensity [**30**]. While P2 reported an RPE range of 3-5, signifying low intensity exercise, this participant was visibly out of breath during high intensity intervals. RPE in HCA should be interpreted with caution [**28**], and future studies should examine the validity and reliability of using RPE in participants with HCA.

As a supplemental measure to assess motor function we digitally evaluated static and dynamic posturography through smartphone application (Mon4t LLC, Binyamina, Israel). While the SARA has been shown to have high inter-rater reliability among trained clinical evaluators [**20**], the evaluation remains clinically subjective, which increases the risk of bias, and scoring may not be sensitive to capture subtle changes across complexities of balance and gait. The use of digital biomarkers may be more sensitive to these changes, and it was encouraging that participants improved in both mSARA and digital measures of balance [**23**].

Limitations

We restricted inclusion to people with mild to moderate impairment on the mSARA to ensure participants would have the ability to safely engage in a challenging exercise protocol. Although frequency, duration, and intensity were managed, there was inherent variability in intervention type per par-

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ticipant. Activities were chosen based on home equipment availability, fitness-level, and disease-specific impairments. Differences in exercise type may have caused variability within zones of moderate and high intensity ratings on the RPE scale.

Conclusions

We describe a novel motor priming intervention delivered over telehealth for people with HCA. Findings show support for this intervention, with all four participants demonstrating improvements in disease-specific function post-intervention. Outcomes are encouraging for exercise-induced neuroplasticity and motor priming interventions in people with HCA, and future studies should explore exercise dosage for motor priming, as well as functional outcomes of motor learning in people with HCA.

List of Abbreviations

ABC: Activities Specific Balance Scale
AE: Aerobic Exercise
BT: Balance training
CR-10: Category Ratio-10
CCAS: Cerebellar Cognitive Affective Syndrome Scale
COVID-19: Coronavirus Disease of 2019
F: Female
HR: Heart Rate
HRR: Heart Rate Reserve
HCA: Hereditary Cerebellar Ataxias
HIIT: Hight-Intensity Interval Training
HTN: Hypertension
INAS: Inventory of Non-Ataxia Signs
M: Male
mSARA: modified Scale for Assessment and Rating of Ataxia
PMHx: Past Medical History
P#: Participant #
PAR-Q: Physical Activity Readiness-Questionnaire
RPE: Rating of Perceived Exertion
SCA: Spinocerebellar Ataxia
SD: Standard Deviation
SPS: Static Postural Sway
TUG: Timed Up and Go Test

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	CEM	BB	MK	AS	SHK	LQ
Research concept and design	√	--	--	--	√	√
Collection and/or assembly of data	√	--	√	√	--	--
Data analysis and interpretation	√	√	√	--	--	√
Writing the article	√	√	√	√	--	√
Critical revision of the article	√	√	--	--	√	√
Final approval of article	√	--	--	--	√	√
Statistical analysis	√	--	--	--	--	--

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