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ORIGINAL COMMUNICATION

Two-year decline in performance on the Cerebellar Cognitive Affective Syndrome Scale in spinocerebellar ataxias

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Abstract

Background and objectives Cognitive deficits are observed in a subset of individuals with spinocerebellar ataxias (SCAs); however, there is limited research on the longitudinal trajectory of such deficits. We investigated longitudinal cognitive performance amongst individuals with SCAs relative to controls, and the relationship of change in cognitive performance with change in self-reported function.

Methods Individuals with symptomatic SCA1, SCA2, SCA3, and SCA6 as well as unaffected controls were administered the Cerebellar Cognitive Affective Syndrome Scale (CCAS-S) at yearly intervals for up to two years. Participants with SCA self-reported day-to-day cognitive and motor function via annual completion of the Patient-Reported Outcome Measure of Ataxia.

Results Significant two-year decline in CCAS-S performance was observed in individuals with SCA ($n = 25$). In a larger cohort of individuals who completed 1-year follow-up ($n = 45$ SCA), greater decline was observed among individuals with better baseline performance, and, at a trending level, those with milder motor ataxia severity. Greater one-year decline on the CCAS-S was significantly associated with greater decline in self-reported day-to-day cognitive function. In contrast, one-year CCAS-S change was not related to change in self-reported motor function.

Conclusions The CCAS-S indexes functionally relevant cognitive change over time in SCAs, with this decline apparent in at least a subset of individuals with SCAs. Decline in cognitive performance may be particularly pronounced in early/mild disease stages. Our results motivate larger and longer-term studies of the CCAS-S in SCAs, including investigating cognitive change across the pre-symptomatic and symptomatic disease course, and identifying risk factors for cognitive decline, to inform appropriate clinical support.

Keywords Spinocerebellar ataxia · Cognition · Longitudinal · Cerebellar Cognitive Affective Syndrome

Introduction

Cognitive deficits are evident in at least a proportion of individuals with spinocerebellar ataxias (SCAs) [1]. Cognitive symptoms remain under-recognized in the sequelae of these progressive neurological conditions, despite growing evidence of the prevalence and impact of these deficits on quality of life.

An emerging body of longitudinal studies indicates that cognition may decline over time [2, 3]. Specifically,

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executive function, processing speed, and attention have been shown to decline in individuals with SCA types 1, 2, 3 and 6, over periods of 2 to 7.5 years [2, 4]. In SCA3, verbal learning as well as verbal and visual memory abilities were found to decline at a 3.5-year follow-up assessment [3]. Visuo-spatial abilities have also been found to decline from baseline levels in studies of SCA2 [5, 6], although this has not been consistently replicated [4]. It should be noted that these studies involved different study designs, follow-up periods, and cognitive test batteries, making it difficult to compare longitudinal results across studies.

In recent years, the Cerebellar Cognitive Affective Syndrome Scale (CCAS-S) [7] has been increasingly used as a standard cognitive measure in SCAs, given its optimised sensitivity to cognitive change in cerebellar pathologies. The CCAS-S is a 10-item screening tool with items designed to capture deficits in the four domains which comprise the Cerebellar Cognitive Affective Syndrome, namely executive, linguistic, visuospatial, and affective (neuropsychiatric) functions. Additionally, deficits in cued recall on an episodic memory item (reflecting dysfunction in memory storage) indicate cerebral involvement [7]. The CCAS-S provides a total raw score (0–120) and pass/fail cut-offs for each of the 10 domains (total fail score 0–10). SCA cohorts have demonstrated reduced performance on the CCAS-S relative to controls in cross-sectional studies [8–13]. Furthermore, a cross-sectional correlation between CCAS-S performance and time to/after onset among individuals with manifest and pre-manifest SCA3 suggested that performance may decline across the disease course [8]. Recently, the first longitudinal analysis of CCAS-S performance in SCAs was published, involving a large cohort of individuals with SCA1, SCA2, SCA3, SCA7, SCA27B and SPG7 completing the CCAS-S at up to 5 yearly timepoints (baseline and four follow-ups, with $n = 177$ at baseline) [14]. A significant *increase* in CCAS-S total raw score was reported between baseline and each of the first three follow-ups, compared with no significant longitudinal change in total score in a Control group. The majority of follow-ups were reported to use the same CCAS-S form (Version 1A) as at baseline. Alternative forms (Versions 1B, 1C, and 1D) were published by the original scale authors to avoid serial assessment practice effects, although their equivalence has not been validated [7].

The CCAS-S and its language translations have now been used widely in SCAs and other cerebellar disorders. However, the empirical literature has also revealed limitations in the scale's ability to reliably characterise cognitive and affective function in this population. Firstly, insufficient selectivity or high "false positive" rates for CCAS have been reported, including in a study validating the CCAS-S against a formal neuropsychological test battery [15]. High false positive rates may be due at least in part to demographic effects, with several studies reporting that performance is related to age and/or education level [9–11, 15–18]. Correction formulas have been developed to address such demographic effects in the German and Spanish translations of the scale [18, 19]. Moreover, Thieme et al. [19] recently reported a large inherent measurement error via analysis of intrarater test–retest reliability. It was reported that the minimal detectable change (95% confidence interval) in a mixed cerebellar degenerative disease/stroke cohort was 11.4 raw score points, representing the amount of change in the total raw score that would be required to assume real change in CCAS-S performance beyond measurement error. CCAS-S research outcomes should be interpreted in light of these findings.

Further investigation into the progression of CCAS-S performance, and its relationship to changes in day-to-day cognitive function in SCAs, will be important to better understand the natural history of SCAs and to support appropriate management, planning, and patient and family education. In this study, we aimed to (i) investigate yearly change in performance on the CCAS-S amongst individuals with symptomatic SCA, relative to control individuals, and (ii) evaluate the relationship between change in CCAS-S performance over time and change in self-reported functional measures assessed using the Patient-Reported Outcome Measure of Ataxia (PROM-Ataxia) [20].

Methods

Participants

The current analysis is drawn from the SCA-Remote longitudinal study (Monash University, data collection 2021–2024). Written informed consent was obtained from participants (Monash University Human Research Ethics Committee, Project #26568). Study procedures were performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

Symptomatic adults (aged ≥ 18 years) with a molecular diagnosis of SCA1, SCA2, SCA3, SCA6, as well as control participants without SCA, were recruited via internal participant databases, patient advocacy organisations, social media, and word-of-mouth. Inclusion criteria included fluent English speaking and reading, and access to a computer with a microphone and internet, but eligibility was not limited by geographic location. SCA group exclusion criteria included diagnosis of a comorbid neurological condition (including a history of an acquired brain injury), or diagnosis of a psychiatric condition (including problematic substance use). However, individuals with SCA whose psychiatric history included only depression and/or anxiety were included, given the increased prevalence of these features in SCAs

[21]. Control exclusion criteria included diagnosis of any neurological or psychiatric condition.

Procedures

Participants undertook yearly assessments via Zoom videoconferencing [22]. Participants completed online surveys to report their demographic information, and, for participants with SCA, their ataxia onset age and Functional Staging of Ataxia [23]. Assessments took place at Baseline, 1-year follow-up, and, for a subset of SCA participants, 2-year follow-up. Assessments that pertain to the current analyses are as follows:

Cerebellar Cognitive Affective Syndrome Scale (CCAS-S)

Researchers administered the CCAS-S via videoconference, with relevant aspects of the administration modified for the online medium as described in Supplementary Table S1. It is noted that this adaptation has not been validated at present, with the CCAS-S usually administered in a face-to-face setting. Alternate forms were used for the serial assessments to avoid practice effects due to the use of the same stimuli. Version A was administered at Baseline, Version B at 1-year follow-up, and Version C at 2-year follow-up. The CCAS-S contains 10 domains: semantic fluency, phonemic fluency, category switching, digit span forwards, digit span backwards, cube drawing/copying, verbal recall, similarities, go no-go, and affect. Each domain generates a raw score and a pass/fail designation based on a cut-off, producing a total raw score (0–120) and total number of failed domains (fail score; 0–10). Higher raw scores indicate better cognitive performance.

Patient Reported Outcome Measure of Ataxia (PROM-Ataxia)

Participants completed the 70-item PROM-Ataxia [20] via an online questionnaire. The PROM-Ataxia includes the following subscales: "Physical 1" and "Physical 2" (36 items), "Activities of Daily Living (ADLs)" (17 items), "Mental 1 (psychosocial)" (10 items), and "Mental 2 (cognitive)" (7 items). Each item is rated on a scale from 0 to 4, with higher scores reflecting more frequent symptoms or more difficulty completing tasks.

Data analyses

REDCap electronic data capture tools hosted at Monash University provided survey delivery and data management, including use of the REDCap Shared Library and eConsent Framework [24–27]. Data were exported to RStudio (2024.04.2) for analysis using R software (version 4.4.1). Statistical significance was evaluated at $p<0.05$.

We investigated 2-year change in CCAS-S performance in the combined SCA group. A one-way repeated-measures ANOVA was used to evaluate the effect of time on CCAS-S total raw score within the SCA group. The slope of raw scores across time was also calculated and their valence examined (i.e., positive vs. negative). Spearman correlations were used to correlate slopes against baseline demographic and clinical variables, baseline scores on the CCAS-S, PROM-Ataxia Physical and Mental 2 subscales, and slopes of the PROM-Ataxia Physical and Mental 2 subscales.

We also investigated changes in CCAS-S performance over one year in the SCA group relative to controls. One-year change scores for CCAS-S total raw score and total fail score were calculated and compared between the combined SCA group and the Control group using Mann–Whitney *U*-tests. Spearman correlations were then conducted between change scores and baseline CCAS-S scores, and, within the SCA group, between CCAS-S change scores for the PROM-Ataxia Physical and Mental 2 subscales. An exploratory analysis to evaluate differences between the different SCA diagnoses was then conducted.

Results

Participant information is presented in Table 1. This longitudinal cohort is a subset of the baseline SCA-Remote CCAS-S study cohort [34], which consisted of 74 individuals with SCA and 57 controls. There were no significant differences between the SCA cohort who completed baseline and did not return for follow-up, and the cohort who completed baseline and at least one year of follow-up, with regard to age, sex, years of education, distribution of SCA diagnoses, age at disease onset, disease duration, or Functional Staging of Ataxia score (Supplementary Table 2).

Two-year change in CCAS-S performance

Two-year CCAS-S total raw score data (SCA group, $n=25$) is shown in Fig. 1a (see Supplementary Table S3 for descriptive statistics of two-year outcome measures). The assumptions of no extreme outliers, normality, and sphericity were met to conduct a one-way repeated-measures ANOVA for the effect of time on total raw score. Timepoint had a significant, small effect on total raw score, $F(2, 48)=7.417$, $p=0.002$, $\eta^2_G=0.033$. Post-hoc analyses with Bonferroni adjustment indicated a significant decrease in total raw score between Baseline and 2-year follow-up (mean: -6.36 points total [-3.18/year], 7.0%, Standardised Response Mean (SRM) = -0.754, $p_{adj}=0.003$, $p_{unadj}<0.001$). Consistent effect sizes were

Table 1 Participant demographic and clinical information

	SCA	CON	Test
CCAS-S—n completed			
1-year follow-up (1.03 ± 0.05 years)	45	26	–
2-year follow-up (1.97 ± 0.04 years)	25	–	–
Baseline demographic information for 1-year follow-up cohort			
Age	55.4 ± 13.8	57.7 ± 11.4	$U = 633.5$, $p = 0.57$
Sex	26 F; 19 M	19 F; 7 M	$\chi^2 = 1.07$, $p = 0.3$
Years of education	16.5 ± 3.8	17.5 ± 3.3	$U = 676.5$, $p = 0.27$
Baseline clinical information for 1-year follow-up cohort			
SCA1 *n*(%)	6 (13.3%)	–	–
SCA2 *n*(%)	10 (22.2%)	–	–
SCA3 *n*(%)	10 (22.2%)	–	–
SCA6 *n*(%)	19 (42.2%)	–	–
Age at disease onset (years)	44.61 ± 13.07	–	–
Disease duration (current age—age at disease onset; years)	10.5 ± 7.91	–	–
Functional Staging of Ataxia	2.8 ± 1.16	–	–

evident, but did not reach statistical significance, over the 1-year intervals between Baseline and 1-year follow-up (mean: −3.24 points, 3.6%, SRM = −0.401, $p_{adj} = 0.170$, $p_{unadj} = 0.056$) or between 1-year and 2-year follow-up (mean: −3.12 points, 3.6%, SRM = −0.378, $p_{adj} = 0.213$, $p_{unadj} = 0.071$).

There was no effect of timepoint on CCAS-S total fail score, as ascertained by a Friedman test due to normality violation; $\chi^2(2) = 3.844$, $p = 0.146$, $W = 0.077$ (small effect), see Supplementary Figure S1 and Table S3.

Individual slope values for CCAS-S total raw score (reflecting the magnitude of change over time) were significantly correlated with baseline CCAS-S total raw score and PROM-Ataxia Mental 2 score (Fig. 1b), where better baseline outcomes (higher CCAS-S scores and lower PROM-Ataxia scores) were associated with greater decline over time. Trending correlations ($p < 0.1$) were observed for baseline Functional Staging of Ataxia and age, where greater age and less severe ataxia were associated with greater decline over time (Fig. 1b). The relationship of baseline CCAS-S total raw score and rate of CCAS-S total raw score decline was further visualised by dividing the group into quartiles based on baseline score, plotting the mean values for each timepoint within each quartile group and fitting a linear regression line (Fig. 2a). Similarly, the Functional Staging effect was explored by dividing the cohort into Mild (stage 0–1), Moderate (stage 2–3), and Severe (stage 4–5) disease severity groups [28] (Fig. 2b).

No significant correlation was observed between CCAS-S slope and years of education, baseline PROM-Ataxia Physical Function, ataxia onset age, or disease duration. Furthermore, CCAS-S raw slope was not correlated with the slope of the PROM-Ataxia Physical Function or Mental 2 scales. See Supplementary Figure S2 for plots of non-significant correlations.

One-year change in CCAS-S performance relative to controls

As illustrated in Fig. 3 (see Supplementary Table S4 for descriptive statistics), in the larger cohort of individuals who completed the 1-year follow-up, the mean change in CCAS-S raw score over time in the combined SCA cohort ($n = 45$) was equivalent to the 2-year cohort (−3.089 points/year, 3.4%, SRM = −0.370). The control group ($n = 26$) showed only a marginal mean change (−0.770 points, 0.7%, SRM = −0.091). However, substantial individual variability was observed in both groups (Fig. 3a), and there was no significant group difference in CCAS-S total raw score change from Baseline to 1-year follow-up ($U = 680$, $p = 0.259$, point-biserial $r = 0.16$). There was also no significant group difference for the change in total fail score ($U = 429.5$, $p = 0.057$, point-biserial $r = -0.27$; Supplementary Figure S3).

Correlation results for change in CCAS-S total raw score and total fail score are presented in Fig. 3b and Supplementary Figure S3b, respectively. One-year change in CCAS-S total raw score was moderately correlated with baseline raw score in the control group, $r_s = -0.435$, $p = 0.026$, with better baseline performance (higher raw score) associated with greater decline. This association was not significant in the SCA group ($r_s = -0.233$, $p = 0.123$). In both groups, 1-year change in total fail score was significantly associated with baseline fail score (SCA: $r_s = -0.381$, $p = 0.01$; Control: $r_s = -0.675$, $p < 0.001$), indicating that better baseline performance (lower fail scores) was associated with greater decline (Supplementary Figure S3b).

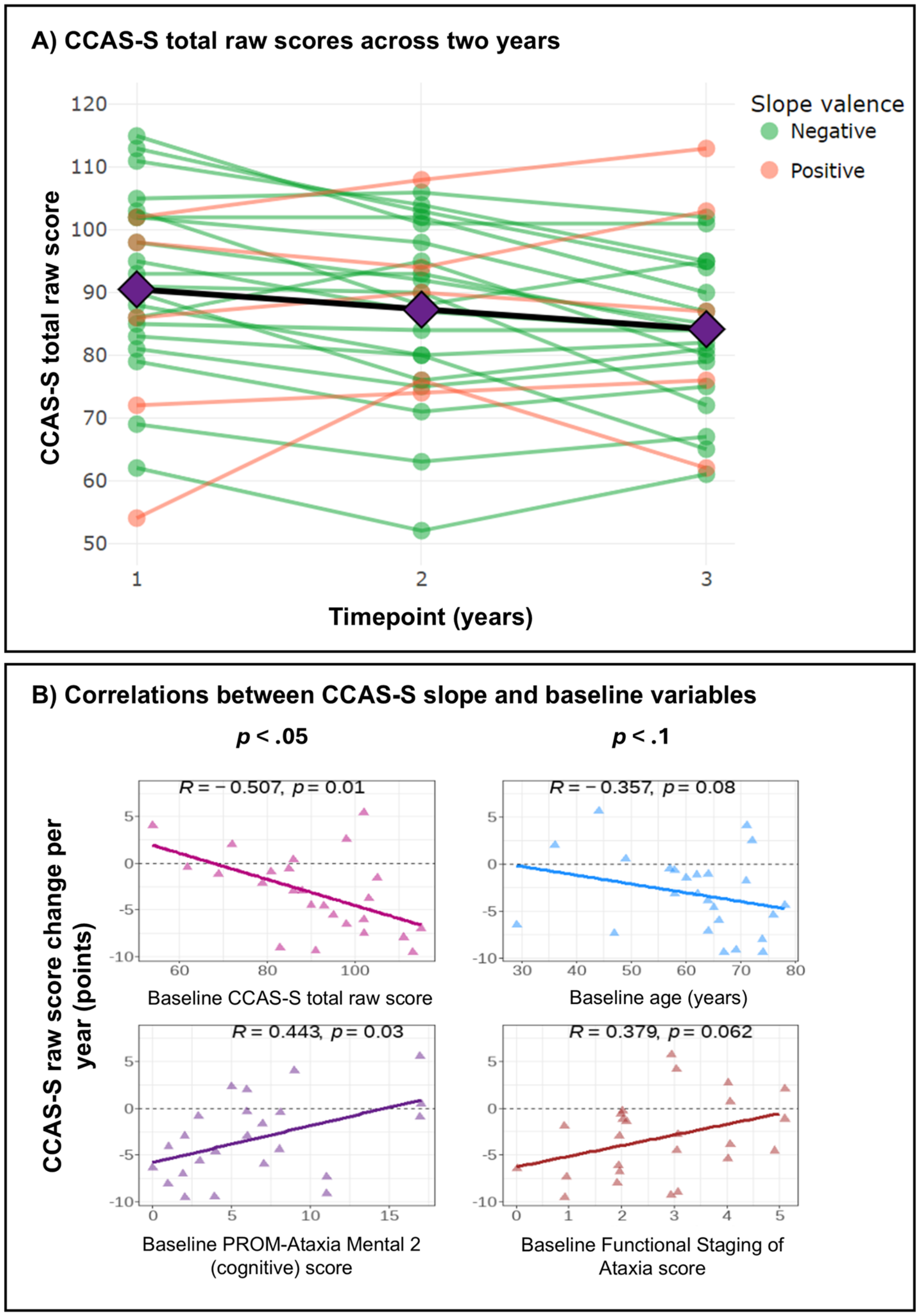

Fig. 1 2-year CCAS-S total raw scores (SCA group). **a** Scores at each of the three study timepoints, coloured by slope valence**.** The group average score at each timepoint is shown by purple diamonds. **b** Correlation plots between change scores and baseline demographic, clinical, and cognitive self-report outcomes, with significant correlations at $p<.05$ in the left column and trending correlations at $p<.1$ in the right. $R=$ Spearman's rho

Amongst participants with SCA, improvements in total raw score were significantly and moderately associated with improvements in self-reported cognition as measured by the PROM-Ataxia Mental 2 ($r_s=0.478$, $p=0.001$). The same effect was not observed for change in total fail score ($r_s=-0.194$, $p=0.208$). Neither raw score nor fail score change was associated with change in the PROM-Ataxia Physical combined score.

Exploratory analysis of individual SCA diagnostic groups

When separated by SCA diagnosis, only modestly sized cohorts were available for each disease (SCA1: $n=6$, SCA2: $n=10$, SCA3: $n=10$, SCA6: $n=19$). However, distinct trends were observed in one-year CCAS-S total raw score change (Fig. 4, Supplementary Table S5), with individuals

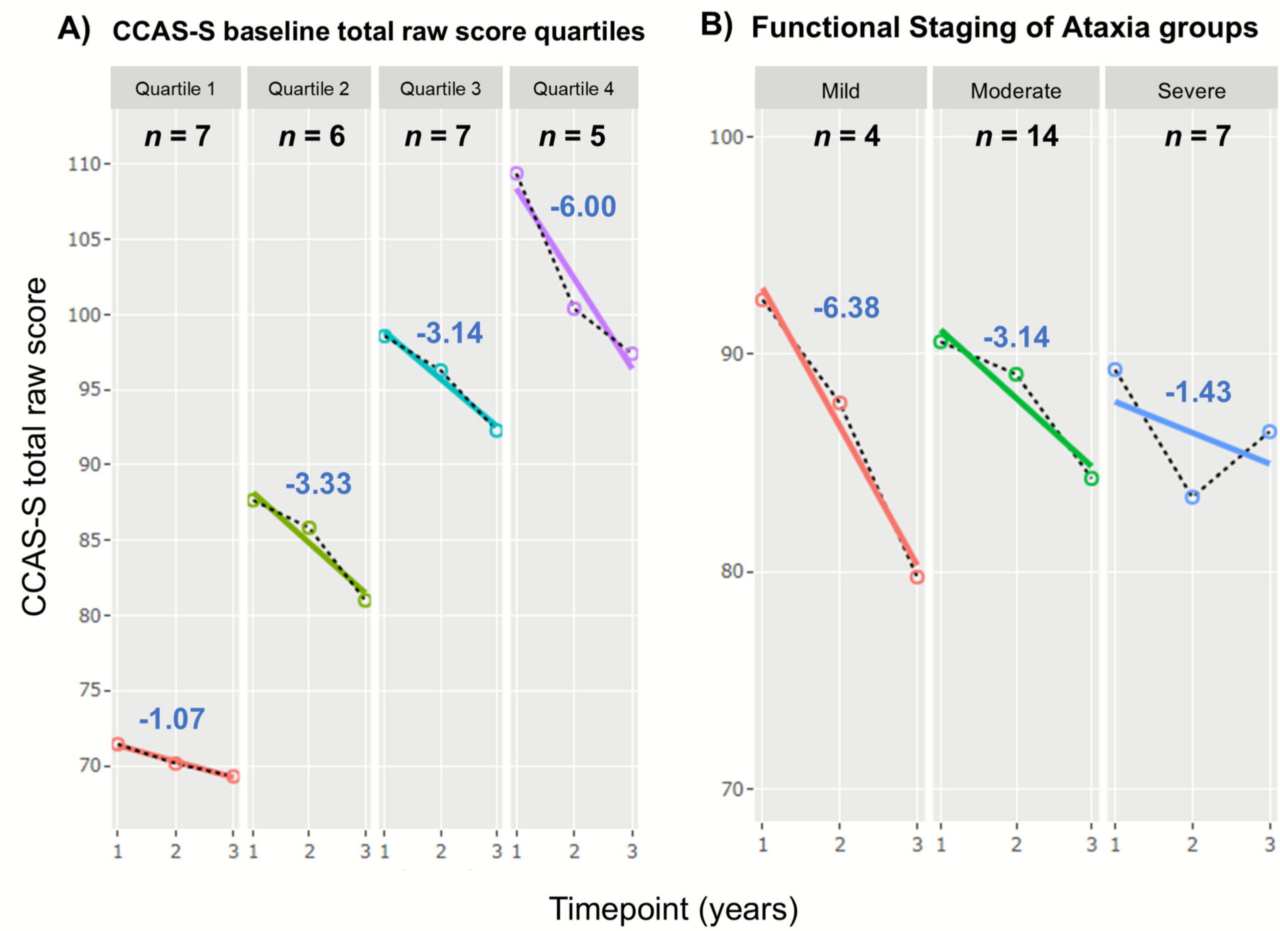

Fig. 2 Cohort subgroup effects for the relationship between two-year CCAS-S total raw score slope and **a** baseline CCAS-S total raw score and **b** baseline Functional Staging of Ataxia score. The mean CCAS-S total raw score at each of the three study timepoints (circles, connected by dashed lines), and the associated linear regression line (solid lines), is shown in separate panels for each discrete subgroup. CCAS-S baseline total raw score subgroups are based on score quartiles. Functional Staging of Ataxia subgroups are based on staging scores as follows—Mild: 0–1; Moderate: 2–3; Severe: 4–5. Subgroup size is indicated in black text (*n* =). Mean slope (change in CCAS-S total raw score, as points per year) within each subgroup is shown in blue text

with SCA2 having the greatest mean longitudinal change over 1 year (− 7.1 points, SRM = − 1.174), more moderate change in SCA3 (− 2.7 points, SRM = − 0.306) and SCA6 (− 2.3 points, − 0.277), and no change evident on average in SCA1 (0.5 points, SRM = 0.049). This was investigated via a series of planned exploratory ANCOVA post-hoc comparisons between each diagnostic group and the control group, with correction for baseline age. One SCA6 datapoint was excluded (total raw change + 22) because it was identified as being an outlier with a standardised residual > 3. It was revealed that the SCA2 group had a significantly greater decline in total raw score compared to the Control group before adjusting for multiple comparisons ($p_{unadj} = 0.029$). This effect did not remain significant after adjustment for multiple comparisons. No other unadjusted subgroup comparisons reached significance (Supplementary Table S6).

Discussion

We present a longitudinal analysis of Cerebellar Cognitive Affective Syndrome Scale (CCAS-S) outcomes amongst individuals with SCAs, using alternative forms of the scale for serial follow-up. Our results demonstrate a significant average decrease in CCAS-S raw score over two years. Furthermore, the one-year change in CCAS-S performance was related to the one-year change in self-reported functional cognition. The decline in cognitive performance appears to be maximal in early disease stages and in those with higher cognitive ability at baseline. Preliminary evidence suggests that cognitive decline may be greatest in people with SCA2.

Our finding of reduced performance over time is consistent with previous literature showing reduction over time in various cognitive assessments [2–6], and with

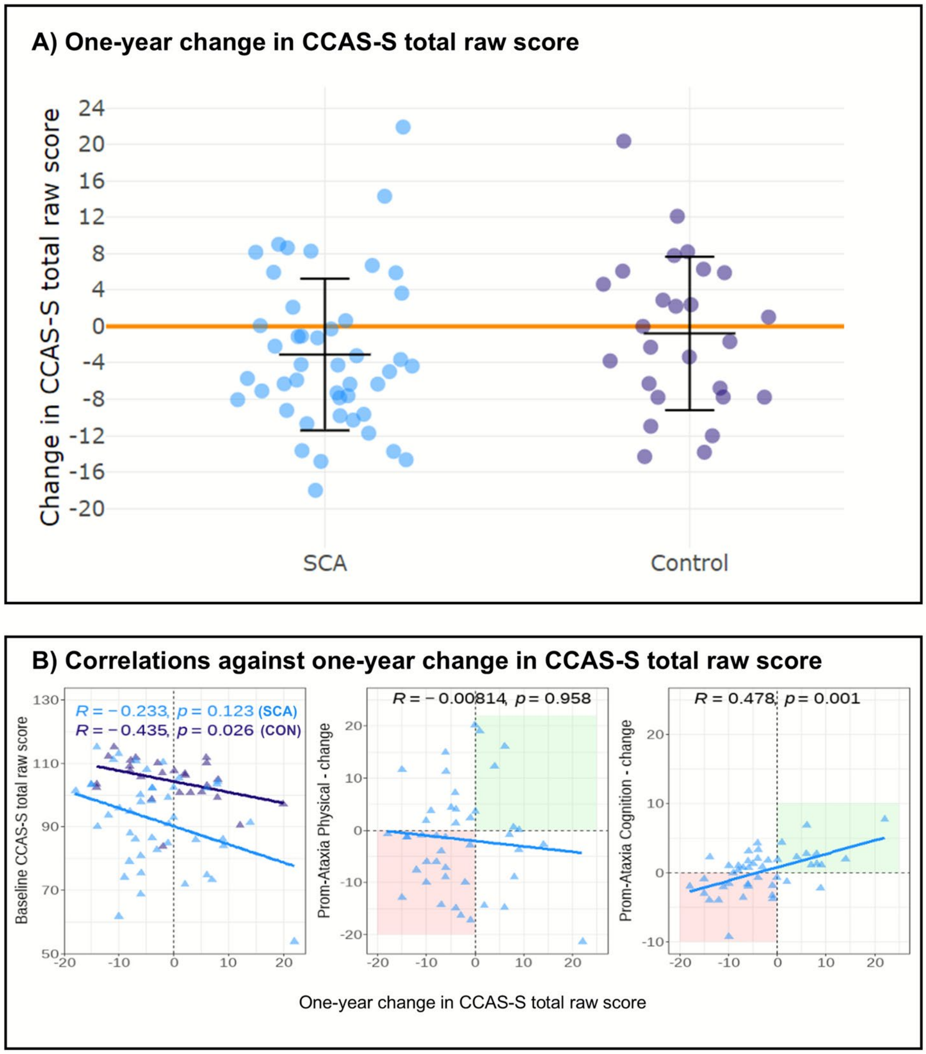

Fig. 3 **a** CCAS-S total raw change scores by participant group, **b** correlations between CCAS-S total raw change scores and CCAS-S baseline raw score (both groups) and PROM-Ataxia change scores (SCA group only). Valence of PROM-Ataxia scores has been reversed in the correlation plots so that higher (positive) values in both PROM-Ataxia and CCAS-S represent improvement over time. Green shaded area = improvement over time in both PROM-Ataxia and CCAS-S; red shaded area = decline over time in both PROM-Ataxia and CCAS-S. *R* = Spearman's rho

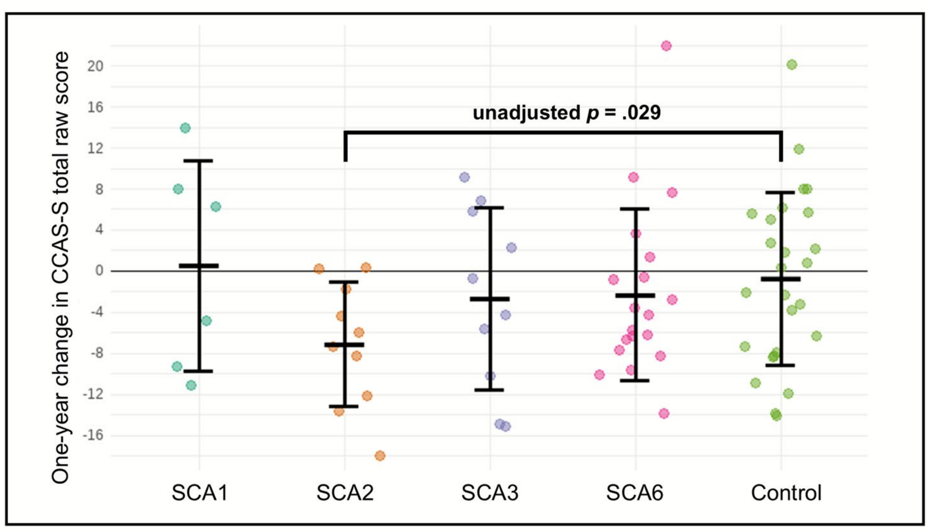

Fig. 4 One-year change in CCAS-S total raw score, by SCA diagnosis group. The significant difference between the SCA2 and control groups, before adjusting for multiple comparisons, is indicated with a square bracket. No other significant (corrected or uncorrected) group differences were observed

cross-sectional evidence of reduction of performance with disease progression [8]. However, our findings contrast with those of Petit et al. [14] who reported increases in CCAS-S total raw score over three years in a large SCA cohort but not in a smaller Control cohort. That study used alternate CCAS-S forms for some but not other serial assessments, although the authors reported equivalence in CCAS-S total raw scores between Versions A and B. The reason for the discrepancy in findings is not readily apparent and may be related to the characteristics of the current cohort; nevertheless, these results together motivate ongoing investigation of cognitive trajectory in SCAs, with further efforts to disambiguate potential test practice effects from change in cognition.

Inter-individual variability was noted in CCAS-S progression, and one-year change in the combined SCA did not significantly differ from change in a control group. This is compatible with the current CCAS-S literature which indicates that only a subset of individuals with SCA shows deficits relative to unaffected individuals. Furthermore, our exploratory analysis suggested important subtype effects, with the SCA2 group, but not other SCA types, showing more decline than Controls. Our SCA2 cohort did have a longer average disease duration than the other SCA diagnoses; however, the absence of a correlation between disease duration and CCAS-S total raw score change indicates that this cohort characteristic is not driving the effect. Some published reports have indicated poorer neuropsychological test outcomes in SCA2 compared to SCA1 [4, 29], although this has not been consistently reported [30], and other studies comparing cognitive outcomes amongst SCA diagnoses have been limited by small cohort sizes (e.g., fewer than 4 individuals with SCA2 included in some studies) [2, 31–33]. Replication of this finding is needed in larger longitudinal studies before making conclusions about differences in longitudinal trajectories between different SCA diagnoses, especially as our SCA2 result did not survive correction for multiple comparisons and our SCA cohort sizes were small.

We report a group-level average decline of 3.18 CCAS-S raw score points per year in our SCA cohort, with variability in cognitive trajectory between individuals. This finding should be interpreted in the context of measurement error, in particular the minimal detectable change of 11.4 points reported by Thieme et al. [19]. Using this criterion, our results indicate that meaningful change in cognition beyond measurement error would occur after 3 to 4 years. This could be a reasonable expectation of cognitive change in these relatively slow-progressing disorders; however, given the limited and inconsistent longitudinal cognitive findings in SCAs thus far, it is not yet possible to quantify how much annual change should be expected.

With regards to the impact of individual differences on CCAS-S change, more decline in performance was observed amongst people with *better* baseline function on multiple measures including subjectively- and objectively-measured cognition and self-reported ataxia severity. There may be multiple explanations for this finding. First, this pattern may reflect a disease-staging effect where the rate of decline in cognition changes across the disease course. Indeed, our work mirrors the findings of a recent study of the PROM-Ataxia in a large spinocerebellar ataxia cohort, which showed that worsening function as indexed by the Mental subscales (psychosocial and cognitive) was more rapid amongst individuals with Functional Staging of Ataxia scores of 0–1 compared to those with higher staging scores [28]**.** Together, this suggests that the greatest change in cognitive function may occur in early disease stages, as characterised by milder severity in the motor ataxia symptoms (rather than shorter disease duration). It is also possible that individuals with higher baseline function have relatively more function to lose, or that self-reported function at the baseline assessment was reduced due to contextual factors, which then improved over the course of the study. Given the important clinical implications of disease staging differences in cognitive change, this finding strongly motivates replication and further investigation of disease staging effects.

Change in CCAS-S performance was significantly related to change in self-reported day-to-day cognitive functioning as measured by the PROM-Ataxia. The cognitive subsection of the PROM-Ataxia assesses word-finding, recall, multitasking, new learning, decision-making, comprehension, and navigation. This builds upon the cross-sectional association between CCAS-S performance and self-reported cognition which we reported in the SCA-Remote baseline cohort [34], and further supports the ecological validity of the scale. Of note, in our cross-sectional work, CCAS-S performance was also correlated with multiple measures of ataxia motor severity including the PROM-Ataxia Physical scale, while in the current analyses, we did not find evidence for a relationship between CCAS-S change and PROM-Ataxia Physical change. Taken together, this finding suggests that although cognitive and physical (motor) changes are both progressive features of SCAs, they likely occur on a different time course.

Limitations in the current study design are acknowledged. We lacked a control group for the two-year analysis of CCAS-S progression, and therefore cannot compare our results to normative data. We also had a limited cohort size with which to explore longitudinal effects within individual SCA diagnoses. However, the present results demonstrate that the CCAS-S can index meaningful cognitive change in SCAs, motivating larger longitudinal studies. Annual follow-ups over a longer period are also recommended, to obtain clearer information about trajectories of cognitive change. For example, some participants' scores did not change in a consistent direction over two years, and some even showed an improvement over time. Further follow-up will help to indicate whether there is an overall pattern of reduced performance versus shorter-term fluctuations. It is also apparent that the CCAS-S may be sensitive to normative age-related decline in some individuals, with controls in our cohort having a near-zero mean decline, but some individuals changing by up to 14 points. Significant relationships between age and CCAS-S performance have been described amongst SCA, control, and combined SCA and control groups [9, 11, 15, 16], although this effect has not been observed in all cohorts [9, 14] Validation of CCAS-S change with change on formal neuropsychological testing would be relevant here as will the publication of age-specific norms and inclusion of tightly age-matched control groups in cohort studies.

We used the alternate forms of the CCAS-S, which have not been validated for equivalence in test difficulty. Our findings that one-year change in CCAS-S total raw score was moderately correlated with change in self-reported cognition, and that Controls did not show the same level of decline as individuals with SCA (albeit a non-significant group difference in cognitive change), suggests that the group-level decrease in performance over time was at least partially related to true change in cognition, and not solely explained by potential differences in test difficulty. However, there remains a possibility that non-equivalence of forms may have influenced the present longitudinal results. Establishing the equivalence of the alternate forms of the CCAS-S will be important for increased confidence in the interpretation of serial assessment outcomes.

We also acknowledge that online administration of the CCAS-S may not be equivalent to in-person administration [8]; therefore our results may not be comparable to other longitudinal CCAS-S findings. Furthermore, individuals who had elected to participate in this online research study, outside of their usual clinic visits, may not be fully representative of the wider population of individuals with SCAs, which could impact the generalisability of the results—in particular, it is possible that our cohort has not included individuals with more severe cognitive difficulties that make it more challenging to participate.

Furthermore, within our remote study design we did not conduct a standard clinician-rated assessment of motor ataxia symptoms such as the Scale for the Assessment and Rating of Ataxia (SARA). We instead characterised motor symptoms via self-report on the PROM-Ataxia (Physical domain) and Functional Staging of Ataxia scales. One-year change in PROM-Ataxia Physical score has been shown to correlate only weakly with change in SARA score [28], and so it is difficult to predict how CCAS-S change may relate to SARA change, based on the present results. Further investigation into the relationship between SARA change and CCAS-S change may be useful given the SARA's role as a key clinical outcome measure in SCAs.

Additionally, future research should investigate the neuroimaging correlates of CCAS-S performance and progression to better understand the mechanisms underlying cognitive change. Correlations between MRI outcomes and CCAS-S performance in SCAs have been reported at a cross-sectional level [14, 35]. Finally, cognitive change in ataxias may be impacted by pharmacological or neuropsychological interventions; however, we did not collect data on whether these factors were present in our cohort. It is possible that such interventions impacted the current findings, potentially by attenuating cognitive decline.

To conclude, we present further evidence of reduced cognitive performance over time in SCAs as indexed by the CCAS-S. The association of CCAS-S change with change in self-reported cognition suggests that change in CCAS-S performance is meaningful, supporting further use of this scale for serial assessment of cognition. This finding also highlights the importance of further focus on the cognitive profile and trajectory of SCAs. This is important given the potential of day-to-day cognitive challenges to impact individuals' level of functioning in their occupational, interpersonal, and other life roles, and thereby impact overall quality of life in addition to the progressive motor impairments. Important avenues for future research in larger, longer-term studies include further characterising the longitudinal progression of cognitive change across the disease course (including prior to the onset of motor symptoms), and elucidating which individuals with SCAs are most at risk of decline in cognition.

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Author contributions LPS: study conceptualization and design, data analyses, draft manuscript preparation. LPS takes responsibility for the integrity of the data and the accuracy of the data analysis. CL: data collection, manuscript preparation. SW: data collection and curation, manuscript review. JM: data collection and curation, manuscript review. KRK: participant recruitment, manuscript review. DJS: study conceptualization and design, participant recruitment, manuscript review. IHH: study conceptualization and design, data analyses, manuscript review.

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Data availability statement The authors confirm that the anonymised data supporting the findings of this study are available upon reasonable request from the corresponding author.

Declarations

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest. The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval The study was approved by the Monash University Human Research Ethics Committee (Project #26568). Study procedures were performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

References

1. Selvadurai LP, Schmahmann JD, Harding IH (2024) Cognitive functioning in spinocerebellar ataxias: an update and future directions. Curr Opin Behav Sci. https://doi.org/10.1016/j.cobeha.2023.101343
2. Moriarty A, Cook A, Hunt H et al (2016) A longitudinal investigation into cognition and disease progression in spinocerebellar ataxia types 1, 2, 3, 6, and 7. Orphanet J Rare Dis 11:82. https://doi.org/10.1186/s13023-016-0447-6
3. Roeske S, Filla I, Heim S et al (2013) Progressive cognitive dysfunction in spinocerebellar ataxia type 3: progressive cognitive dysfunction in SCA3. Mov Disord 28:1435–1438. https://doi.org/10.1002/mds.25512
4. Fancellu R, Paridi D, Tomasello C et al (2013) Longitudinal study of cognitive and psychiatric functions in spinocerebellar ataxia types 1 and 2. J Neurol 260:3134–3143. https://doi.org/10.1007/s00415-013-7138-1
5. Le Pira F, Giuffrida S, Maci T et al (2007) Dissociation between motor and cognitive impairments in SCA2: evidence from a follow-up study. J Neurol 254:1455–1456. https://doi.org/10.1007/s00415-007-0548-1
6. Nigri A, Sarro L, Mongelli A et al (2020) Progression of cerebellar atrophy in spinocerebellar ataxia type 2 gene carriers: a longitudinal MRI study in preclinical and early disease stages. Front Neurol 11:616419. https://doi.org/10.3389/fneur.2020.616419
7. Hoche F, Guell X, Vangel MG et al (2018) The cerebellar cognitive affective/Schmahmann syndrome scale. Brain 141:248–270. https://doi.org/10.1093/brain/awx317
8. Bolzan G, Müller Eyng ME, Leotti VB et al (2023) Cognitive-affective manifestations since premanifest phases of spinocerebellar ataxia type 3/machado-joseph disease. Cortex. https://doi.org/10.1016/j.cortex.2023.09.021
9. Selvadurai LP, Perlman SL, Ashizawa T et al (2024) The cerebellar cognitive affective/schmahmann syndrome scale in spinocerebellar ataxias. Cerebellum 23:1411–1425. https://doi.org/10.1007/s12311-023-01651-0
10. Rodríguez-Labrada R, Batista-Izquierdo A, González-Melix Z et al (2022) Cognitive decline is closely associated with ataxia severity in spinocerebellar ataxia type 2: a validation study of the Schmahmann Syndrome Scale. Cerebellum. https://doi.org/10.1007/s12311-021-01305-z
11. Maas RPPWM, Killaars S, van de Warrenburg BPC, Schutter DJLG (2021) The cerebellar cognitive affective syndrome scale reveals early neuropsychological deficits in SCA3 patients. J Neurol 268:3456–3466. https://doi.org/10.1007/s00415-021-10516-7
12. Tezenas Du Montcel S, Petit E, Olubajo T et al (2023) Baseline clinical and blood biomarkers in patients with preataxic and early-stage disease spinocerebellar ataxia 1 and 3. Neurology 100:e1836–e1848. https://doi.org/10.1212/WNL.0000000000207088
13. Thieme A, Faber J, Sulzer P et al (2022) The CCAS-scale in hereditary ataxias: helpful on the group level, particularly in SCA3, but limited in individual patients. J Neurol. https://doi.org/10.1007/s00415-022-11071-5
14. Petit E, López Domínguez D, Marelli C et al (2025) Prevalence, severity, and progression of cerebellar cognitive-affective syndrome in patients with spinocerebellar ataxias. Neurology 105:e213980. https://doi.org/10.1212/WNL.0000000000213980
15. Reumers SFI, Maas RPPWM, Van Den Brandt VJM et al (2025) Validation of the cerebellar cognitive affective syndrome (CCAS) scale in CCAS patients and cerebellar controls. J Int Neuropsychol Soc. https://doi.org/10.1017/s1355617725101033
16. Thieme A, Röske S, Faber J et al (2021) Reference values for the cerebellar cognitive affective syndrome scale: age and education matter. Brain 144:e20–e20. https://doi.org/10.1093/brain/awaa417
17. Liu Q, Rubarth K, Faber J et al (2025) Subtypes of cognitive impairment in cerebellar disease identified by cross-diagnostic cluster-analysis: results from a German multicenter study. J Neurol 272:83. https://doi.org/10.1007/s00415-024-12831-1
18. Serrano-Munuera C, Martínez-Regueiro R, Martínez Fernández EM et al (2025) Validation of the Spanish version of the cerebellar cognitive-affective syndrome scale. Clin Neuropsychol. https://doi.org/10.1080/13854046.2025.2488453
19. Thieme A, Rubarth K, Van Der Veen R et al (2025) Optimizing selectivity of the cerebellar cognitive affective syndrome scale by use of correction formulas, and validation of its German version. J Neurol. https://doi.org/10.1007/s00415-025-13083-3
20. Schmahmann JD, Pierce S, MacMore J, L'Italien GJ (2021) Development and validation of a patient-reported outcome measure of ataxia. Mov Disord. https://doi.org/10.1002/mds.28670
21. Karamazovova S, Matuskova V, Ismail Z, Vyhnalek M (2023) Neuropsychiatric symptoms in spinocerebellar ataxias and Friedreich ataxia. Neurosci Biobehav Rev 150:105205. https://doi.org/10.1016/j.neubiorev.2023.105205
22. Zoom Communications, Inc. (2021) Zoom
23. Subramony SH, May W, Lynch D et al (2005) Measuring Friedreich ataxia: interrater reliability of a neurologic rating scale. Neurology 64:1261–1262. https://doi.org/10.1212/01.WNL.0000156802.15466.79
24. Harris PA, Taylor R, Minor BL et al (2019) The REDCap consortium: building an international community of software platform partners. J Biomed Inform 95:103208. https://doi.org/10.1016/j.jbi.2019.103208
25. Harris PA, Taylor R, Thielke R et al (2009) Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 42:377–381. https://doi.org/10.1016/j.jbi.2008.08.010

26. Obeid JS, McGraw CA, Minor BL et al (2013) Procurement of shared data instruments for research electronic data capture (REDCap). J Biomed Inform 46:259–265. https://doi.org/10.1016/j.jbi.2012.10.006
27. Lawrence CE, Dunkel L, McEver M et al (2020) A REDCap-based model for electronic consent (eConsent): moving toward a more personalized consent. J Clin Transl Sci 4:345–353. https://doi.org/10.1017/cts.2020.30
28. Burt AL, L'Italien G, Perlman SL et al (2025) Spinocerebellar ataxia progression measured with the patient-reported outcome measure of ataxia. Mov Disord. https://doi.org/10.1002/mds.30158
29. Colucci F, Stefanelli S, Contaldi E et al (2024) Cognition in patients with spinocerebellar ataxia 1 (SCA1) and 2 (SCA2): a neurophysiological and neuropsychological approach. J Clin Med 13:4880. https://doi.org/10.3390/jcm13164880
30. Bürk K, Globas C, Bösch S et al (2003) Cognitive deficits in spinocerebellar ataxia type 1, 2, and 3. J Neurol 250:207–211. https://doi.org/10.1007/s00415-003-0976-5
31. Klinke I, Minnerop M, Schmitz-Hübsch T et al (2010) Neuropsychological features of patients with spinocerebellar ataxia (SCA) types 1, 2, 3, and 6. Cerebellum 9:433–442. https://doi.org/10.1007/s12311-010-0183-8
32. Sokolovsky N, Cook A, Hunt H et al (2010) A preliminary characterisation of cognition and social cognition in spinocerebellar ataxia types 2, 1, and 7. Behav Neurol 23:17–29. https://doi.org/10.1155/2010/395045
33. Ma J, Wu C, Lei J, Zhang X (2014) Cognitive impairments in patients with spinocerebellar ataxia types 1, 2 and 3 are positively correlated to the clinical severity of ataxia symptoms. Int J Clin Exp Med 7:5765–5771
34. Selvadurai LP, Gullia S, Morgan J et al (2025) Psychomotor and non-motor correlates of cognition in spinocerebellar ataxias types 1, 2, 3, and 6. Brain Commun. https://doi.org/10.1093/braincomms/fcaf425
35. Chandrasekaran J, Petit E, Park YW et al (2023) Clinically meaningful magnetic resonance endpoints sensitive to preataxic spinocerebellar ataxia types 1 and 3. Ann Neurol 93:686–701. https://doi.org/10.1002/ana.26573