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ORIGINAL ARTICLE

Quality of Life Changes Following the Onset of Cerebellar Ataxia: Symptoms and Concerns Self-reported by Ataxia Patients and Informants

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Abstract

Semi-structured interviews of patient accounts and caregiver, or informant, perspectives are a beneficial resource for patients suffering from diseases with complex symptomatology, such as cerebellar ataxia. The aim of this study was to identify, quantify, and compare the ways in which cerebellar ataxia patients' and informants' quality of life had changed as a result of living with ataxia. Using a semi-structured interview, responses were collected from patients and informants regarding motor, cognitive, and psychosocial variables. Responses were also collected from patients and informants to open-ended questions that were subsequently categorized into 15 quality of life themes that best represented changes experienced by the patients and informants. Ataxia patients and informants agreed as to the severity of posture/gait, daily activities/fine motor tasks, speech/feeding/swallowing, and oculomotor/vision impairment. It was also demonstrated that severity ratings for specific motor-related functions strongly correlated with corresponding functions within the International Cooperative Ataxia Rating Scale (ICARS), and that this interview identified frequency associations between motor impairments and specific psychosocial difficulties, which could be useful for prognostic purposes. Overall, the information obtained from this study characterized the symptoms and challenges to ataxia patients and their caregivers, which could serve as a useful educational resource for those affected by ataxia, clinicians, and researchers.

Keywords Cerebellar ataxia · Caregivers · Quality of life · Cerebellum · Cognition · Patient-reported outcome measures

Introduction

Progressive cerebellar degeneration is a rare disease, often with a hereditary component that leads to cerebellar ataxia. Presentation of symptoms can vary, depending on the etiology, along with other intrinsic factors, such as the age-of-onset and trinucleotide repeat length [1, 2]. Ataxia patients report a combination of several symptoms that effect movement and fine motor tasks such as difficulty with walking or balance, fine motor movements (precision and accuracy), gait (wide-based or shuffled), speech (slurred), eye movements (nystagmus), tremors (limbs, trunk, voice), and daily activity and fine motor tasks, such as eating or swallowing liquids [3, 4]. In addition to the physical manifestation of the disease, ataxia patients may also experience cognitive and neuropsychiatric symptoms [5–12]. Cerebellar degeneration may disrupt not only the processes within the cerebellum, but also the interconnectedness of the cerebellum with the cerebral cortex (e.g., motor regions and dorsolateral prefrontal cortex) and subcortical structures, such as the basal ganglia [13–16]. Thus, degeneration of the cerebellum may alter critical pathways resulting in motor and non-motor changes [17, 18].

A new diagnosis of cerebellar ataxia may elicit surprise, dread, fear, and anxiety for a patient and their family. The best way to help prepare the patient and family for living with ataxia is through education, such as by providing a characterization of the motor and non-motor aspects of the disorder. While much is known about the motor components

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of ataxia, much less is known about the cognitive and emotional symptoms or the impact these have on patients' and family's daily lives.

A useful way to characterize the impact of ataxia on those directly affected by it is through careful and thorough interviews with patients and family members. The cerebellar cognitive affective/Schmahmann syndrome (CCAS) scale is a clinical assessment designed to be administered specifically to ataxia patients [19, 20]. The CCAS scale probes the patient's capability on an array of cognitive functions. The CCAS has been helpful in providing a test of mental function in those with cerebellar injury as tests developed for use in patients with dementias have been shown to be insensitive to cognitive deficits associated with cerebellar dysfunction [19]. In validation and reliability tests of the CCAS scale, correlations with motor functions were minimal, suggesting that motor and cognitive impairments followed dissociable trajectories. However, it is unknown how well the CCAS scale captures trait changes over time versus short-term state fluctuations. Furthermore, this type of assessment does not directly generalize to activities of daily living or quality of life, leaving out important information about how a patient's real-world function may be affected by cerebellar degeneration. There are only a handful of patient-reported outcome measures currently being used in ataxia research [21–24], and only one has been designed specifically for use with cerebellar ataxia patients [25]. Moreover, to our knowledge, there are no semi-structured interviews that collect data from both ataxia patients and informants. The importance of including caregiver and patients' perspectives was demonstrated from a report released by the National Ataxia Foundation (NAF) on the experiences of caregivers and patients diagnosed with SCA types 1, 2, 3, 6, 7, 8, 17 or Dentatorubral–Pallidoluysian Atrophy (DRPLA) [26]. The outcome of the report led to three key elements based on responses from patients and caregivers: 1) disease manifestations vary across patients, 2) current treatments are not effective for eliminating symptoms, and 3) disease progression directly impacts interpersonal relationships that can lead to social isolation, emotional stress, or physical burden placed on the patient, family, and caregivers. These findings illustrate the need for including both caregiver and patient perspectives in ataxia to improve patient care and treatment outcomes in clinical trials.

The first and only cerebellar ataxia scale available to capture changes in cognitive function or changes that matter most to individuals with ataxia in terms of their quality of life to date (released in 2021) [25] is the Patient-Reported Outcome Measure of Ataxia (PROM-Ataxia), which includes three domains encompassing physical, daily activities, and mental health. The PROM-Ataxia is test-retest reliable and validated against external measures [27, 28]. The PROM-Ataxia is divided into a 2-part physical section (frequency versus severity), a 2-part mental section (neuropsychiatric versus cognitive), and a section on activities of daily living. Importantly, the PROM-Ataxia was developed according to the patients' experience and reporting of symptom relevance within the past two weeks, thereby relying fully on the patient's perspective. Validation tests of the PROM-Ataxia indicated that the physical sections correlated strongly with external measures of motor deficits, and the neuropsychiatric section correlated moderately with measures of anxiety and depression. The cognitive section was not validated against standard cognitive measures, but it correlated moderately with external measures of motor deficits.

We began a similar line of questioning in 2013, before the PROM-Ataxia was released, by creating our own interview directed toward those with cerebellar ataxia. We were interested in identifying and characterizing the difficulties faced by people with cerebellar ataxia from their own perspective. We reasoned that this sort of information could be useful in the clinic in terms of care (including prognostics) and patient education. We focused our questioning along several domains, including motor function (generally following the sub-domains of the ICARS), physical and mental daily activities, mood, and cognition. Our interview differed from the PROM-Ataxia in three important ways: 1) questions of cognition were separated from emotion, with a deep interrogation of cognitive functions in real-world terms, 2) the questionnaires were extended to include study caregivers, or informants (e.g., spouse or sibling), who knew the patients before and after the onset of ataxia, and 3) open-ended questions were included for patients and informants regarding each group's unique quality of life issues affected by ataxia. Informants were included in order to assess their perspective on symptomatology, explore consensus between patients and informants, and probe the informants' greatest concerns and hardships in relation to supporting their loved one with ataxia (See Supplement 1 for interview materials).

The aim of this study was, foremost, to use our interviews to better understand how cerebellar ataxia affected the quality of life in people with cerebellar ataxia and their informants. The relation between interview responses and the International Cooperative Ataxia Rating Scale (ICARS) was explored to examine how well patient self-report tracked with clinical observational measures. Symptom category clusters were also explored in order to help characterize symptom profiles, which could inform prognostication.

Methods

Study Participants and Procedures

In this study, 55 cerebellar ataxia patients and 47 "informants" were recruited through the Ataxia Center at Johns Hopkins and the National Ataxia Foundation's 2017 Annual Ataxia Conference. Research was primarily

focused on those with progressive cerebellar degeneration that was due to hereditary causes (e.g., genetic conformation of SCA) or to unknown etiology. Those with a diagnosis of Friedrich's ataxia (FA), multiple systems atrophy- cerebellar type (MSA-C), episodic-ataxia type 2 (EA2), and autosomal recessive cerebellar ataxia (ARCA) were excluded. Four cerebellar ataxia patients ($n = 4$) and their respective study partners ($n = 4$) were excluded from analysis after chart review, as diagnoses were later established as FA, EA2, ARCA, and MSA-C respectively, leaving a total of 51 cerebellar ataxia patients (mean age = 56.6 years, SD = 12.7) and 43 informants (mean age = 57.2 years, SD = 15.2) in the analyses.

Patients were diagnosed according to a clinician's general assessment, which was based on genetic confirmation (if available), family history, neuroradiological readings of brain structure, overall health history, and additional clinical information to rule out other possible diagnoses. Participants were excluded if they had a history of an additional neurological disorder aside from ataxia, a history of head injury with loss of consciousness lasting longer than 5 min and/or resulting in neurological sequelae, learning disability, substance dependence, or a history of a primary psychiatric condition prior to development of ataxia. Informants were not screened for any of the above considerations. They knew the patient before and after the onset of ataxia and were the patient's spouse or significant other ($n = 30$), close family member (e.g., parent ($n = 2$), sibling ($n = 5$), adult child ($n = 5$), or certified medical caregiver ($n = 1$). In one pair of sibling patients, both were diagnosed with SCA 6 and also served as each other's informants. Eight patients were interviewed without informants due to a lack of availability.

Diagnoses were confirmed by a neurologist with expertise in cerebellar ataxia (LR). Genetic ataxias included SCA 1 ($n = 2$), SCA 2 ($n = 5$), SCA 3 ($n = 6$), SCA 5 ($n = 1$), SCA 6 ($n = 10$), and SCA 8 ($n = 2$). Patients without genetic confirmation or no family history of confirmed SCA subtype were categorized as nonfamilial: Cerebellar Ataxia Unknown Etiology (CAUE) ($n = 15$). Familial history of ataxia was categorized as: Autosomal Dominant Cerebellar Ataxia (ADCA) ($n = 3$), which applied to a subset of CAUE participants who had a family history of ataxia in the 1st, 2nd, or 3rd degree relatives but without SCA confirmation ($n = 7$). Ataxia patients were combined into one group ($n = 51$) and compared with the number of total informants ($n = 43$) for statistical analyses. Patient and informant demographic information is presented in Table 1.

Written informed consent was obtained from all patients and informants in the study prior to participating. The study protocol was approved by the Johns Hopkins Medical Institute Institutional Review Board and performed in accordance with the Declaration of Helsinki.

Semi-structured interview

Patients and informants received a semi-structured interview, which was administered by five trained researchers, to patients and informants separately. The interview consisted of structured and open-ended questions designed to capture a patient's unique perspective on their condition. There were also questions designed to gather historical information, such as a description of initial symptoms and course to diagnosis, and an assessment of the patient's perspective on their quality of life. Informants received a similar interview, asking about the patient's abilities within the domains and diagnostic history, along with questions about issues specifically related to the informants' experience.

The semi-structured interview probed the patient's and informant's perspectives regarding how ataxia symptoms have impacted the patient's motor function, daily activities, cognition, emotion, and quality of life. The interview began with open-ended questions regarding demographic and medical history. Participants were then asked to rate their ability to perform motor functions and daily activities using Likert scales from 1–5, 0–3, or 0–1 (no/yes for absence or presence of an impairment; each scale is detailed in the Data Abstraction section below). Motor functions were divided into three domains: 1) posture and gait, 2) daily activities and fine motor skills, and 3) speech, feeding, and swallowing, each of which reflected ICARS Part 1- posture and gait disturbances, Part-II kinetic functions, and Part-III speech disorders, respectively. In the posture and gait portion of the interview, participants were asked about their ability to walk, stand on two feet, stand on one foot, stand from toe to heel, sit down in a chair, stand up from a chair, get in and out of bed, and climb stairs. In the daily living and fine motor skills portion, they were asked about their ability to write with a pen or pencil, drive a car, eat with utensils, and wash or groom themselves. Finally, in the speech and swallowing portion, participants were asked about their ability to speak at sufficient speeds, speak with precision, articulate their words, chew food, swallow food and liquid. They were also asked if people had difficulty understanding them, if they were asked to repeat themselves often, if they had control over the timing of their speech, if they coughed or cleared their throat often, if they reduced the amount of volume of liquid they consumed when drinking, and if they took smaller bites when eating. These questions were reported on a Likert scale. Next, participants were asked about cognitive functions, specifically topics that addressed psychosocial domains, such as difficulty paying attention in social situations, ability to multitask as home or work, feeling impulsive, ruminating, and feeling easily overwhelmed by responsibilities. These were also reported on a Likert scale. A separate cognition section contained yes/no and open-ended questions regarding memory that addressed common

Table 1 Demographics

Group	Age (years, SD)	Sex (M:F)	Race (*n*)				Education (years)	Duration of Illness (years)	ICARS (total score)	Employment Status (*n*)			
			White	African American	Asian	Hispanic				Retired	Full-Time	Part-Time	Unemployed
Genetic ($n=28$)	55.3 ± 9.9	6:22	22	4	2	–	16.5 ± 3.2	11.6 ± 6.4	34.1 ± 15.4	16	9	1	2
Familial ($n=8$)	66.3 ± 10.9	5:3	8	–	–	–	16.9 ± 1.4	12.1 ± 8.4	27.3 ± 7.3	5	3	–	–
Nonfamilial ($n=15$)	53.9 ± 16.1	7:8	14	–	1	–	14.8 ± 3.3	20.2 ± 17.8	39.3 ± 13.3	8	5	2	–
Informant ($n=42$)	57.2 ± 15.2	18:24	36	4	1	2	15.6 ± 2.7	–	–	21	19	1	2

Demographic and clinical features of ataxia patients and informants. SD = standard deviation, M:F = male: female

daily living tasks that may be affected by memory changes since the onset of ataxia, such as: forgetting appointments or reminders, spending time looking for misplaced objects, forgetting what was said in conversations, remembering names and faces, and completing mental math. The emotional awareness section contained open-ended questions pertaining to changes in emotion since the onset of ataxia. Afterward, participants were asked open-ended questions regarding their vision that were divided into the following domain: oculomotor and vision, which reflected part IV of the ICARS. Patients were asked about their experiences with vision trouble and nystagmus. These responses were scored as yes/no for the presence or absence of an impairment. Lastly, participants were asked open-ended questions that addressed changes to their quality of life and how ataxia directly impacted their lives. Informants were asked nearly identical questions about the patient. The informants had supplementary questions that probed their unique concerns and challenges regarding living with a loved one with ataxia.

Because the interview was revised throughout a four-year timespan, not all interviews were identical. Specifically, these revisions added newer questions to the interview, without replacement of original questions. More recent iterations of the interview added questions that pertained to communication and swallowing, vision impairment, unintentional weight loss, changes sleeping at night, and changes in appetite. Those who received an early pilot version (5 patients, 2 informants) were excluded from the current dataset, as this version excluded too many variables to be comparable to later interviews. Patients and informants who were administered the second version ($n=57$) did not receive questions about swallowing, speech, appetite, sleep, and vision that were added in the third version ($n=37$). However, all available data from those who received the second or third interview versions were included in the dataset. Medical records were also used to supplement information regarding ataxia diagnosis, cerebellar sign severity, and speech/swallowing patterns, although this was available to us only for those recruited through the Ataxia Center at Johns Hopkins ($n=37$). Administration time of the interviews ranged from 30 – 60 min.

Data Abstraction

Questions about motor function broadly assessed four domains that were consistent with the primary categories represented in the ICARS: 1) posture and gait disturbances, 2) daily activities and fine motor skills, 3) speech, feeding, and swallowing, and 4) oculomotor and vision. The patient's ability to perform motor tasks in the posture/gait and daily living categories was reported on a Likert scale from 1 to 5, with one meaning "Yes, easily," two

meaning "Yes, but with effort," three meaning "Yes, but occasionally requires assistance," four meaning "Yes, but almost always requires assistance," and five meaning "Not at all." The patient's perceptions of their difficulties speaking, chewing, and swallowing were reported on a Likert scale of 0–3, with zero meaning "Rarely," one meaning "Sometimes," two meaning "Often", and three meaning "Always". Additional responses regarding communication and swallowing were reported as 0 or 1, with 0 meaning "No" or 1 meaning "Yes" regarding changes with the onset of ataxia. Oculomotor and vision questions were also open-ended questions that were transcribed as a 0 (no change) or 1 (change with ataxia). Questions regarding changes in memory since the onset of ataxia were also reported as a 0 (no change) or 1 (change with ataxia). Questions regarding emotional awareness and quality of life consisted of several open-ended questions about emotional changes after ataxia onset, subject awareness of problems (informant only), the biggest challenge to the caregiver (informant only) and biggest challenge to patient/what patient would like to most see improve.

Responses to open-ended questions were categorized into 15 quality of life themes, based on patient and informant responses. These included: fitness and physical recreation, nonphysical recreation, vocation or chores, independence, relationships, mobility, fine motor function, visual function, eating, cognition, general health, communication, self-care, self-image, and mood/emotion. Data were scored as 0 (absent) or 1 (present) if the verbal responses matched within any of the 15 themes. Frequency was calculated as the total of each variable and entered into a word cloud for visualization [29].

An ICARS exam was administered to 26 of the ataxia patients on the day of the interview. Medical charts for the 37 patients that were recruited from the Ataxia Center at Johns Hopkins were reviewed to confirm or supplement information gathered in the interview. Medical chart review included up to 6 months on either side of the interview date.

To quantify the degree of neurological impairment across all patients, a disease stage variable was determined for each patient that was determined by the degree of gait impairment according to Klockgether and colleagues [30]. Disease stages ranged from 0–3: Stage 0 indicated no gait difficulties ($n = 3$), Stage 1 indicated onset of gait difficulties ($n = 14$), Stage 2 indicated loss of independent gait and reliance on walking aid such as a walker or a cane ($n = 28$), and Stage 3 indicated confinement to a wheelchair ($n = 6$). With this method, each patient was assigned a neurological impairment score, including those without an ICARS score.

Data Transformation

Regardless of response format (except open-ended questions), data that were originally scored on a Likert scale, whether 1–5 or 0–3, were converted to a five-point scale, with five representing the most severe impairment and one representing no impairment at all. Each variable within the respective domain was then averaged to obtain the overall score. The reason for using the average rather than the total to represent the overall score for each motor impairment was to allow for comparison across scores regardless of the number of questions asked in each domain. The following formula was used to transform the individual responses to a 1–5 scale:

$$X = \left[(a - b) \times \frac{(x - B)}{(A - B)}\right] + b$$

a = The maximum of the new scale, 5

b = The minimum of the new scale, 1

A = The maximum of the current scale

B = The minimum of the current scale

x = Current score

X = Scaled score

Additionally, the overall score for the patient's oculomotor abilities was calculated by taking the average of two binary responses to the questions in that category. Since the speech/swallowing subsection of the interview included responses from a Likert scale and a binary scale, the overall score used for ICARS comparison tests was an average of the two responses on a Likert scale that aligned closely with the ICARS' speech assessment—specifically if the patient had difficulty speaking at sufficient speeds and speaking with precision.

The only case that permitted the overall score to be calculated with a sum rather than an average was the questions regarding changes in memory. Since the same set of questions was asked in all versions of the semi-structured interview, the overall score for each section was the sum of the binary responses that were reported for each question.

Statistics

Participants with ataxia (genetic, familial, and nonfamilial) were combined into group 1 and informants into group 2 for these analyses to assess any differences between patient and informants. These differences were tested using independent t-tests for continuous data and Pearson Chi-Square

for categorical data as appropriate. For independent *t*-tests, Levine's Test for Equality of Variances was used to identify unequal variances. Correlations were run between the four domains of the semi-structured interview and the ICARS using Spearman's Rank for categorical data. Two-Step Cluster Analyses were performed on discrete variables (posture/gait, daily activities/fine motor) to detect latent groupings within the dataset. In the questionnaire, there were eight posture and gait questions whose responses were analyzed to form two clusters. These questions pertained to the patient's ability to walk, stand on two feet, stand on one foot, stand toe to heel, sit down in a chair, stand up from a chair, get in and out of bed, and climb stairs. The second analysis was run on responses to five daily activities /fine motor questions, which also revealed two clusters in the data set. These questions pertained to the patient's ability to write with a pen/pencil, drive a car, eat with utensils, wash and groom themselves, and dress themselves. To draw further conclusions, independent *t*-tests were used for comparisons regarding psychosocial skills and changes in memory after each subject had been assigned to a cluster. Data were normalized and scaled to ensure the generation of good quality clusters and visualized using *R* [31]. All analyses were performed using IBM SPSS Statistics, Macintosh, version 27.0 (IBM Corp., Armonk, NY, USA).

Results

The ataxia patients and informants were compared on response differences for the following domains: posture and gait, daily activities and fine motor tasks, speech, feeding and swallowing, and oculomotor and vision (Table 2). Patient and informant ratings did not differ significantly within the domains 1) posture and gait, 2) daily activities and fine motor tasks, 3) speech, feeding, and swallowing, or 4) oculomotor and vision scores. This suggested that there was agreement between the two groups regarding the patient's ability to perform most motor tasks.

Tests were conducted to determine presence of correlations between the patients' responses to the four domains in the interview and the corresponding subdomains within the ICARS. Results indicated that responses within all four domains positively correlated with the ICARS. The posture and gait scores positively correlated with the posture and gait disturbances of the ICARS $r(25) = 0.58$, $p = 0.003$ (Fig. 1). Daily living and fine motor scores positively correlated with the kinetic functions of the ICARS $r(25) = 0.41$, $p = 0.040$. Trouble speaking at sufficient speeds and precision positively correlated with the speech disorders of the ICARS $r(13) = 0.57$, $p = 0.041$. Lastly, oculomotor scores positively correlated with oculomotor disorders of the ICARS $r(17) = 0.64$, $p = 0.006$. Overall, these findings suggested that the four domains within the interview using real-world terms and self-report for how ataxia impacted day-to-day life, coincided with clinical, observational assessments.

Disease stages (0–3) of the ataxia participants ($M = 1.7$, $SD = 0.75$) positively correlated with the total ICARS score $r(26) = 0.63$, $p = 0.001$, posture and gait disturbances (Part I- ICARS) $r(25) = 0.70$, $p = < 0.001$, kinetic functions (Part II- ICARS) $r(25) = 0.39$, $p = 0.05$, and speech disorders (Part III- ICARS) $r(25) = 0.41$, $p = 0.03$. However, disease stages did not correlate with oculomotor disorders (Part IV-ICARS) $r(25) = 0.34$, $p = 0.10$. Regarding interview questions across the four domains, disease stages positively correlated with posture and gait scores $r(51) = 0.53$, $p = < 0.001$ and daily living fine motor scores $r(51) = 0.57$, $p = < 0.001$, but did not correlate with speech scores $r(23) = 0.28$, $p = 0.195$ or oculomotor scores $r(30) = -0.02$, $p = 0.935$.

Ataxia patients and informants were also asked about changes in psychosocial functions. These focused specifically on the ability to pay attention in social situations, ability to complete household or professional tasks, whether the patient was easily distracted or had a hard time concentrating, ability to multitask, whether they ruminated, whether

Table 2 Main categories of the interview divided into analogous ICARS domains

Domain	Ataxia ($n = 51$) (mean, SD)	Informants ($n = 43$) (mean, SD)	*P*-value
Posture & Gait Score	2.75 ± 0.71	2.88 ± 0.67	0.37
Daily Activity & Fine Motor Tasks Score	1.98 ± 0.74	1.96 ± 0.81	0.88
Speech, Feeding, & Swallowing Score			
Trouble speaking at sufficient speeds & precision	2.22 ± 0.89	2.17 ± 1.17	0.91
Speech*	0.65 ± 0.32	0.57 ± 0.41	0.30
Trouble Chewing & Swallowing	1.81 ± 0.75	1.67 ± 1.07	0.67
Swallowing*	0.46 ± 0.31	0.39 ± 0.34	0.54
Oculomotor & Vision Score*	0.48 ± 0.44	0.57 ± 0.33	0.47

The scores reported for ataxia patients and informants were divided into analogous ICARS domains. *Represents data that were reported as binary (presence/absence). SD, standard deviation

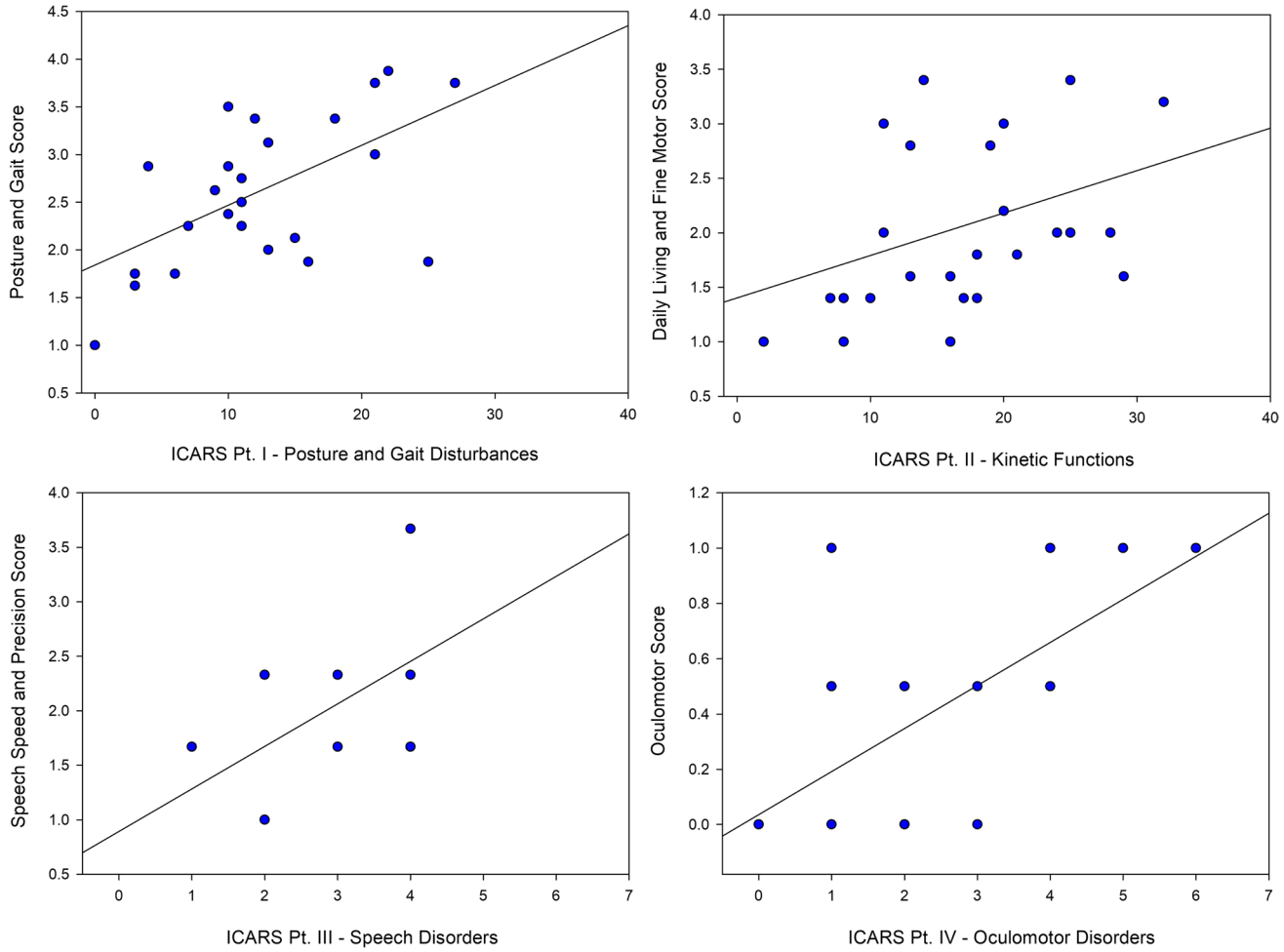

Fig. 1 Correlations between the ICARS subsection scores and interview domains given to ataxia participants. Scores for all four domains of the ICARS positively correlated with the analogous domain within the interview

they were impulsive, easily overwhelmed by household or professional tasks, and could switch attention easily. Patients and informants were in general agreement in their responses; however, for ability to switch attention, the groups disagreed: informants, at 51.2% (M = 3.9, SD = 1.4), felt strongly that ataxia patients were rarely able to switch attention (Table 3), whereas, ataxia patients (56.9%) responded that they were able to switch attention with relative ease (M = 2.0, SD = 1.3), t(92) = 6.5, $p = < 0.001$, d = 0.58. Informants, at 51.2% (M = 2.2, SD = 1.4), also believed that ataxia patients rarely ruminated, while ataxia patients, at 31.4% (M = 2.8, SD 1.4), t(92) = 1.9, marginally significant at $p = 0.06$, d = 0.21, reported that they sometimes ruminated or thought about the same topics constantly.

Patients and informants generally agreed on the patient's changes in memory since the onset of ataxia. Each participant answered questions from the interview, and three scores were generated that each reflected a subset of memory symptoms. The first score represented the patient's forgetfulness (general changes in memory, forgetting appointments, needing lists, repeating stories, forgetting what others say in conversations, and spending time looking for misplaced objects), the second score represented the patient's communication skills (finding the right words, talking, and explaining ideas), and the third score represented the patient's ability to remember names and faces. Patients and informants reported marginally significant differences for communication skills: patients (M = 1.14, SD = 1.02) reported more difficulty than did informants (M = 0.72, SD = 1.05), t(88) = 1.94, $p = 0.056$, d = 0.402.

Further correlations were run between each participant's psychosocial functions scores and ICARS subscores. There was a positive correlation between Part II- ICARS (kinetic functions) and the ability to switch attention (r(25) = 0.410, $p = 0.042$). Correlations were repeated using ICARS subscores and changes in memory scores, which reflected each patient's general forgetfulness, communication skills, and ability to remember names and faces. There was a negative

Table 3 Daily functions with a cognitive or psychiatric basis

Topic	Group (Ataxia, $n=51$ Informants, $n=43$)	Rarely	Sometimes	Often	Always	*P*-Value
Able to pay attention in social situations	Ataxia	2.0	5.9	25.5	**66.7**	0.60
	Informants	2.3	9.3	25.6	**62.8**	
Able to complete household or professional tasks	Ataxia	5.9	17.6	17.6	**58.8**	0.48
	Informants	7.5	17.5	27.5	**47.5**	
Distractible or hard time concentrating	Ataxia	**58.8**	21.6	13.7	5.9	0.45
	Informants	**46.5**	34.9	9.3	9.3	
Able to multitask	Ataxia	21.6	**29.4**	23.5	25.5	0.45
	Informants	**34.9**	20.9	18.6	25.6	
Ruminate or think about the same topics constantly	Ataxia	27.5	**31.4**	23.5	17.6	0.06
	Informants	**51.2**	20.9	16.3	11.6	
Impulsive or act or speak without thinking first	Ataxia	**54.79**	33.3	5.9	5.9	0.69
	Informants	**62.8**	23.3	9.3	4.7	
Easily overwhelmed by household or professional tasks	Ataxia	**58.8**	15.7	11.8	13.7	0.58
	Informants	**48.8**	20.9	18.6	11.6	
Able to switch attention	Ataxia	7.8	15.7	19.6	**56.9**	<0.001
	Informants	**51.2**	25.6	9.3	14.0	

Ataxia participant and informant data are represented as percent response rate to questions pertaining to cognitive and psychiatric domains ranging from rarely, sometimes, often, and always. Bold represents highest response rate in the Likert scale

correlation between Part III-ICARS (speech disorders), and the ability to remember names and faces (r(25) = -0.442, $p=0.027$), i.e., lower speech ability correlated with higher memory for faces and names. It should be noted, however, that visual inspection of the scatterplot for this last correlation suggested that results were skewed by two patients with low face/name recall ability.

Within the ataxia group, scaled scores for posture/gait and daily activities/fine motor (higher score indicating a higher level of impairment) were correlated with each psychosocial function ability that was asked about in the interview (Table 4). Posture/gait and daily activities/fine motor tasks each positively correlated with the inability to complete light household duties or responsibilities, such as sending emails, organizing files, etc. [r(51) = 0.30, $p=0.036$ and r(51) = 0.43, $p=0.002$, respectively]. Posture/gait and daily activities/fine motor tasks each positively correlated with impulsive behaviors [r(51) = 0.32, $p=0.024$ and r(51) = 0.43, $p=0.002$, respectively]. Finally, a positive correlation was observed between daily activities/fine motor tasks and the inability to multitask, r(51) = 0.38, $p=0.007$. The same tests were run to detect any correlations between scaled scores for posture/gait and daily activities/fine motor and each total score that reflected a category of memory changes, but none were found to be significant.

Two-step cluster analyses were performed with the inputs being either the responses to the interview related to posture/gait responses (8 variables) or the daily activities and fine motor responses (5 variables). The two-step analysis used a distance measure to separate groups and create subgroups [32, 33]. The results from both cluster analyses indicated two clusters of "fair" quality, with Cluster 1 showing higher severity of impairment for all motor variables compared to that of Cluster 2. The two groups were then compared on the psychosocial items from the interview. An independent samples t-test between the two clusters formed by the posture/gait responses revealed that patients in Cluster 1 (M = 2.04, SD = 1.30) were marginally more impaired at controlling impulsive behavior relative to patients in Cluster 2 (M = 1.49, SD = 0.66), t(48) = 1.99, $p=0.051$, d = 0.496. Comparisons between the two groups formed by the daily activities and fine motor cluster analysis revealed additional differentiations. Multitasking impairments were higher for patients in Cluster 1 (M = 3.89, SD = 1.11) than for patients in Cluster 2 (M = 2.67, SD = 1.46), t(24) = 3.06, $p=0.005$, d = 0.874. Additionally, keeping track of household tasks was marginally more difficult for Cluster 1 (M = 2.67, SD = 1.52) than for Cluster 2 (M = 1.72, SD = 1.14), t(15) = 1.99, $p=0.064$, d = 0.769. Cluster 1 also had marginally more difficulty controlling their impulsive behavior (M = 2.56, SD = 1.69) compared to Cluster 2 (M = 1.62, SD = 0.80), t(13) = 1.86, $p=0.086$, d = 0.881. Finally, Cluster 1 had a marginally higher tendency to feel overwhelmed (M = 2.89, SD = 1.75) compared to Cluster 2 (M = 1.82, SD = 1.32), t(15) = 1.95, $p=0.070$, d = 0.749. (Fig. 2). Further independent samples tests were run to detect any significant differences between the clusters regarding changes in memory, but none were found to be significant.

Open-ended questions about the changes in the patient's quality of life since disease onset were examined

Table 4 Bivariate correlations between motor impairments and psychosocial impairments

Psychosocial Item	Posture/Gait $n=51$ (Correlation Coefficient, *P*-Value)	Daily Activities/ Fine Motor Tasks $n=51$ (Correlation Coefficient, *P*-Value)
Able to Pay Attention in a Social Situation	-0.045 $p=0.753$	0.059 $p=0.679$
Distractible	-0.011 $p=0.937$	0.050 $p=0.727$
Able to Multitask	0.236 $p=0.096$	0.375 $p=$**0.007**
Able to Switch Attention	-0.197 $p=0.165$	-0.049 $p=0.735$
Able to complete housework	0.295 $p=$**0.036**	0.428 $p=$**0.002**
Ruminate or think about the same concepts constantly	0.082 p=0.566	0.047 p=0.745
Impulsivity or speaking without thinking first	0.315 $p=$**0.024**	0.428 $p=$**0.002**
Easily overwhelmed by household or professional tasks	-0.088 $p=0.538$	0.213 $p=0.133$

Bivariate correlations are shown between the posture/gait and daily activities/fine motor domains and each psychosocial item included in the interview for cerebellar ataxia patient responses only. Listed in the table are each test's correlation coefficient and *p*-value. Bolded numbers represent significant correlations

(Fig. 3). Patients were asked in what way they thought having cerebellar ataxia had the biggest impact on their daily living, and which area/s of their life would they most like to see improve. Responses were categorized into 15 quality of life themes. Out of all of the quality of life themes, ataxia patients reported that the biggest challenge or area they desired improvement in was fitness and physical recreation (73.0%), followed by mobility (51.0%), independence (43.0%), vocation or chores (41.0%), and nonphysical recreation (41.0%). One ataxia patient reported, *"Balance, walking, physical activities like dancing or running. I cannot work or do things like a normal parent such as attend school functions. I want to do more things with my son."*

Informants were asked the same open-ended questions about their ataxia partners. Informants (61.0%) felt that fitness and physical recreation were very important to the patients followed by independence (54.0%), mobility (51.0%), relationships (30.0%), and vocation or chores (28.0%). One informant reported, *"They miss recreational physical activities. It's been difficult for them to accept the ataxia diagnosis. Mobility has been impacted causing difficulty with steps and poor coordination. They cannot do what they love to anymore."*

Finally, informants were asked what the biggest challenges were while supporting their loved ones (Fig. 4). Examples of informant responses were:

"Watching them get worse. Having to deal with strangers' reactions."
"The emotional impact of watching them go through the disease."
"It's hard to watch them deteriorate. There is a sense of urgency now for retirement for me now, and I want to retire while they are still able to do things."

More frequently reported words were reflected as a larger size in the word cloud in comparison to less frequently reported words [29]. From highest frequency to lowest frequency, emotional impact, responsibility, watching the disease progress, feelings of helplessness, and health (personal and their loved ones) were areas that trended from the informants' responses.

Discussion

In this study, a semi-structured interview was created that captured the perspectives of ataxia patients and informants to assess their changes in daily function and quality of life as a result of having cerebellar ataxia. Tests were run to assess potential differences and/or similarities between patients' and informants' responses, and to see whether the responses aligned with clinical observations (i.e., the ICARS).

Ataxia patients and informants agreed on the patient's ability to perform tasks for the following domains: posture and gait, daily activities and fine motor tasks, and speech,

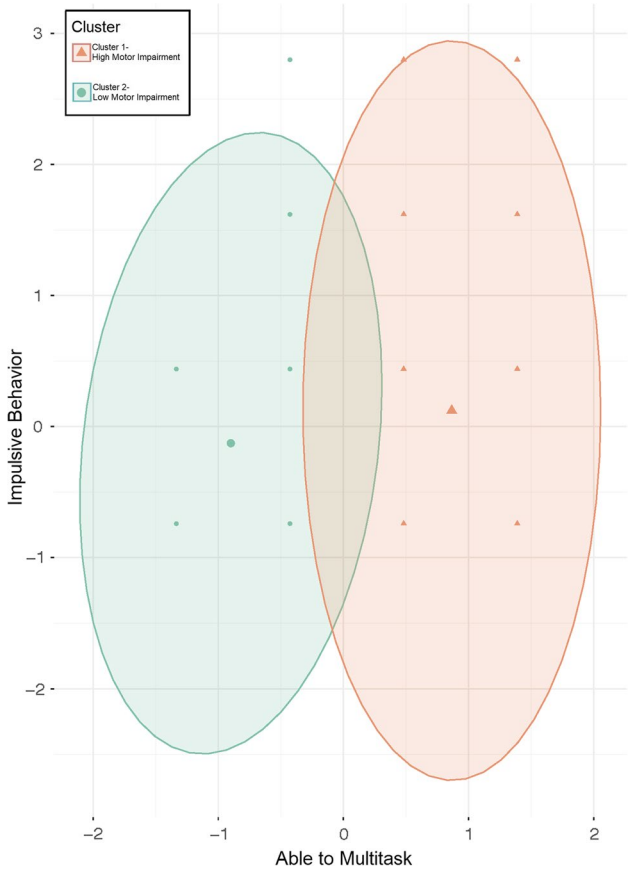

Fig. 2 Cluster analysis of daily activity and fine motor responses from ataxia patients. Data points are reported to the closest center based on their respective Euclidean distances. The X and Y scales represent the distance between points for the following topics: 1) able to multitask and 2) impulsive behavior. Patients in Cluster 1 were more impaired in their ability to multitask and showed more impulsive behavior compared to that of patients in Cluster 2

feeding, and swallowing. This indicated that informants were aware of changes due to disease progression and how these domains impacted their loved one's ability to perform day-to-day activities. Regarding oculomotor and vision, informants felt that their loved ones may have slightly more vision issues than what the patients self-reported. This may have been due to the ability of the informants to notice outward ocular changes such as nystagmus. Alternatively, for the ataxia patients, it is possible that there were compensatory mechanisms in place for convergence insufficiency that mitigated symptoms, such as double or blurred vision that led to decreased reporting [34], which may have rendered vision issues less noticeable to themselves, relative to other physical symptoms.

The four domains of the interview strongly correlated with the four ICARS subscales (posture and gait disturbance, kinetic function, speech disorder, and oculomotor disorders). The results provided evidence that within the categories of our interviews, the simple, straightforward questions that the patients were asked about their everyday lives revealed the same issues that a neurologist or clinician would observe during a neurological examination. A benefit of this type of interview, therefore, is its feasibility. Asking for real-world descriptions of how ataxia impacts the patient's lives accurately reflected the neurological impairments that the patient was experiencing.

The responses to questions concerning the patient's psychosocial abilities were correlated to the responses to the posture/gait and daily activities/fine motor questions to identify any associations between motor impairments and cognition. It was found that severity of motor impairments (especially for daily activities/fine motor) positively correlated with difficulty in multitasking, completing housework, and behaving impulsively. Examining the connections between specific motor impairments and specific cognitive impairments can help inform patients and caregivers of what non-motor deficits they might experience if their existing motor impairments match a certain profile. Moreover, data from this study supported an association between motor and psychosocial trajectories in cerebellar ataxia when cognition was considered in real-world terms rather than as scores from direct neuropsychological tests (e.g., in the CCAS scale). No correlation was found between memory changes and ICARS scores. This differed from the PROM, which found a correlation between the cognitive section of their "Mental" measure and motor deficits. However, cognitive questions in the current interview focused specifically on memory changes that occurred after ataxia onset. By contrast, cognitive questions in the PROM did not focus on memory per se and were referable to changes within the past two weeks. The resultant differences between the two studies is revealing because it indicates that cognitive difficulties related to ataxia are complex and not driven by memory-related issues. For example, associations were observed through our cluster analyses between motor function and psychosocial skills, which included aspects of cognition, as described below.

The two-step cluster analyses that were performed on both the posture/gait responses and the daily living and fine motor responses indicated the presence of two different profiles of motor impairments, with one cluster showing a higher severity of motor deficits than the other. Comparisons between the two clusters revealed a higher number of group differences in the psychosocial abilities between the clusters formed by the daily living categories compared to those formed by the posture/gait motor domains. Additional tests indicated no differences between the posture/gait clusters or the daily living/fine motor task clusters with regard to changes in memory since ataxia onset. Thus, changes in daily living and fine motor tasks may be impacted by psychosocial factors rather than frank memory impairments. In the clinic, when

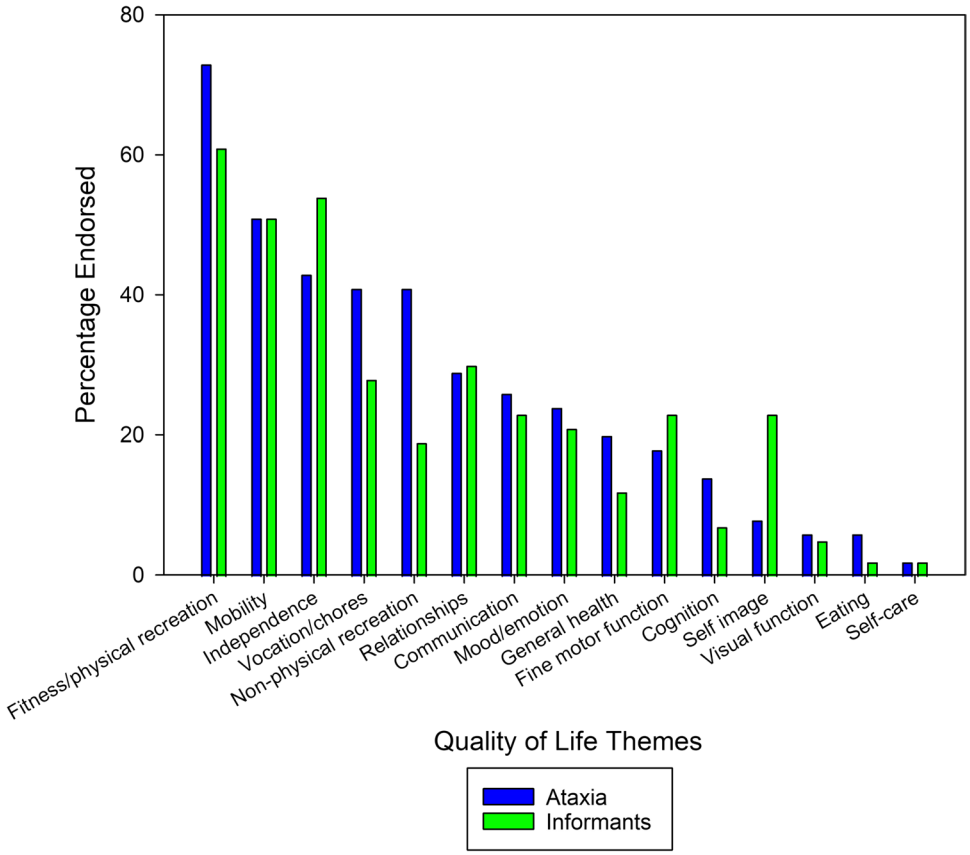

Fig. 3 The percent response rate of ataxia and informants is reported across 15 quality of life themes. The ataxia participants shown in blue, indicated that fitness/physical activities were the biggest challenge or area desiring improvement. Informants shown in green, responded that independence was the biggest challenge or area desiring improvement for ataxia patients

Fig. 4 Responses from informants were categorized from an open-ended question, "What are the biggest challenges while supporting your loved one?" The frequency of responses were reflected as a word cloud, where bigger words represent a higher instance of reporting and smaller words represent a lower instance of reporting from the informants

a patient is associated with a particular motor symptom profile, they could be informed of non-motor difficulties commonly linked to that profile. Methods such as these can help prepare patients who have been recently diagnosed (as well as their caregivers) for what symptoms they might experience in the future, telling a story about ataxia that has been primarily absent from many previous studies on the disease.

Currently, ataxia-based clinical assessments primarily focus on disorders of movement, where changes in psychosocial domains are often underrepresented. As the cerebellum contributes to cognition and mood, clinicians would benefit from asking questions regarding cognitive changes and neuropsychiatric symptoms [17, 35–38]. Our results revealed that patients and informants generally agreed on changes in the ability to perform

certain tasks in the cognitive domain. However, informants felt that the patients were rarely able to switch attention and rarely ruminated, while patients felt that they were always able to switch attention and sometimes ruminated. The ability to switch attention and rumination both involve executive functions [39–42], which are impaired in ataxia [19, 43–46]. This may explain, in part, why ataxia patients are less self-aware of their abilities related to attention and rumination.

Asking questions that address changes to the quality of life in ataxia patients can be useful for patients and family members that may want to learn more about what to expect with disease progression. In addition, these conversations can be useful for providers to assess how quickly or what aspects of the patient's day-to-day activities are changing (e.g., physical, such as biking or running; social activities such as spending time with family and friends; emotion/mood, cognitive, etc.) Ataxia patients felt that areas of their lives that they would like to see improve were fitness and physical recreation, mobility, vocation or chores, independence, and nonphysical recreation, and informants agreed. Both groups also agreed on the significant impact ataxia has had on their quality of life. When informants were asked what the biggest challenge was for them while supporting their loved one, emotional impact, responsibility, watching the disease progress, feelings of helplessness, and health (personal and their loved ones) were the most frequently reported answers. Such conversations can better prepare caregivers for the emotional toll of what to expect over time and provide coping mechanisms or strategies. This information can also be used to guide ataxia-oriented organizations to use as discussion tools for caregivers and ataxia patients.

Including a dynamic discussion between patients and caregivers using semi-structured interviews and questions that address changes in the patient's quality of life may positively impact treatment and care for ataxia patients. It can serve as an educational resource for newly diagnosed patients and their loved ones for what to expect with disease progression. This type of interview would also be beneficial during telemedicine visits, which have become an increasingly viable form of healthcare. Given that patients' report of real-world difficulties correlated with clinical assessments (e.g., ICARS scores), results here demonstrated the feasibility of asking patients and caregivers about everyday challenges that could reasonably inform clinicians in the absence of in-person visits.

This study has several limitations. First, diagnoses of FA, MSA-C, EA2, and ARCA were excluded from the study population as these disorders differ from other forms of cerebellar ataxia. Future research may benefit from studying these cohorts separately, or combined with a larger cohort. Such information would speak to the generalizability of these findings to additional forms of ataxia. Second, total scores were unable to be ascertained within the interview, such as the type used for ICARS and other functional measures. Interview totals would have provided a quick reference point to make it more user-friendly, but due to the evolving nature of the interview, not all participants received all parts that were included in the final version of the interview, making it difficult to compare totals with different ranges. Third, due to relatively low participant numbers, findings from cerebellar ataxia subtypes were unable to be characterized, which, with more participants, may reveal clinical phenotypes and disease trajectory that differ by disease etiology.

Conclusion

In summary, these descriptive findings demonstrated the effectiveness of semi-structured interviews that revealed the patient's and informants' perspectives regarding quality of life changes due to ataxia, and how these interviews can be useful in clinical settings and as a learning resource for patients and their families. Results of the study demonstrated that informants were a reliable asset as responses throughout the interview were synonymous with changes in quality of life that mattered the most to ataxia patients. Lastly, this interview was able to identify connections between specific motor impairments and specific cognitive impairments, as seen from the results of the correlation and cluster analyses. Such information may help patients and informants understand what additional deficits they may experience or expect if their existing motor impairments match a particular profile. Exploratory analysis may benefit from using the patient and informant interviews as an outcome measure in clinical trials to effectively target treatment and therapeutic options. As the interview can range from 30–60 min, a future direction will be to fine-tune the questionnaire length so that it can be used more efficiently and to validate it against external measures.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12311-022-01393-5.

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Declarations

The authors have no relevant financial or non-financial interests to disclose.

Conflict of Interest The authors declare that they have no conflict of interest.

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