RESEARCH ARTICLE



Cerebellar impulsivity_compulsivity assessment scale

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Abstract

Objective: The cerebellum has been identified as the key brain region that modulates reward processing in animal models. Consistently, we recently found that people with cerebellar ataxia have impulsive and compulsive behaviors (ICBs), the main symptoms related to abnormal reward processing. Due to the lack of a validated scale to quantitatively measure ICBs in cerebellar disorders, we aim to develop and validate a new scale, Cerebellar Impulsivity-Compulsivity Assessment (CIA). Methods: We recruited 62 cerebellar ataxia cases, categorized into those with ICBs and those without. We developed a preliminary version of CIA, containing 17 questions. We studied the internal consistency, test-retest reliability, and inter-rater reliability to formulate the final version of CIA, which constitutes only 10 questions. The receiver operating characteristic curve (ROC) was generated to assess the sensitivity and specificity of CIA. Results: Cerebellar ataxia cases with ICBs have threefold higher total preliminary CIA scores than those without ICBs (12.06 ± 5.96 vs. 4.68 ± 3.50 , p = 0.038). Cronbach's alpha revealed good internal consistency across all items $(\alpha > 0.70)$. By performing the test–retest reliability and inter-rater reliability on the preliminary version of CIA, we excluded seven questions (r < 0.70) and generated the final version of CIA. Based on the ROC, a score of 8.0 in CIA was chosen as the cut-off for ICBs in individuals with cerebellar ataxia with 81% sensitivity and 81% specificity. Interpretation: CIA is a novel tool to assess ICBs in cerebellar ataxia and broaden our understanding of the cerebellum-related cognitive and behavioral symptoms.

Introduction

The cerebellum was traditionally considered a brain region important for motor control, such as movement coordination and motor learning.^{1,2} However in the past decade, the role of the cerebellum in cognitive and behavioral functions has gained increasing visibility.^{3–5} People with cerebellar disorders of a variety of causes, including ischemic strokes, hemorrhages, tumors, and genetic or degenerative forms of ataxia, can have a constellation of cognitive and behavioral symptoms called cerebellar

cognitive affective syndrome/Schmahmann syndrome.^{6–8} Cerebellar cognitive affective syndrome contains but is not limited to deficits in executive and visuospatial functions, verbal memory, verbal fluency, and emotion-affect regulation.^{6,7}

In recent animal studies, the cerebellum has been identified to play a role in modulate complex reward processing.^{9–13} Several neuronal elements of the cerebellum have been found to involve in reward processing^{10–13}: granule cell neuronal firing encodes the reward anticipation and delivery,¹³ climbing fiber firing conveys reward prediction

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error, and Purkinje cells are highly involved in the reinforcement learning,¹² which is crucial to inform the reward processing in the brain. From neural network perspective, the cerebellum has dense connections with the traditional reward circuitry^{9,14–16}; specifically, the ventral tegmental area (VTA).^{17–21} Via the cerebello-VTA connections, the cerebellum sends excitatory signals to modulating the neuronal activity of VTA.^{9,16} Collectively, these animal studies support the role of the cerebellum in reward processing.

The classical symptoms related to abnormal reward processing in humans are impulsivity and compulsivity,²² which can have tremendous impacts on individuals' lives.^{23–25} Consistent with animal studies,¹² we recently found that people with cerebellar ataxia have increased impulse control behaviors (ICBs), including but not limited to excessive video game playing, binge eating, and hoarding,^{23,24} further supporting the hypothesis that an intact cerebellum is crucial for reward processing in humans. These clinical observations further strengthen the new role of the cerebellum in reward processing actually occurs in humans.

One of the prevalent neurological disorders associated with ICBs is Parkinson's disease. To further explore the differences between ICBs in Parkinson's disease and cerebellar ataxia, we also recently compared impulsive and compulsive "traits" in these two disorders. We found Parkinson's disease patients have impulsive traits across different impulsive domains whereas individuals with cerebellar ataxia have impulsive traits centered around non-planning domain only, demonstrating different types of impulsivity in different neurological disorders.²⁶ Therefore, impulsive and compulsive scales developed for Parkinson's disease may not be ideal to measure ICBs in people with cerebellar ataxia.²⁷ To measure and track the ICBs reliably in cerebellar ataxia, there is a need for developing a validated scale specifically in this population. We thus performed the present study to develop a scale for cerebellar ICBs, and to create a new tool to study behavior symptoms associated with cerebellar dysfunction for future clinical studies.

Methods

Study design and participants

We conducted a cross-sectional study by recruiting individuals with cerebellar ataxia from the Ataxia Clinic at Columbia University Medical Center from 2019 to 2021. The diagnosis of cerebellar ataxia was made by two ataxia specialists (S.H.K. and C.R.L.). The diagnoses of our ataxia participants included genetically-confirmed autosomal dominant spinocerebellar ataxia (SCA), multiple system atrophy - cerebellar type (MSA-C), Friedreich ataxia, immune-mediated ataxia, Fragile X-associated tremor/ataxia syndrome, and idiopathic late-onset cerebellar ataxia (ILOCA). Participants were diagnosed with MSA-C based on the proposed diagnostic criteria.²⁸ The diagnosis of ILOCA was made after the extensive search for autoimmune, metabolic, paraneoplastic, and genetic testing for repeat expansion-related SCAs, the absence of a family history of ataxia, and the absence of parkinsonism or autonomic features.²⁹ A comprehensive medical and neurological history and examination was reviewed for each study participant. All subjects had no prior neurological and psychiatric diseases known to be associated with impulsivity and compulsivity, including dementia, attention deficit hyperactivity disorders, autism spectrum disorders, bipolar disorders, or substance abuse. The ataxia symptoms were measured by the scale of rating and ataxia assessment (SARA).³⁰

Development and validation of CIA

We first designed the preliminary version of Cerebellar Impulsivity-Compulsivity Assessment (CIA) scale with 17 questions, labeled as Q1 to Q17 (Table S1). As the preliminary CIA was designed to comprehensively capture the impulsive and compulsive patterns, these 17 questions included modified questions from the Yale-Brown Obsessive Compulsive Scale,^{31,32} the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V),³³ and additional questions considered commonly observed in people with cerebellar ataxia via the patient focus group discussion and gauged by two ataxia neurologists (S.H.K. and C.R.L.). These 17 questions were categorized into three domains: the impulsivity, the compulsivity, and the social appropriateness considering that the consequences of impulsivity and compulsivity were often perceived as inappropriate social behaviors.^{34–36} We recruited 62 cerebellar ataxia subjects to the study, who received the qualitative interview using DSM-V and were categorized into those with and without ICBs. Specifically, we interviewed the participants using the diagnostic criteria of "disruptive, impulse-control, and conduct disorders (p.461 - p.480)" and "obsessive compulsive related disorders (p.235 - p.264)." In the former, we excluded the oppositional defiant disorder, intermittent explosive disorder, conduct disorder, and antisocial personality disorder. In the latter, we excluded body dysmorphic disorder, trichotillomania, excoriation, substance/medicationinduced obsessive compulsive related disorders and obsessive-compulsive related disorders due to other medical conditions. Taken as a whole, for cerebellar ataxia cases who met the DSM-V diagnostic criteria for obsessivecompulsive disorders, hoarding disorder, other specified and unspecified obsessive–compulsive related disorders, as well as other specified and unspecified impulse-control disorders were categorized as having cerebellar ICBs. This methodology is consistent with other published literatures studying impulsivity and compulsivity.^{27,31,32} All participants then received preliminary CIA evaluation.

To test internal consistency, we collected three measurements using the preliminary CIA scale - the first measurement delivered by a trained rater (T1), the patient self-rating measurement (P1), and the second measurement by a trained rater (T2). Raters were blinded to the results of the DSM-V diagnostic interview. The timing between T1 and P1 was within 2 weeks, and the timing between T1 and T2 was between 2 and 6 weeks. Each participant's rating at T1 and T2 was done by the same rater. We had 62 participants who completed T1. Among these 62 participants, 41 completed both T1 and P1 (for inter-rater reliability), and 27 completed T1 and T2 assessments (for test-retest reliability). We used Cronbach's alpha reliability test for data collected in T1, P1, and T2, to test internal consistency and Cronbach's alpha >0.70 was considered the standard for good internal consistency.³⁷ We studied the inter-rater reliability using data collected between T1 and P1 with intraclass correlation analysis, and r > 0.7 was considered good reliability.³⁸

We also applied the same methodology to study the testretest reliability between data collected in T1 and T2.39 We then removed the questions that did not meet the good standard of internal consistency, inter-rater reliability, and test-retest reliability. The remaining questions then formed the revised version of CIA. We further tested the validity of the revised version of CIA by generating the receiver operating characteristic (ROC) curve and area under curve (AUC). The cut-off value of CIA was assessed via the AUC to reach the high sensitivity and specificity (i.e., both >80%) to detect ICBs,40 based on the qualitative interview using DSM-V. The complete algorithm for scale development is listed in a flow chart (Fig. 1). After the final version of CIA was developed, we further examined if there are differences between the ICB and non-ICB groups in each domain: impulsivity, compulsivity, and social appropriateness using Student's ttest. We also conducted the factor analysis to examine the variability of the 10 questions by domain to support the grouping of these questions into three domains. To validate our finding in the final version of CIA, we additional recruited 15 patients with cerebellar ataxia as a validation cohort and conducted the ROC analysis.

We next asked if the existing impulsivity and compulsivity scale gearing toward Parkinson's disease, the

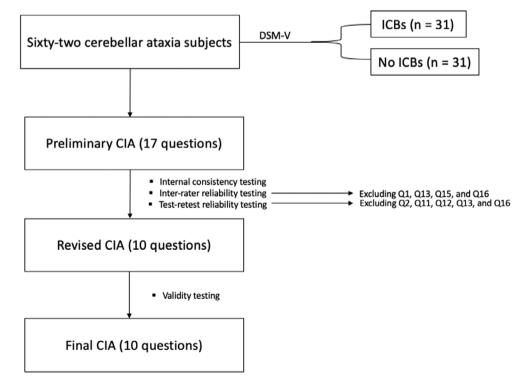


Figure 1. The validation process of the cerebellar impulsivity and compulsivity assessment scale. CIA, cerebellar impulsivity and compulsivity assessment scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICB, impulsive and compulsive behaviors; Q = each question of the cerebellar impulsivity and compulsivity assessment scale.

Impulsivity scale in cerebellar ataxia

Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale (QUIP-RS) assessment,²⁷ can reliably capture the cerebellar ICBs. We thus conducted the ROC analysis to examine if QUIP-RS can validly assess cerebellar ICBs diagnosed by DSM-V. We also examined if there is a correlation between the QUIP-RS and the final version of CIA.

All the statistical analyses were conducted using SPSS statistics software version 25.

Results

Demographics

Via the qualitative interview using DSM-V, we recruited 31 cerebellar ataxia cases with ICBs and 31 cerebellar ataxia cases without ICBs as previously published.^{23,24} The ICB and non-ICB groups had no differences in sex, and the disease duration. Individuals with ICBs were 2.61 years older than those without ICBs (60.67 \pm 11.38 vs. 58.06 \pm 17.82, p = 0.010). Consistently, those with ICBs had 1.94 years longer disease duration than those without ICBs $(47.00 \pm 17.42 \text{ vs. } 45.06 \pm 20.86, p = 0.137)$, while not statistically significant. Those with ICBs had slightly more severe ataxia than those without ICBs (SARA score:12.94 \pm 9.08 vs. 11.82 \pm 4.41, p = 0.008). Seven participants were taking carbidopa/levodopa, and one participant were on pramipexole. The comprehensive demographic data, including age, gender, ataxia diagnosis, and the severity of ataxia were listed in Table 1.

Internal consistency investigation

We first investigated whether the preliminary CIA, containing 17 questions, are ideal to investigate ICBs in cerebellar ataxia. We found that Cronbach's alpha for the preliminary CIA was 0.846, which was above the pre-set cutoff of 0.7, indicating a good overall internal consistency. To further explore the internal consistency of CIA in our cohort, we conducted Cronbach's alpha with an exclusion of each question - our results showed that the Cronbach's alpha still remained above 0.80, even after excluding each of the 17 questions, with lowest 0.824 and highest 0.850 (Table S2). Therefore, we kept all 17 questions in the preliminary CIA scale for further investigation of the reliability and validity of the scale.

Inter-rater reliability of CIA

We next examined the inter-rater reliability of the preliminary CIA. There were 41 cases who completed both T1 (i.e., the first measurement delivered by a trained rater) and P1 (i.e., the patient self-rating measurement within

 Table 1. Demographics and scores of all cerebellar ataxia and controls at baseline.

	ICB ^a (+)	ICB ^a (–)	<i>p</i> -value
n	31	31	
Age (years)	60.67 ± 11.38	58.06 ± 17.82	0.010 ^b
Sex (Male:Female)	17: 14	14: 17	0.612 ^c
Diagnosis	SCA: 8 (26%)	SCA: 10 (32%)	
	MSA: 6 (19%)	MSA: 6 (19%)	
	FA: 2 (7%)	FA: 3 (10%)	
	ILOCA: 6 (19%)	ILOCA: 7 (23%)	
	Others ^d : 9 (29%)	Others ^d : 5 (16%)	
Disease duration (years)	47.00 ± 17.42	45.06 ± 20.86	0.137
Ataxia severity (SARA score)	12.94 ± 9.08	11.82 ± 4.41	0.008 ^b

FA, Friedreich's ataxia; ICB, impulsive and compulsive behaviors; ILOCA, idiopathic late-onset cerebellar ataxia; MSA, multiple system atrophy; SARA, Scale for Assessment and Rating of Ataxia; SCA, Spinocerebellar ataxia (genetically).

^aDiagnosed via the qualitative interview of Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V).

^bIndependent *t* test.

^cChi-square test.

^dImmune-mediated ataxia, tacrolimus-induced ataxia, post-surgical cerebellar ataxia, Fragile X-associated tremor/ataxia syndrome.

2 weeks after T1) assessment. Thus, we assessed the interrater reliability by conducting intraclass correlation reliability test between the rater-rating scores (T1) and patient self-rating (P1) using these 41 cases' measurement. The total preliminary CIA has a strong correlation between rater rating scores and patient self-rating scores (Intraclass correlation coefficient for inter-rater reliability r = 0.849, $r^2 = 0.722$; 95% CI: 0.707–0.931, p < 0.001) (Fig. 2A). However, when we assessed the inter-rater reliability in each of the 17 questions, we found that 4 questions are below the good reliability standard (i.e., r > 0.7): Q1 (r = 0.515), Q13 (r = 0.653), Q15 (r = 0.700), and Q16 (r = 0.477) (Table S3). Therefore, we removed these four questions from the preliminary version of CIA (Fig. 1).

Test-retest reliability of CIA

Twenty-seven cases completed both T1 (i.e., the first measurement delivered by a trained rater) and T2 assessment (i.e., the second measurement by a trained rater). We then examined the test-retest reliability by conducting intraclass correlation reliability using these 27 cases' measurement. Again, the 17-item total preliminary CIA has a strong correlation between first rater-rating scores and the second rater-rating scores (Intraclass correlation coefficient for test-retest reliability r = 0.883, $r^2 = 0.780$; 95% CI: 0.788–0.937, p < 0.001) (Fig. 2B), demonstrating a good test-retest reliability. However, further analyses in

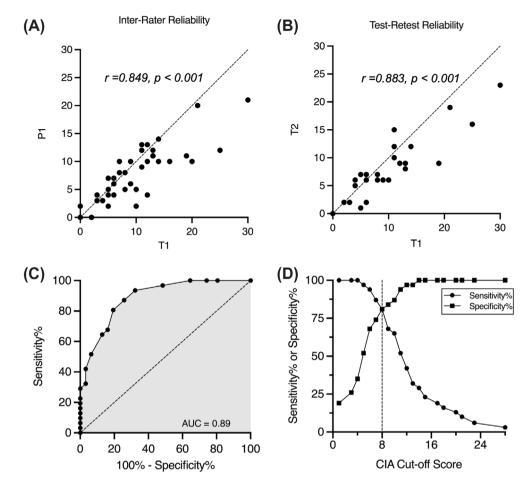


Figure 2. (A) The correlation between cerebellar ataxia cases' self-rating (P1) and trained trainer's first rating (T1). (B) The correlation between the same trainer's first rating (T1) and second rating (T2). (C) The receiver operating characteristic curve and its area under the curve value to exhibit the sensitivity and specificity of the cerebellar impulsivity and compulsivity assessment scale. (D) Sensitivity and specificity plot showing the cutoff CIA score of 8, as indicated by a dotted line. The time interval between T1 and P1 took place within 2 weeks, and the time interval between T1 and T2 was 2 to 6 weeks. The dotted line in Figure 2(A) and 2(B) is the bisector line (i.e., the line of identity). Total number of dots is less than 41 in Figure 2(A) and less than 27 in Figure 2(B) due to overlapping datapoints.

individual questions demonstrated that five questions did not reach the standard of good reliability (i.e., r > 0.7): Q2 (r = 0.669), Q11 (r = 0.429), Q12 (r = 0.574), Q13 (r = 0.526), and Q16 (r = 0.045) (Table S4). Therefore, these five questions were removed in the preliminary version of CIA (Fig. 1).

Sensitivity and specificity of CIA

After removing seven questions (i.e., Q1, 2, 11, 12, 13, 15, and 16) by examining the inter-rater reliability and test–retest reliability, we next assessed the sensitivity and specificity of this 10-question CIA in assessing ICBs in cerebellar ataxia. We plotted the sensitivity and specificity of ROC curve (AUC = 0.887, p < 0.001, Fig. 2C). We found the best possible cut-off value of total CIA score was 8.0

with sensitivity = 81% and specificity = 81% (Table S5, Fig. 2D). Given that AUC is greater than 0.7, our result demonstrated the validity of this final version of CIA scale (Table 2) to assess ICBs in cerebellar ataxia.

Validation cohort for the final CIA

To further replicate our own findings, we recruited a validation cohort (n = 15) with its demographics listed in Table S6. The AUC of the ROC analysis for CIA and cerebellar ICBs in this cohort was 0.830, p = 0.043. By selecting the cut-off score 8.0, the sensitivity was 60%, and the specificity was 80%. The sensitivities and specificities for the different cutoff values of the validation cohort was listed in the Table S7, showing the trend is overall on par with the discovery cohort (n = 62). C.-Y. R. Lin et al.

 Table 2. Cerebellar impulsivity and compulsivity scale.

nstruction: we are going to examine the broader domain of the emotion and affect affected by the of furthering the understanding of the cerebellum, which might lead to the therapeutics development	in the future if any of the cerebellar ataxia patients
have problems of such kind. Please answer/rate each question by circling the number, based on you	
Questions	Degree Scor
Q1: I make rash decisions/Do you or your family and friends feel that you tend to make rash	(0) None
decisions?	(1) Rarely
	(2) Sometimes
	(3) Often
	(4) Very often
Q2: I am not good at planning ahead/Do you or your family and friends feel that you are <u>not</u> good	(0) None
at planning ahead?	(1) Rarely
	(2) Sometimes
	(3) Often
	(4) Very often
Q3: Others might see me as irresponsible/Would people (family and friends) feel you irresponsible?	(0) None
	(1) Rarely
	(2) Sometimes
	(3) Often
	(4) Very often
24: Do you have any unpleasant thoughts, urges, or images that repeatedly enter your mind?	(0) None
	(1) Rarely
	(2) Sometimes
	(3) Often
	(4) Very often
25: Do you feel driven to perform certain behaviors or mental acts over and over again? Examples:	(0) None
washing hands, tapping the table, making sounds, pacing around, placing objects in a certain	(1) Rarely
order, storing a lot of objects, etc.	(2) Sometimes
	(3) Often
	(4) Very often
Q6: On average, how much <u>time</u> is occupied by these thoughts or behaviors each day?	(0) None $(1) < 1$ have a day
	(1) < 1 hour a day
	(2) $2-3$ hours a day
	(3) 3–8 hours a day
	(4) > 8 hours a day or more than half of
	the time you are awake
Q7: How much distress do these thoughts or behaviors cause you?	(0) None
	(1) Slightly disturbing
	(2) Disturbing, but manageable
	(3) Very disturbing
	(4) Overwhelming distress
28: How much <u>control</u> do you have over these thoughts or behaviors? How successful are you in	(0) Completely controllable
stopping or diverting these thoughts or behaviors? Can you dismiss them?	(1) Usually able to
	(2) Sometimes able or unable to
	(3) Most of the time unable to
	(4) Totally unable to
9: You have trouble not interrupting with people's conversation? You tend to interrupt with	(0) None
people's conversation, either filling in your opinion, words, or shouting out answers?	(1) Rarely
	(2) Sometimes
	(3) Often
	(4) Very often
210: Do you think a lot about how others perceive you? Are you concerned how others think	(0) None,
about you?	(1) Rarely
	(2) Sometimes
	(2) Sometimes (3) Often
	(4) Very often

 Total score of Q1-Q3 (impulsivity).
 _____.

 Total Score of Q4-Q8 (compulsivity)
 _____.

 Total score of Q9-Q10 (social appropriateness)
 _____.

 Total CIA score
 _____.

QUIP-RS in cerebellar ICBs

Among movement disorders, Parkinson's disease is the most well-known neurological disorder to have impulsive and compulsive symptoms. The current existing rating scale for impulsivity and compulsivity was primarily designed for Parkinson's disease, specifically the OUIP-RS. Thus, we further tested how the existing rating scale of impulsivity and compulsivity gearing toward Parkinson's disease performs in measuring ICBs in cerebellar ataxia patients. Our results showed that on ROC analysis, the AUC of total QUIP-RS for cerebellar ICBs was 0.557 (<0.7, unacceptable for differentiation those who have ICBs vs. without ICBs), p = 0.584 and the AUC of QUIP-RS ICD score for cerebellar ICBs was 0.509 (<0.7, unacceptable) for differentiation, p = 0.931. In addition, using Pearson's correlation, we found that there is no correlation between total CIA with total QUIP-RS (correlation coefficient r = 0.042, p = 0.818) or total CIA with QUIP-RS ICD scores (r = -0.069, p = 0.700), demonstrating the differences between CIA and QUIP-RS. These studies further demonstrate the differences between CIA and QUIP-RS, and support that CIA is specific in measuring cerebellar ICBs.

Domain-specific assessment of CIA

We next compared the scores of each domain in final CIA between cerebellar ataxia cases with and without ICBs. We found cerebellar ataxia cases with ICBs, compared to non-ICB cases, had significantly higher scores in the domains of impulsivity (3.58 \pm 2.21 vs. 1.39 \pm 1.40, p = 0.020, compulsivity (6.73 ± 4.06, vs. 0.83 ± 1.58, p < 0.001), and social appropriateness (3.54 \pm 2.06 vs. 2.19 \pm 1.72, p = 0.007) (Fig. 3). Our results exhibited that the factor analysis determinant of the final CIA version was 0.721 for the impulsivity (Q1 to Q4), 0.140 for compulsivity (Q5 to Q8), and 0.969 for social appropriateness (Q9 and Q10). All determinants were >0.001, indicating that the grouping of questions in each category represents the same construct, which further supports the use of final version of CIA to measure the overall cerebellar ICBs.

Discussion

In the present study, we developed a new scale, CIA, with 10 questions through an extensive validation process to tailor the ICB assessment in cerebellar ataxia. CIA exhibits good test–retest reliability and good inter-rater reliability when measuring ICBs in individuals with cerebellar ataxia. The ROC analysis is similar in the discovery and the validation cohort, further demonstrates the solidity of our findings.

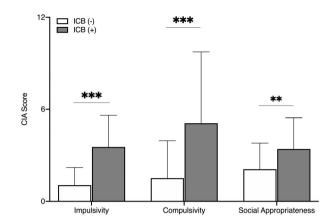


Figure 3. The cerebellar impulsivity and compulsivity scale domain comparisons in cerebellar ataxia cases with and without impulsive and compulsive behaviors. Significance: (*) p < 0.05, (**) p < 0.01, (***) p < 0.001.

Our results indicated that the scale designed to measure the impulsivity and compulsivity in Parkinson's disease, the QUIP-RS, is not an optimal tool to measure cerebellar ICBs. This is consistent with the recently reported findings of distinctive impulsive patterns between Parkinson's disease and cerebellar ataxia.²⁶ The traditional reward mesolimbic pathway connects the VTA to ventral striatum.^{19,41} Recent animal studies have exhibited the important role of the cerebellum in different stages of reward processing.9-13 Consistently, we found patients with cerebellar ataxia have increased ICBs, supporting the notion of abnormal reward processing.²⁴ Given that the impulsivity and compulsivity could greatly impact the quality of life for people living with ataxia and their families,²³ such as the non-planning impulsive traits (e.g., spending money without thinking about the consequences) identified in cerebellar ataxia,²⁶ a validated scale to allow further probing the mechanism of ICBs in cerebellar disorders is necessary. CIA can be used at bedside and office as a time and cost-effective screening tool. CIA can also be used to correlate with physiology or neuroimaging measurements to explore the mechanisms of the cerebellar contributions to reward processing. Moreover, the CIA is an outcome based on the patient report, which can potentially be implemented in future clinical trials as a non-motor measure for ataxia. Recently, the cerebellar cognitive affective syndrome (CCAS) scale was developed to quantify the cognitive and behavioral dysfunction severity in cerebellar ataxia.^{4,8,42,43} In addition to CCAS which serves as a performance test, the patient-reported outcome measure of ataxia was recently developed to measure the degree of patient care improvement and clinical trial application.⁴⁴

Structural change of the cerebellum and cerebro-cerebellar network alteration contribute to the non-motor features in multiple neurodevelopmental and neurodegenerative diseases.^{45–50} Along this line, it would be of importance to conduct future studies to examine the functional connectivity and structural alterations between the cerebellum and other reward regions in the mesolimbic and mesocortical pathways to further the understanding of the cerebellar ICBs, a part of the cerebellar cognitive affective syndrome. To our knowledge, this is the first study to demonstrate a validated scale for ICBs in cerebellar disorders, which will serve as the basis for future mechanistic studies in patients.

The limitation of the present study is that part of the CIA questions were modified from existing scales, the DSM-V and Yale-Brown Obsessive Compulsive Scale which has been extensively used in clinical and research settings.³¹⁻³³ It is possible that other ICBs may be specific to cerebellar disorders and thus not entirely captured. In addition, cerebellar ataxia cases in the present study are of various diagnoses, often involving the extra-cerebellar brain structures. To elaborate on the selection of cases with "pure" cerebellar involvement, future research should focus on recruiting SCA6 cases or cases with cerebellar lesions. The prevalence of ICBs in the ataxia population is not well studied; therefore, applying CIA needs to consider positive and negative predictive values, and different thresholds of CIA to detect ICBs may be considered in the different population. Future studies are needed to broadly understand ICBs in cerebellar ataxia.

As we began to understand the cognitive and behavioral function of the cerebellum, CIA can serve as a tool that can be broadly implemented to study ICBs, decision making, and reinforcement reward and also be a potential clinical outcome measurement to assess therapeutic effects on ICBs in this population.

Author Contributions

Chi-Ying R. Lin: study concept, study supervision, data interpretation, manuscript draft, and critical revision; Nadia Amokrane: study coordination and data acquisition; Serena Chen: data acquisition; Tiffany X. Chen: data acquisition, statistical analysis, and figure making; Ruo-Yah Lai: data acquisition; Paula Trinh: data acquisition; Michael J. Minyetty: data acquisition; Haidyn Emmerich: data acquisition; Ming-Kai Pan: critical revision of the manuscript for important intellectual content; Daniel Claassen: study concept, critical revision of the manuscript for important intellectual content; Sheng-Han Kuo: study concept, study supervision, data interpretation, and critical revision of the manuscript for important intellectual content.

Conflict of Interest

All authors report no disclosures relevant to the manuscript.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. The preliminary version of the cerebellar impulsivity and compulsivity scale with a total of 17 questions.

Table S2. Internal consistency examination of the preliminary version of the cerebellar impulsivity and compulsivity scale.

Table S3. Inter-rater reliability examination of the preliminary version of the cerebellar impulsivity and compulsivity scale. Questions not meeting the standard of good reliability (i.e., r > 0.7) were removed.

Table S4. Test–retest reliability examination of the preliminary version of the cerebellar impulsivity and compulsivity scale. Questions not meeting the standard of good reliability (i.e., r > 0.7) were removed.

 Table S5.
 Sensitivities and specificities for the selected cutoff value based on the receiver operating characteristics

curve for the cerebellar impulsivity–compulsivity assessment scale on the 62 ataxia cases with and without impulsivity and compulsivity behaviors. CIA, cerebellar impulsivity-compulsivity assessment.

Table S6. The demographics of the validation cohort with 15 newly recruited cerebellar ataxia cases to test the final cerebellar impulsivity–compulsivity assessment scale. ICB, impulsive and compulsive behaviors; ILOCA, idiopathic late-onset cerebellar ataxia; MSA, multiple system atrophy; SARA, Scale for Assessment and Rating of Ataxia; SCA, Spinocerebellar ataxia (genetically). ^aIndependent t test; ^bChi-Square test. *Diagnosed via the qualitative interview of Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V).

Table S7. Sensitivities and specificities for the selected cutoff value based on the receiver operating characteristics curve for the cerebellar impulsivity–compulsivity assessment scale on the 15 validation cases with and without impulsivity and compulsivity behaviors. CIA, cerebellar impulsivity-compulsivity assessment.