

# Intensive coordinative training improves motor performance in degenerative cerebellar disease



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## ABSTRACT

**Objectives:** The cerebellum is known to play a strong functional role in both motor control and motor learning. Hence, the benefit of physiotherapeutic training remains controversial for patients with cerebellar degeneration. In this study, we examined the effectiveness of a 4-week intensive coordinative training for 16 patients with progressive ataxia due to cerebellar degeneration ( $n = 10$ ) or degeneration of afferent pathways ( $n = 6$ ).

**Methods:** Effects were assessed by clinical ataxia rating scales, individual goal attainment scores, and quantitative movement analysis. Four assessments were performed: 8 weeks before, immediately before, directly after, and 8 weeks after training. To control for variability in disease progression, we used an intraindividual control design, where performance changes with and without training were compared.

**Results:** Significant improvements in motor performance and reduction of ataxia symptoms were observed in clinical scores after training and were sustained at follow-up assessment. Patients with predominant cerebellar ataxia revealed more distinct improvement than patients with afferent ataxia in several aspects of gait like velocity, lateral sway, and intralimb coordination. Consistently, in patients with cerebellar but without afferent ataxia, the regulation of balance in static and dynamic balance tasks improved significantly.

**Conclusion:** In patients with cerebellar ataxia, coordinative training improves motor performance and reduces ataxia symptoms, enabling them to achieve personally meaningful goals in everyday life. Training effects were more distinct for patients whose afferent pathways were not affected. For both groups, continuous training seems crucial for stabilizing improvements and should become standard of care.

**Level of evidence:** This study provides Class III evidence that coordinative training improves motor performance and reduces ataxia symptoms in patients with progressive cerebellar ataxia.

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## GLOSSARY

**BBS** = Berg balance score; **GAS** = goal attainment score; **ICARS** = international cooperative ataxia rating scale; **SARA** = scale for the assessment and rating of ataxia.

Cerebellar ataxic gait is typically characterized by an increased step width, variable foot placement, irregular foot trajectories, and a resulting unstable stumbling walking path<sup>1-3</sup> with a high risk of falling.<sup>4</sup>

Despite greatly improved understanding of the genetic underpinnings of ataxia,<sup>5</sup> no cure is yet available for the disease. Thus, physiotherapy remains a cornerstone in current ataxia therapy. However, the benefit of physiotherapeutic training is under dispute for patients with degenerative ataxia since the cerebellum is known to play an important role in the generation and adaptation of appropriate patterns of limb movements and dynamic regulation of bal-

Editorial, page 1818

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**Table 1** Clinical data of the study participants

Patient	Age, y	Age at onset, y	Gender	Diagnosis	Pre/post training	SARA				ICARS			
						E1	E2	E3	E4	E1	E2	E3	E4
C1	55	52	F	IDCA	No/yes	11	17	13	13.5	37	52	33	38
C2	79	76	F	SCA 6	No/yes	11.5	13.5	6	5	36	43	24	26
C3	66	56	M	ADCA	Yes/yes	15	15	9	6.5	45	43	29	23
C4	71	67	M	IDCA	No/yes	11	13.5	9.5	10	36	43	26	34
C5	56	53	F	IDCA	No/no	14	14.5	10	11	42	44	32	36
C6	47	31	M	IDCA	Yes/yes	13.5	14	8.5	9.5	40	43	25	25
C7	67	43	M	IDCA	No/no	20	24.5	19	16.5	55	56	49	44
C8	69	57	M	SCA 2	No/yes	11	11.5	8.5	9	41	41	31	30
C9	71	51	F	SCA 6	Yes/yes	16.5	17	13	12	45	48	39	37
C10	65	60	F	IDCA	Yes/no	12.5	12.5	8	9.5	34	34	25	34
A1	44	34	F	SANDO	No/yes	15.5	14	12	11	37	44	32	32
A2	69	56	M	IDCA with SN	No/no	21	23	16.5	16.5	57	54	43	50
A3	40	22	F	SANDO	Yes/no	15	12.5	8	13	44	38	26	39
A4	51	31	M	FA	Yes/no	23	19	16	17	59	44	41	44
A5	69	44	M	FA	Yes/yes	24	20	17	16	62	52	45	47
A6	64	44	F	FA	Yes/no	18	17	14	17.5	51	44	37	39

Ataxia was clinically assessed at the 4 examinations E1–E4 using the scale for the assessment and rating of ataxia (SARA) as primary outcome measure. SARA covers a range from 0 (no ataxia) to 40 (most severe ataxia). In addition, scores of the International Cooperative Ataxia Rating Scale (ICARS) are provided. In the patient column, “C” indicates individuals with predominantly cerebellar ataxia while “A” indicates patients with afferent ataxia. Pre training: (yes/no) categorization whether patients performed other physiotherapeutic training before intervention. Post training: (yes/no) categorization based on interview data, assessing whether patients performed daily training after intervention.

IDCA = idiopathic cerebellar ataxia; SCA 6 = spinocerebellar ataxia type 6; ADCA = autosomal dominant cerebellar ataxia; SCA 2 = spinocerebellar ataxia type 2; SANDO = sensory ataxic neuropathy with dysarthria and ophthalmoparesis caused by mutations in the polymerase gamma gene (POLG); SN = sensory neuropathy; FA = Friedreich ataxia.

ance.<sup>2,6,7</sup> Impairments of cerebellar patients in (short-term) practice-dependent motor learning have been shown for various motor tasks.<sup>8-12</sup> Motivated by these studies, it has been hypothesized that patients with degenerative cerebellar disease may not benefit from physiotherapy with respect to movement adaptation and increased coordination and balance capabilities.<sup>6,13,14</sup>

Very few clinical studies have evaluated physiotherapeutic interventions for patients with cerebellar ataxia. Some case studies have examined physiotherapeutic concepts to retrain posture and balance control using increasingly demanding balance and gait tasks.<sup>15-17</sup> Recently, locomotor training on treadmills with<sup>18</sup> or without<sup>19</sup> body weight support have been proposed. Further studies are needed to understand the potential benefit of rehabilitation for cerebellar ataxia patients. Open questions are whether such patients have lost the ability of practice-dependent

motor learning or whether they require longer-duration or higher-intensity training to learn.<sup>13</sup>

Here we present a prospective cohort study of the influence of coordinative training on patients with degenerative cerebellar disease. The goal of this study was to examine whether these patients can improve interjoint coordination and dynamic balance by intensive coordination training over a longer duration.

**METHODS Patients.** We examined 16 patients with degenerative cerebellar disease, including 10 patients (C1–C10) with predominant effects on the cerebellum (group C: 5 women, 5 men, age  $64.6 \pm 9.38$ ) and 6 patients (A1–A6) with predominant afferent ataxia (group A: 3 women, 3 men, age  $56.2 \pm 12.9$ ; for clinical details see table 1). Patients with afferent ataxia were positive for genetic mutations known to cause primarily afferent ataxia: 3 patients with genetically confirmed Friedreich ataxia and 2 with sensory ataxic neuropathy with dysarthria and ophthalmoparesis caused by mutations in the polymerase gamma gene (*POLG*). Furthermore, 1 patient with combined idiopathic ataxia and highly severe sensory neuropathy (as indicated by loss of sensory nerve action potentials in nerve conduction studies) was included in the afferent ataxia group.

Patients with afferent ataxia had earlier disease onset than patients in the cerebellar group ( $38.5 \pm 11.9$  vs  $54.6 \pm 13.3$  years of age; Mann-Whitney  $U$  test:  $U = 11$ ,  $p = 0.039$ ) and also presented with more severe disease (scale for the assessment and rating of ataxia [SARA]:  $19.7 \pm 4.2$  vs  $13.6 \pm 2.9$ ,  $U = 5.5$ ,  $p = 0.005$ ). All patients were able to walk a distance of 10 meters with or without a walking aid. Before study onset, 7 patients received physiotherapy once a week with different protocols (e.g., strength training, isometric and isotonic stabilization).

**Standard protocol approvals, registrations, and patient consents.** All experimental procedures were approved by the local ethics committee. Patients gave written informed consent.

**Study design.** We assessed the effectiveness of a 4-week course of intensive coordinative training, followed by 8 weeks during which the patients were asked to continue exercises at home. Patients were examined 4 times: 8 weeks before intervention (E1), immediately before the first coordinative training (E2), immediately after the last training (E3), and after 8 weeks for follow-up assessment (E4).

To control for variability in disease progression, patients were taken as their own controls in an intraindividual control design where performance changes with and without training were compared (level of evidence class III). Three different comparisons were performed: 1) by comparing E1 with E2, we determined the variability of test performance not caused by the intervention. This variability might be due to progression of diseases, variability of daily condition, or practice effects; 2) we assessed intervention effects by comparing E2 and E3; 3) comparison of E2 with E4 and E3 with E4 allowed the assessment of retention effects.

Motor performance was evaluated on 3 levels independently: 1) effects on neurologic symptoms assessed by clinical ataxia and behavioral rating scales, 2) quantitative movement analysis, 3) improvements in personally relevant activities of daily living assessed by an individual goal attainment score.

**Coordinative physiotherapy.** The strategy of the physiotherapeutic intervention was to activate and demand control mechanisms for balance control and multijoint coordination. Furthermore, the intervention trained the patients' ability to select and use visual, somatosensory, and vestibular inputs to preserve and retrain patients' capability for reacting to unforeseen situations and for avoiding falls as much as possible.

The physiotherapy program consisted of a 4-week course of intensive training with 3 sessions of 1 hour per week. Exercises included the following categories: 1) static balance, e.g., standing on 1 leg; 2) dynamic balance, e.g., sidesteps, climbing stairs; 3) whole-body movements to train trunk-limb coordination; 4) steps to prevent falling and falling strategies; 5) movements to treat or prevent contracture. Appendix e-1 on the *Neurology*<sup>®</sup> Web site at [www.neurology.org](http://www.neurology.org) provides a detailed description of the physiotherapeutic exercises.

After the 4-week intervention period, all patients received an individual written training schedule. They were asked to perform exercises by themselves at home for 1 hour each day. Patients were instructed to perform only safe exercises at home and to omit any exercises which they could only perform with aid. After assessment E4, we assessed by interview which patients regularly performed training at home (see table 1). None of the data of the movement analysis or the interview were available to the examiners during clinical ratings.

**Clinical outcome measures.** The primary outcome measure was SARA,<sup>20</sup> which has been approved as a valid measure of

**Table 2** Example for a personally selected goal of the goal attainment score

Individual goal: Walking around a table with small distance without swaying	Score
The patient walks around the table mainly by touching the table	-2
The patient can walk around the table without touching the table most of the time	-1
The patient can walk around the table without touching the table	0
The patient can walk around the table without touching the table and is able to look around sometimes	+1
The patient can walk around the table without touching the table and is able to look around the whole time	+2

Personally selected goal of the goal attainment score exemplarily shown for patient C4. Five levels of goal attainment were defined before the intervention started (at examination E2). At examination E3, the goal attainment is rated subjectively from the patient. Scores range from -2 to 2 (-2 baseline, -1 less than expected outcome, 0 expected outcome, 1 greater than expected outcome, 2 much greater than expected outcome).

disease severity in spinocerebellar ataxias and idiopathic ataxias.<sup>21</sup> The SARA score includes 8 items: 3 items rating gait and posture, 1 item for speech disturbances, and 4 items for limb-kinetic functions (table 1). Additionally, we assessed ataxia by the international cooperative ataxia rating scale (ICARS).<sup>22</sup> SARA and ICARS were assessed by a neurologist experienced in ataxia (M.S.). Independently and blinded for these scores, a physiotherapist (S.B.) rated balance control capacities using the Berg balance score (BBS).<sup>23</sup> In addition, patients selected individual goals using a goal attainment score (GAS)<sup>24</sup> (table 2) to determine the relevance of the intervention for everyday life.

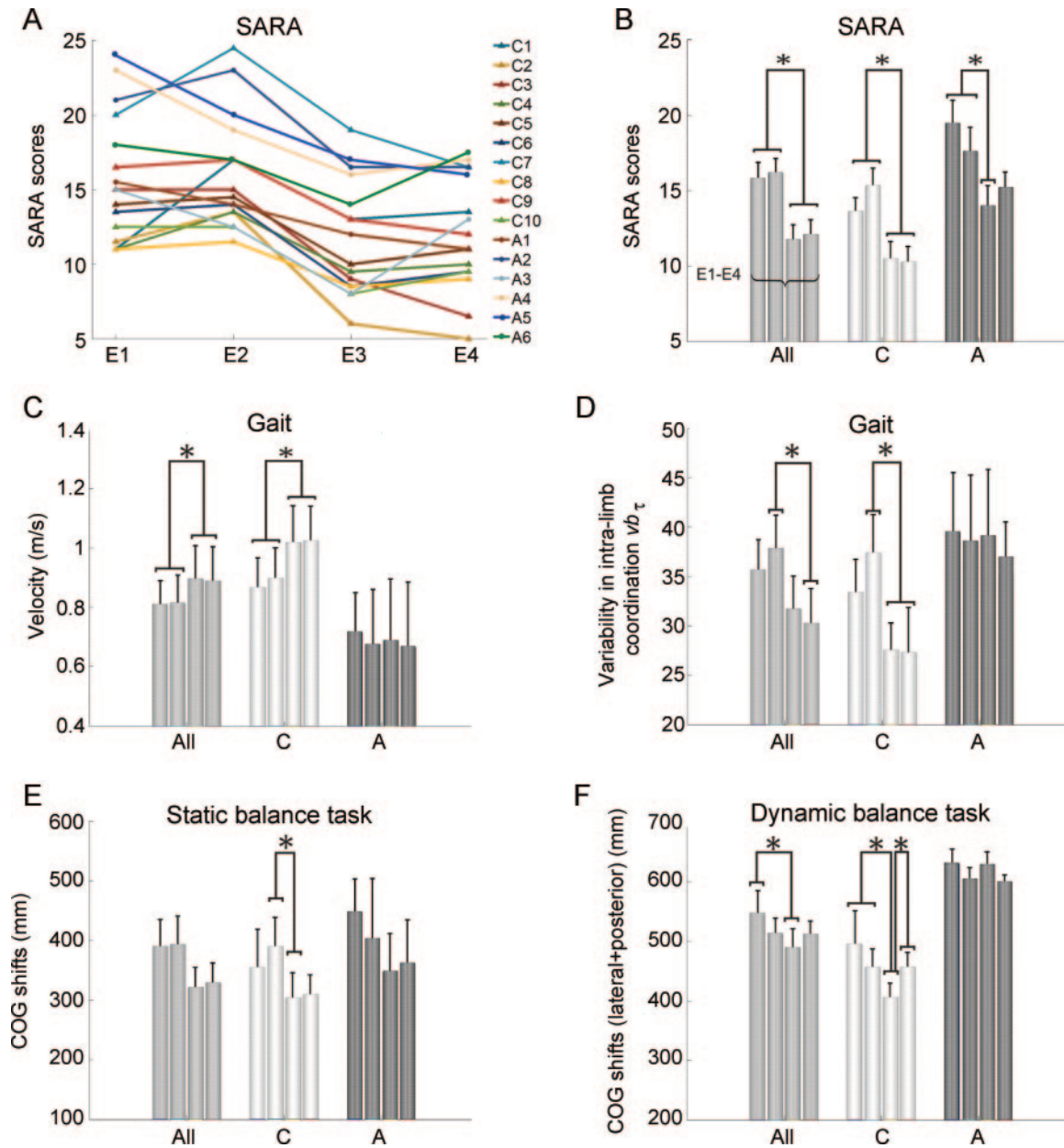
**Quantitative movement analysis.** Motor performance was evaluated by quantitative movement analysis using a VICON 612 motion capture system with 8 cameras (see appendix e-2 for details). We examined gait as well as a static and a dynamic balance task. For gait analysis, patients were instructed to walk normally at a self-determined pace. Patients were walking with shoes and without walking aids except for patients A4 and C7 who used a trolley for the recording of gait. From each patient we recorded 12–15 gait cycles, within 3 walking trials.

We examined standard gait measures like velocity, step length, step width, and lateral body sway. Lateral body sway was defined as the lateral component of the path of the center of gravity, normalized to the anterior-posterior component for each trial.

Furthermore, we determined a specific measure for the temporal variability of intralimb coordination. This measure *vb<sub>t</sub>* has been shown in previous work to detect temporal abnormalities in intralimb coordination in gait that are specific for patients with cerebellar dysfunctions<sup>25,26</sup> (see appendix e-2). Temporal variability in gait has been suggested as an indicator for the risk of falling.<sup>27</sup>

In the static balance task, patients had to stand for 30 seconds with their eyes open, feet together, and arms in front of the body. We determined body sway by measuring the motion of the center of gravity.

In the dynamic balance task, subjects stood in an upright position with both legs on a treadmill and were warned that the



(A) Scale for the assessment and rating of ataxia (SARA) scores at examinations E1-E4 of individual patients. "C" indicates the group with predominantly cerebellar ataxia and "A" means patients with afferent ataxia. (B) Group comparisons of SARA scores and measures from quantitative movement analysis (C-F). Groups of 4 bars indicate the examinations E1-E4. Asterisks indicate significant differences between examinations (\* $p < 0.05$ ).

treadmill would be activated in the next few seconds. The treadmill was programmed to run for 1 second with an acceleration of  $6 \text{ m/s}^2$  and a maximal velocity of  $0.4 \text{ m/s}$  in posterior direction. The mechanical stimulus had a translatory amplitude of  $18 \text{ cm}$ . Subjects were protected from falling by a safety harness. They were instructed to compensate the perturbation by anteriorly directed steps. In each session, 3 trials were conducted, the second and the third trial being analyzed with respect to lateral and posterior body sway. The first trials were not analyzed in order to allow patients to get used to the treadmill and the task.

**Statistical analysis.** Comparisons between the cerebellar group and the afferent group were executed by using the non-parametric Mann-Whitney  $U$  test ( $U$  and  $p$  values). Significances are reported with the significance level  $p < 0.05^*$ . Repeated mea-

surements analyses were performed using the nonparametric Friedman test ( $\chi^2$  and  $p$  values) to determine within-group differences between examinations E1 and E4. When the Friedman test yielded a significant effect ( $p < 0.05$ ) or a trend ( $p < 0.1$ ), post hoc analysis was performed using a Wilcoxon signed-rank test for pairwise comparisons between assessments ( $Z$  and  $p$  values). For the latter we report 2 significance levels: uncorrected ( $p < 0.05^*$ ) and Bonferroni corrected for multiple comparisons ( $p < 0.05/3^{**}$ ). Statistical analysis was performed using the software packages MATLAB and SPSS.

**RESULTS Clinical scores.** Differences in ataxia symptoms (measured by SARA) across the 4 assessments were confirmed using a Friedman test ( $\chi^2 =$



**Table 3** Comparison of ataxia symptoms and motor performance before and after the intervention

	SARA, total	ICARS, total	BBS, total	Gait				Static balance, COG sway	Dyn. balance, COG sway
				Velocity	Step length	Lateral sway	$vb_{\tau}$		
All patients	0.001*/0.001*	0.001*/0.001*	0.001*/0.001*	0.007*/0.04*	0.004*/0.13	0.3/0.3	0.09/0.02*	0.27/0.45	0.28/0.65
Cerebellar ataxia	0.005*/0.005*	0.005*/0.008*	0.005*/0.01*	0.007*/0.02*	0.005*/0.01*	0.04*/0.02*	0.04*/0.02*	0.04*/0.14	0.02*/0.75
Afferent ataxia	0.026*/0.11	0.027*/0.08	0.03*/0.06	0.75/0.91	0.43/0.6	0.6/0.25	0.75/0.6	0.68/0.84	0.22/0.14

For each combination of patient group and measure 2  $p$  values are given (Mann-Whitney  $U$  test). The first  $p$  value denotes the comparison of measures at examinations E2 and E3, the second compares examinations E2 and E4. Asterisks indicate significance ( $p < 0.05$ ).

SARA = scale for the assessment and rating of ataxia; ICARS = International Cooperative Ataxia Rating Scale; BBS = Berg balance score;  $vb_{\tau}$  = measure for the temporal variability of hip-knee coordination (see Methods); COG = center of gravity.

30.7,  $p < 0.0001$ ). Comparisons between specific examinations of the SARA score revealed reduction ( $-5.2$  points on average) comparing pre/post intervention (E2/E3, Wilcoxon signed-rank test:  $Z = -3.52$ ,  $p < 0.001^{**}$ ) and retention of improvements in the follow-up assessment (E2/E4,  $Z = -3.36$ ,  $p = 0.001^{**}$ ) (figure, A and B). Subgroup analyses revealed pre/postintervention differences for both the cerebellar ( $Z = -2.81$ ,  $p = 0.005^{**}$ ) and the afferent groups ( $Z = 2.21$ ,  $p = 0.027^{*}$ ), whereas retention was found for the cerebellar group only ( $Z = -2.6$ ,  $p = 0.008^{**}$ ) (table 3). In contrast, there is no improvement comparing preintervention examinations (E1/E2,  $Z = 0.56$ ,  $p = 0.57$ ), indicating that there is no relevant influence of factors beyond intervention.

Categorized by training intensity at home (table 1), the group of patients performing daily training showed a slight improvement (decrease) in the SARA score in the follow-up assessment E4 compared to E3 (average  $-0.4$  points), whereas the complementary group revealed an average increase of the SARA score (1.0 point).

We found comparable results for ICARS and BBS, showing significantly improved performance for all patients after interventions, while significant retention was restricted to the cerebellar group (table 3).

The tendency of cerebellar patients profiting more than afferent patients was confirmed in the goal attainment scores (table 4). For all patients, the average rating was 0.5 ( $0 \approx$  expected outcome,  $1 \approx$  greater than expected outcome). For the cerebellar group, average rating was 0.8 compared to 0.1 in patients with afferent ataxia.

**Quantitative movement analysis.** Gait analysis revealed an increased velocity for cerebellar patients ( $\chi^2 = 13.56$ ,  $p = 0.004$ ) in the comparison of pre/postintervention ( $Z = -2.7$ ,  $p = 0.007^{**}$ ) and retention ( $Z = -2.29$ ,  $p = 0.02^{*}$ ). In contrast, velocity was not increased for the afferent group (figure, C; table 3).

Consistent with these results, cerebellar patients showed persistent increase in step length ( $\chi^2 = 17.4$ ,  $p = 0.001$ ) (E2/E3:  $Z = -2.8$ ,  $p = 0.005^{**}$ ; E2/E4:  $Z = -2.4$ ,  $p = 0.013^{**}$ ) and a decrease in lateral body sway ( $\chi^2 = 9.1$ ,  $p = 0.02$ ) (E2/E3:  $Z = -1.98$ ,  $p = 0.047^{*}$ ; E2/E4:  $Z = -2.29$ ,  $p = 0.022^{*}$ ) indicating an improvement of dynamic balance in gait. Quantifying the joint coordination variability using the measure  $vb_{\tau}$  (see Methods) revealed a reduced temporal variability ( $\chi^2 = 6.9$ ,  $p = 0.07$ ) in hip-knee coordination (this joint combination has been shown to be most indicative for changes in intralimb coordination in previous studies<sup>25,28</sup>) after training ( $Z = -1.98$ ,  $p = 0.047^{*}$ ) and at follow-up ( $Z = -2.29$ ,  $p = 0.022^{*}$ ) for the group of cerebellar patients (figure, D; table 3).

The dynamic balance task on the treadmill revealed a nonsignificant decrease in body sway comparing E1 and E2, which is probably caused by practice effects (figure, F). Patients with afferent ataxia were not able to reduce body sway after training, whereas cerebellar patients improved ( $\chi^2 = 8.2$ ,  $p = 0.04$ ) in comparison of pre/postintervention (E2/E3,  $Z = -2.29$ ,  $p = 0.02^{*}$ ). This result implies an improvement in dynamic balance control with strong everyday relevance. However, follow-up assessment revealed an increase of body sway for cerebellar patients (E3/E4,  $Z = -2.09$ ,  $p = 0.03^{*}$ ), indicating that improvements in dynamic balance did not fully persist. See appendix e-2 for more details.

**DISCUSSION** In this study, we focused on coordinative training for patients with degenerative ataxias. This might be the most difficult group of ataxias to treat, due to their progressive nature and effect on virtually all parts of the cerebellum. In contrast, ataxia following stroke, neurosurgery, trauma, or multiple sclerosis generally affects only some regions of the cerebellum, but leaves other regions intact, which might be trained to compensate for the defective parts.

Subjects served as their own controls by comparing the preintervention disease course (examinations

Patient	Goal	Score
C1	Walking on a narrow path (<50 cm)	2
C2	Walking up a staircase without using railway	2
C3	Reaching the mailbox in a distance of 600 m without using a walking aid	0
C4	Walking around a table with small distance without swaying	1
C5	Walking without a walking aid over a distance >10 m	1
C6	Walking over a distance of about 300 m without a walking aid or a helping person	2
C7	Walking over a distance of 50 m with a trolley, without bumping with the feet into it	1
C8	Walking free on a small staircase (3 steps) in an alternating way with a distance of 1 m to the railway	-1
C9	Walking with a trolley over a distance of 50 m	0
C10	Walking without a walking aid over a distance of about 100 m	0
A1	Walking independently over longer distances (>500 m)	1
A2	Reducing danger of falling	0
A3	Walking a distance of 30 m with a full cup without to spill something	-1
A4	Walking with a trolley over a distance of 2,000 m without dropping feet and strong support from the arms	-1
A5	Walking over a distance of 100 m with a trolley, without bumping with the feet into it	2
A6	Walking with a trolley over a distance of 500 m	-1

Personally selected goals of the goal attainment scale and the scores obtained after the intervention period. Described goals correspond to score 0. Scores range from -2 to 2 (-2 baseline, -1 less than expected outcome, 0 expected outcome, 1 greater than expected outcome, 2 much greater than expected outcome).

E1/E2) with the disease course during intervention (examinations E2/E3). This allowed for control of factors like daily condition, practice effects, or progression of disease. The advantage of taking the patients as their own control group is the comparability of disease progression.

The results of our study reveal a significant reduction of ataxia symptoms measured by the clinical scale SARA for all patients. The natural disease progression of degenerative cerebellar ataxias is 0.6–2.5 points per year on the SARA scale depending on genotypes (data of the EUROSICA natural history study; Thomas Klockgether, personal communication, 2008). The average improvement obtained by the coordinative training of -5.2 SARA points therefore means that the patients gained back func-

tional performance equivalent to 2 or more years of disease progression. Follow-up assessment revealed retention of this improvement for the cerebellar group.

Quantitative movement analysis revealed more distinct changes for patients with cerebellar ataxia. These patients showed significant improvement in specific measures quantifying intralimb coordination as well as balance control in gait and balance tasks, whereas patients with predominant afferent ataxia did not improve. This discrepancy is most likely caused by a loss of afferent information in these patients, which inhibits necessary inputs for adequate cerebellar processing. Consistently, cerebellar patients achieved more of their personal goals concerning activities of daily living, as indicated by their higher goal attainment score.

Another main result consists of the observation that retention crucially depends on continuous training. Our interview-based data on training intensity at home indicate that patients who regularly performed training according to a “homework protocol” had a better long-term outcome than patients who did not train at home regularly. The necessity of continuous training also became obvious in the dynamic balance task on the treadmill. For the cerebellar group, body sway was significantly reduced in comparison of pre/postintervention, but also significantly increased in the follow-up assessment. This finding indicates that the improvements gained by the coordinative training could not be preserved for this demanding task of reactive balance control. This phenomenon is most likely explained by the patients’ limited training of demanding whole body coordination exercises at home for safety reasons. We therefore recommend professionally administered physiotherapy units to focus on whole body coordination exercises as an ideal complement of home training.

In order to prove the specificity of our results, we tested for several interference factors. Differences concerning age may limit comparability of the afferent and the cerebellar groups. However, better motor learning would be expected in the younger rather than in the older group. Similarly, differences in disease severity are unlikely to explain discrepancies between the afferent and the cerebellar group since the physiotherapy effect did not correlate with disease severity ( $r = -0.158$ ,  $p = 0.57$ , Spearman rank correlation). Additionally, there is no difference in improvement of ataxia symptoms (SARA) depending on whether patients have done physiotherapeutic training before the intervention ( $U = 83$ ,  $p = 0.87$ ).

We cannot fully exclude the influence of repetitive practice effects, in particular for the balance

task on the treadmill. The greatest influence of practice effects would be expected between the first and the second assessment (E1/E2). But changes between E1 and E2 were not significant and changes between E3 and E4 went in the opposite direction. For the examinations included in the clinical ataxia scales (SARA, ICARS), it is unlikely that practice effects predominantly influenced these results, since patients have undergone clinical ratings for years and scores did not improve between assessments without training.

The specificity of improvements in motor performance is supported by highly significant correlations between specific items of clinical ataxia ratings and specific movement measures reflecting multijoint coordination and dynamic balance control (figure e-5). Additionally, the difference in dynamic balance improvements for afferent and cerebellar groups indicates that these improvements are not predominantly due to strengthening of ankle and hip muscles, but that they are influenced by increased capacities in the dynamic regulation of balance.

We delivered evidence for the hypothesis that patients are able to improve multijoint coordination and dynamic balance by intensive and continuous physiotherapeutic training despite ongoing neurodegeneration. Thus, our findings stimulate further studies in degenerative cerebellar disorders. These include long-term learning studies as well as imaging analyses to clarify whether the degenerating cerebellum is still able to adapt motor coordination, or whether the learning deficit is compensated by other brain structures.

We focused on ambulatory patients, who are able to walk with or without walking aid, as patients with more severe impairments are usually not able to perform most of the exercises. Thus, further studies are needed to examine whether patients with more severe impairments would also benefit from physiotherapeutic training (adjusted to their impairments, e.g., for arm movements) or whether the capacity to improve motor performance relies on a specific level of residual cerebellar integrity.

## AUTHOR CONTRIBUTIONS

Statistical analysis was conducted by Dr. Winfried Ilg.

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## DISCLOSURE

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