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The cerebellar cognitive affective/Schmahmann syndrome scale

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Cerebellar cognitive affective syndrome (CCAS; Schmahmann's syndrome) is characterized by deficits in executive function, linguistic processing, spatial cognition, and affect regulation. Diagnosis currently relies on detailed neuropsychological testing. The aim of this study was to develop an office or bedside cognitive screen to help identify CCAS in cerebellar patients. Secondary objectives were to evaluate whether available brief tests of mental function detect cognitive impairment in cerebellar patients, whether cognitive performance is different in patients with isolated cerebellar lesions versus complex cerebrocerebellar pathology, and whether there are cognitive deficits that should raise red flags about extra-cerebellar pathology. Comprehensive standard neuropsychological tests, experimental measures and clinical rating scales were administered to 77 patients with cerebellar disease—36 isolated cerebellar degeneration or injury, and 41 complex cerebrocerebellar pathology—and to healthy matched controls. Tests that differentiated patients from controls were used to develop a screening instrument that includes the cardinal elements of CCAS. We validated this new scale in a new cohort of 39 cerebellar patients and 55 healthy controls. We confirm the defining features of CCAS using neuropsychological measures. Deficits in executive function were most pronounced for working memory, mental flexibility, and abstract reasoning. Language deficits included verb for noun generation and phonemic > semantic fluency. Visual spatial function was degraded in performance and interpretation of visual stimuli. Neuropsychiatric features included impairments in attentional control, emotional control, psychosis spectrum disorders and social skill set. From these results, we derived a 10-item scale providing total raw score, cut-offs for each test, and pass/fail criteria that determined 'possible' (one test failed), 'probable' (two tests failed), and 'definite' CCAS (three tests failed). When applied to the exploratory cohort, and administered to the validation cohort, the CCAS/Schmahmann scale identified sensitivity and selectivity, respectively as possible exploratory cohort: 85%/74%, validation cohort: 95%/78%; probable exploratory cohort: 58%/94%, validation cohort: 82%/93%; and definite exploratory cohort: 48%/100%, validation cohort: 46%/100%. In patients in the exploratory cohort, Mini-Mental State Examination and Montreal Cognitive Assessment scores were within normal range. Complex cerebrocerebellar disease patients were impaired on similarities in comparison to isolated cerebellar disease. Inability to recall words from multiple choice occurred only in patients with extra-cerebellar disease. The CCAS/Schmahmann syndrome scale is useful for expedited clinical assessment of CCAS in patients with cerebellar disorders.

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Abbreviations: BARS = Brief Ataxia Rating Scale; CCAS = cerebellar cognitive affective syndrome; CNRS = Cerebellar Neuropsychiatric Rating Scale; D-KEFS = Delis Kaplan Executive Function System; DSB = Digit Span Backward; DSF = Digit Span Forward; FRSBE = Frontal System Behavior Scale; JLO = Judgement of Line Orientation test; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; SCDC = Social and Communication Disorder Checklist; WAIS-IV = Wechsler Adult Intelligence Scale–fourth edition; WIAT-II = Wechsler Individual Achievement Test–second edition

Introduction

Cerebellar cognitive affective syndrome (CCAS) is characterized by deficits in executive function, linguistic processing, spatial cognition and affect regulation (Schmahmann and Sherman, 1998). It arises from damage to the cognitive cerebellum in the cerebellar posterior lobe (lobules VI, VII, possibly lobule IX), and is postulated to reflect dysmetria of thought analogous to the dysmetria of motor control from damage to the sensorimotor cerebellum in the anterior lobe (lobules III–V) and lobule VIII (Schmahmann, 1991, 1996, 2010; Schmahmann and Sherman, 1998; Stoodley and Schmahmann, 2009*a*, 2010; Stoodley *et al.*, 2012, 2016). The CCAS may occur separately or together with the cerebellar motor syndrome and the vestibular syndrome from damage to the flocculonodular lobe, and is the third cornerstone of clinical ataxiology (Schmahmann's syndrome; Manto and Mariën, 2015).

The defining features of CCAS have been replicated in studies across disease types and in patients of different ages (Malm *et al.*, 1998; Levisohn *et al.*, 2000; Neau *et al.*, 2000; Riva and Giorgi, 2000; Exner *et al.*, 2004; Paulus *et al.*, 2004; Van Harskamp *et al.*, 2005; Schmahmann *et al.*, 2007; Caroppo *et al.*, 2009; Mariën *et al.*, 2009, 2014; Fallows *et al.*, 2011; Tedesco *et al.*, 2011; Wingeier *et al.*, 2011; Hoche *et al.*, 2014; Koziol *et al.*, 2014; Van Overwalle *et al.*, 2015; Adamaszek *et al.*, 2017). Diagnosis presently relies on neuropsychological testing, although the traditional behavioural neurology approach to bedside cognitive testing (Critchley 1953; Heilman and Valenstein, 1979; Mesulam, 1985; Strub and Black, 2000) was the basis for the original diagnosis of cognitive and neuropsychiatric impairment in patients with cerebellar injury and the formulation of the concept of CCAS (Schmahmann and Sherman, 1998). There is presently no reliable or validated brief test of mental function to elicit the presence of CCAS in a patient with cerebellar dysfunction analogous to the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975) or the Montreal Cognitive Assessment (MoCA) (Nasreddine *et al.*, 2005), which were developed to detect patients with amnestic and other dementias. There is, therefore, a critical need for a concise screening battery of cognitive tasks proven to be sensitive for the detection of CCAS to determine whether an individual with cerebellar dysfunction has the non-motor manifestations of the cerebellar lesion.

The principal objectives of this study were (i) to examine the neuropsychological profile in a large cohort of patients with lesions of the cerebellum to test and further explore the original conclusions regarding CCAS; and (ii) to investigate the resulting pattern of strengths and deficits to develop a cerebellar cognitive test battery for use in the office or bedside setting sensitive to the deficits of CCAS, and selective enough to differentiate patients from healthy controls. Our secondary objectives were (iii) to evaluate whether the MMSE and MoCA detect cognitive impairment in cerebellar patients; and (iv) whether cognitive performance is different in patients with isolated cerebellar lesions versus those with complex cerebrocerebellar pathology. We took advantage of the inclusion of some patients with advanced cerebrocerebellar pathology to examine (v) whether there are cognitive skills assessed in the neuropsychological test battery or the resulting short test of cerebellar cognition that should raise red flags (Köllensperger *et al.*, 2008) about pathology outside the cerebellum (i.e. what can reasonably be considered non-cerebellar cognition?). Finally, (vi) we validated this new scale in another cohort of cerebellar patients and matched controls.

Subjects and methods

Participants

Adult patients were recruited from the Ataxia Unit of the Massachusetts General Hospital Department of Neurology with hereditary or other neurodegenerative ataxias, or acquired injury to the cerebellum. Detailed history was elicited, neurological examination performed, and brain MRI evaluated. Group assignments of patients into isolated cerebellar disease, isolated cerebellar injury and complex cerebrocerebellar disease were based on analysis of genotypes, published pathological features of the spinocerebellar ataxias and related disorders (Koeppen, 2002; Lin *et al.*, 2014, 2016), and expert consensus criteria (Manto *et al.*, 2013). Seventy-seven patients (age range 17–80 years, 42 males, mean education 15.01 years) were included in the study, of whom 36 had disease confined to cerebellum. Demographics are listed in Table 1. Radiographic images representative of every diagnosis encountered in the study are presented in the Supplementary Fig. 1. Fifty-eight healthy controls were matched for age, gender and education (matching age interval 5 years, education intervals $\leqslant$12 years, 13–16 years, $\geqslant$18 years, gender male or female). Two controls were excluded because of test anxiety, and two because of previously undisclosed attention deficit disorder. This study was approved by the Institutional Review Board of the Massachusetts General Hospital. Written, informed consent was obtained from all participants.

Cognitive assessment

Neuropsychological assessment comprised standard tests from widely-used neuropsychological test batteries (e.g. Wechsler Adult Intelligence Scales, WAIS; Wechsler, 2008) and experimental tasks derived from functional neuroimaging studies showing cerebellar activation (e.g. verb for noun task; Fiez, 1996). Patient performance was compared to standard norms and healthy controls. Supplementary Table 2 lists the tests administered and the domains they are thought to represent. Some tests tap functions that cover more than one domain, as exemplified by phonemic and semantic fluency, which are language tasks that also reflect executive search functions and semantic memory (Shao *et al*., 2014).

Neuropsychiatric assessment

In our earlier analysis that introduced the concept of the neuropsychiatry of the cerebellum, patients demonstrated, or family members reported, neuropsychiatric phenomena that were categorized according to five domains of behaviour—attentional control, emotional control, autism spectrum, psychosis spectrum, and social skill set (Schmahmann *et al*., 2007). Within each of these five domains, symptoms were further grouped according to hypermetric/overshoot/positive and hypometric/undershoot/negative symptoms (Supplementary Table 3). Based on this approach, we developed a novel test instrument, the Cerebellar Neuropsychiatric Rating Scale (CNRS) (Daly *et al*., 2016), which we used in this study. The CNRS was completed by first degree relatives of the patients and healthy controls. It was complemented by use of the Frontal System Behavior Scale (FRSBE) (Grace *et al*., 1999) and the Social and Communication Disorder Checklist (SCDC) (Skuse *et al*., 1997) (Supplementary Table 2).

Neurological examination and assessment of ataxia severity

A comprehensive medical and neurological history and examination was documented for every patient. The cerebellar

Table 1 Exploratory cohort: patient diagnoses and demographic features

Disease entity	Patients *n*	Gender (F/M)	Age (years, mean)	Education (years, mean)
Isolated cerebellar pathology				
Left cerebellar injury (L-haemorrhage, L-tumour, L-SCA stroke)	3	1/2	54.6	17.0
Posterior fossa injury [medulloblastoma, haemorrhage (*n* = 2)]	3	1/2	28.3	15.0
Right cerebellar injury [R-PICA stroke, R-SCA stroke (*n* = 2)]	3	2/1	43.0	16.0
Post-infectious cerebellitis	1	1/0	33.0	12.0
Non-progressive isolated cerebellar ataxia	2	1/1	19.0	13.0
SCA5	1	0/1	56.0	16.0
SCA6	6	3/3	61.7	15.2
SCA8	4	3/1	57.5	15.0
ARCA-1	3	1/2	50.8	15.1
EA-2	2	1/1	23.5	13.0
ILOCA	8	3/5	47.9	15.0
Complex cerebro-cerebellar pathology				
Cerebellar and brainstem haemorrhage	2	1/1	64.0	18.0
Complex cerebrocerebellar degeneration with gene variants[a]	2	1/1	58.0	14.3
Pontine cavernous malformation	1	1/0	45.0	14.0
AOA2	1	1/0	20.0	14.0
Friedreich's ataxia	2	0/2	41.5	16.0
SCA1	7	3/1	59.4	14.3
SCA2	5	2/3	54.5	14.8
SCA3	12	6/6	56.3	14.6
SCA7	2	0/2	62.0	16.0
SCA17	1	1/0	48.0	16.0
MSA-C	6	3/3	57.3	14.5

Seventy-seven patients were investigated (isolated cerebellar pathology, *n* = 36; complex cerebrocerebellar pathology, *n* = 41).

AOA2 = ataxia oculomotor apraxia type 2; ARCA-1 = autosomal recessive cerebellar ataxia type 1, DRPLA = dentatorubropallidoluysian atrophy; EA-2 = episodic ataxia type 2; ILOCA = idiopathic late onset cerebellar ataxia; L = left; MSA-C = multiple system atrophy of the cerebellar type; PICA = posterior inferior cerebellar artery; R = right, s/p = status post; SCA = spinocerebellar ataxia; SCA stroke = infarction in the territory of the superior cerebellar artery.

[a]Complex cerebrocerebellar degeneration with gene variant: one patient with late onset cerebellar ataxia with white matter hyperintensities and mutational variant in senataxin (*SETX*) gene; one with late onset cerebellar ataxia, peripheral motor neuropathy and variant X-linked recessive *ATP2B3* gene.

motor syndrome was evaluated, and ataxia severity was assessed by means of the Brief Ataxia Rating Scale (BARS) (Schmahmann *et al.*, 2009; Supplementary Table 4). This clinical score assesses the five cardinal motor manifestations of the cerebellar motor syndrome, namely, gait, lower extremity and upper extremity dysmetria, dysarthria, and oculomotor abnormalities. The maximum severity score is 30: a normal exam scores 0, mild cerebellar motor syndrome 1–9, moderate cerebellar motor syndrome 10–20, and severe cerebellar motor syndrome >20. Motor performance was also evaluated using 25-foot timed walk and 9-Hole Pegboard Test (9HPT; Mathiowetz *et al.*, 1985).

Data analysis

Analysis of cognitive performance in comparison to standard norms and controls

Thirty-six tests were administered [e.g. Delis-Kaplan-Executive Function System (D-KEFS)], providing 71 measures (e.g. set loss errors within D-KEFS), each of which was scored (Table 2). Behavioural data were analysed using SSPS v21 (SSPS Inc.). All tests were administered in their English version, and USA reference norms were used for standard tests. Raw scores were converted to z-scores measuring deviation from the mean to compare all measures on a common scale. Z-scores were calculated using normative data for standardized tests, or control data from our study, e.g. for the oral sentence production test. Each patient was then matched with a group of controls of the same gender and similar age and years of education. A multivariate comparison between patients and controls within each cognitive domain was performed using Hotelling's T square test (Hotelling, 1931). This was followed by one-tailed paired Student's *t*-test for each individual test. Tests that were not significantly different between patients and controls were excluded from further analysis. Differences in cognitive performance between patient groups (complex cerebrocerebellar disease, isolated cerebellar disease, isolated cerebellar injury) were analysed using one-way ANOVA.

Development of the cerebellar cognitive affective/Schmahmann syndrome scale

To develop the CCAS scale the data were analysed in the following manner:

(i) Since some patients were unable to complete all tests because of fatigue or time constraints, data were analysed only for those missing $<15\%$ of the test items. We excluded tests in which the difference between mean raw scores of patients and controls reached significance but the absolute value difference was not sufficient to allow for derivation of a clear diagnostic cut-off (e.g. months backwards raw score, Table 2).

(ii) The remaining tests were ranked by group differences in mean z-scores. From this ranking, tests were selected that met the *a priori* requirement representing the core CCAS domains—executive, linguistic, visual spatial, and affective.

(iii) Tests inappropriately lengthy for a screening instrument were excluded. These included tests for which the number of items could not be meaningfully reduced, e.g. verb for noun generation; or those requiring repeated administration across a delay of >10 min, e.g. verbal paired associates delayed recall.

(iv) A threshold (or cut-off) was then applied to maximize selectivity to prevent diagnosing controls as patients. A secondary aim was to maintain reasonable sensitivity, i.e. detecting the deficits that would indicate that a patient belongs in the patient group. We emphasized selectivity in determining thresholds to prevent overly optimistic sensitivity. Raw scores of individual controls were used to calculate cut-offs.

(v) A final item in the scale captures subjective assessment of affective range, derived from the CNRS questions that survived into the final rank order of cumulative diagnosis.

(vi) We then used Cronbach's alpha (Cronbach, 1951), a measure of internal consistency, to assess the inter-relatedness of the items within the test, i.e. whether all test items in the scale measure the same concept—in this case, the same cognitive domain. Using this coefficient of inter-item correlations, Cronbach $\alpha \geqslant 0.7$ represents acceptable internal consistency, $\geqslant 0.8$ is good and $\geqslant 0.9$ is excellent. A Cronbach $\alpha \leqslant 0.6$ is poor (Cronbach, 1951; Nunnaly, 1978; Loewenthal, 2004).

Validation of the cerebellar cognitive affective/Schmahmann syndrome scale

The resulting novel scale was then validated in 39 new patients with cerebellar diseases (Table 3) and 55 healthy control subjects.

Results

Analysis of cognitive performance in comparison to standard norms and controls

Performance on current brief tests of cognition

On the MMSE, patients and controls tested within the normal range ($\geqslant 25$; Folstein *et al.*, 1975). Patient mean = 28.70, standard deviation (SD) 1.25; control mean 29.56, SD 0.72, not significant (Supplementary Table 5).

On the MoCA, mean performance of both the patient and control groups was in the normal range, i.e. $\geqslant 26$. This result obscures the finding that patient mean scores (26.45, SD 2.52) were lower than control mean scores (28.77, SD 1.22, $P < 0.001$), that patients were impaired on a number of subscores within the MoCA battery (Supplementary Table 5), and that of the 35 patients who completed all MoCA items, six scored $\leqslant 25$. Further, some

Table 2 Performance of patients and controls on tests of cognitive and emotional processing

	Hotelling's T square *F*	Hotelling's T square *P*	Patients				Controls				One tailed paired *t*-test		
			Raw		z		Raw		z		*t*	*df*	*p*
			Mean	SD	Mean	SD	Mean	SD	Mean	SD			
EXECUTIVE FUNCTION TESTS													
Trails A (s)	20.535	0.000	51.65	23.14	−2.29	2.94	24.55	5.47	0.88	0.72	−8.133	62	0.000
Trails B (s)			124.07	79.99	−6.72	24.73	57.29	15.64	0.58	0.9	−6.535	62	0.000
Trails B − Trails A (s)			60.19	65.13	−1.11	3.22	32.74	13.29	−0.3	0.72	−2.156	76	0.017
Category switching accuracy (TC)			**10.25**	**3.3**	**−0.49**	**1.15**	**13.82**	**1.45**	**0.78**	**0.51**	**−7.235**	**49**	**0.000**
Category switching set loss (TM)			0.6	1.08	0.12	1.15	0.34	0.54	−0.16	0.57	1.692	56	0.048
Total D-KEFS set loss (TM)			1.55	1.61	0.21	0.69	0.95	1.6	0.61	0.49	−3.675	49	0.001
D-KEFS repetition errors (TM)			1.45	1.82	0.27	0.75	1.76	1.26	0.26	0.43	0.258	49	0.399
Letter-number sequencing (TS/2)			0.97	0.89	−0.55	1.14	1.19	0.65	−0.26	0.83	−2.012	66	0.024
Letter-number sequencing time (s)			83.31	30.15	0.91	1.36	63.75	16.03	0.03	0.72	3.702	45	0.001
Go/No-go Test (TS/2)			**1.09**	**0.87**	**−1.41**	**1.75**	**1.8**	**0.3**	**0.03**	**0.61**	**−6.381**	**63**	**0.000**
Go/No-go Test omissions (TM)			0.04	0.28	n.a.	n.a.	0	0	n.a.	n.a.	1	51	0.161
Go/No-go Test commissions (TM)			1.21	1.23	3.16	3.59	0.1	0.15	−0.1	0.45	6.55	51	0.000
VERBAL MEMORY TESTS													
Word immediate recall (TS/5)	33.025	0.000	4.88	0.4	−0.7	2.94	4.94	0.16	−0.28	1.18	−1.134	68	0.131
Word delayed recall (TS/15)			**12.09**	**3.33**	**−1.17**	**2.2**	**13.8**	**0.73**	**−0.03**	**0.48**	**−3.987**	**68**	**0.000**
Verbal paired associates - I (TS/32)			16.89	9.52	0.08	1.19	23.03	2.98	0.78	0.49	−4.354	59	0.000
Learning slope			2.48	2.8	−0.52	1.06	4.29	1.24	0.18	0.56	−4.304	59	0.000
Verbal paired associates - II (TS/8)			5.46	2.63	0.13	1.02	7.28	0.64	0.81	0.4	−4.683	58	0.000
WORKING MEMORY TESTS													
DSF (TS/16)	106.353	0.000	9.94	2.38	−0.08	0.95	11.79	1.82	0.47	0.51	−4.698	60	0.000
Longest DSF (TS/9)			**6.25**	**1.19**	**−0.77**	**0.91**	**7.29**	**0.91**	**0.02**	**0.69**	**−5.7**	**62**	**0.000**
DSB (TS/16)			7.81	2.16	−0.25	0.87	11.36	2.09	1.12	0.79	−9.408	59	0.000
Longest DSB (TS/8)			**4.56**	**1.13**	**−1.1**	**0.72**	**6.2**	**1.05**	**−0.05**	**0.67**	**−8.541**	**61**	**0.000**
Months backwards (TS/1)			0.87	0.38	−0.47	1.94	0.97	0.14	0.02	0.71	−1.997	68	0.025
Months backwards time (s)			18.55	9.79	0.64	1.22	13.63	5.45	0.03	0.68	2.515	46	0.008
LINGUISTIC TESTS													
Production of Derived Words (TS/5)	25.002	0.000	4.72	0.69	−1.72	4.57	5	0.04	0.12	0.25	−2.694	45	0.005
Oral Sentence Production (TS/20)			19.26	1.37	−0.38	1.47	19.72	0.53	0.12	0.56	−1.982	37	0.028
Word Repetition (TS/4)			3.94	0.25	−0.3	1.71	4	0.02	0.13	0.11	−1.675	46	0.051
Verb for Noun (TS/17)			12.72	3.25	−6.05	5.37	16.62	0.37	0.39	0.62	−8.342	49	0.000
Pseudoword Decoding at 60 s (TS/52)			40.27	8.92	−1.55	2.24	44.71	2.84	−0.44	0.71	−4.153	45	0.000
Pseudoword Decoding at 30 s (TS/52)			22.6	6.67	−1.55	1.04	28.98	4.5	−0.55	0.7	−6.015	41	0.000
Word Stem Completion (TS/22)			21.27	1.11	−1.67	3.15	21.96	0.15	0.28	0.42	−4.272	48	0.000
Naming (TS/3)			2.88	0.4	n.a.	n.a.	3	0	n.a.	n.a.	−1.955	39	0.029
Phonemic fluency (TC) (F,A,S words in 3 min)			**32.3**	**12.66**	**−0.51**	**1.29**	**50.04**	**6.75**	**1.27**	**0.64**	**−8.434**	**49**	**0.000**
F-letter phonemic fluency (TC) (/1 min)			10.90	4.82	−0.96	0.83	16.20	2.75	−0.05	0.48	−7.308	59	0.000
A-letter phonemic fluency (TC) (/1 min)			9.5	4.42	−1.27	0.94	15.40	2.72	−0.01	0.58	−9.009	59	0.000
S-letter phonemic fluency (TC) (/1 min)			11.48	4.75	−1.23	0.85	18.38	2.63	0.01	0.47	−10.891	59	0.000

(continued)

Table 2 Continued

	Hotelling's T square *F*	Hotelling's T square *P*	Patients				Controls				One tailed paired *t*-test		
			Raw		z		Raw		z		*t*	*df*	*p*
			Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Semantic fluency (TC) (Animals and Boys' names in 2 min)			**32.82**	**8.54**	**−0.7**	**1.19**	**45.61**	**6.27**	**1.02**	**0.63**	**−8.335**	**49**	**0.000**
Animals semantic fluency (TC) (/1 min)			17.06	5.08	−0.91	0.80	22.29	3.88	−0.09	0.61	−6.306	59	0.000
Boys' names fluency (TC) (/1 min)			15.85	4.20	−0.99	0.64	22.34	4.25	0.00	0.65	−8.467	58	0.000
VISUAL-SPATIAL ABILITY TESTS													
Star (TS/1)	29.917	0.000	0.92	0.27	−0.45	2	1	0	0.14	0	−2.313	61	0.012
Pentagon (TS/1)			0.94	0.25	−0.33	1.25	0.97	0.12	−0.17	0.6	−1.12	61	0.134
Cube (TS/2)			**1.52**	**0.72**	**−0.91**	**1.43**	**1.93**	**0.13**	**−0.1**	**0.26**	**−4.442**	**61**	**0.000**
Clock (TS/5)			4.39	0.93	−0.72	1.47	4.75	0.56	−0.15	0.88	−2.97	58	0.002
JLO (TS/15)			11.57	3.49	0.13	1.07	13.08	1.58	0.57	0.42	−3.233	58	0.001
ABSTRACT REASONING TESTS													
Addition (TS/6)	34.577	0.000	5.48	0.78	−0.29	1.19	5.77	0.36	0.15	0.55	−2.613	62	0.006
Subtraction (TS/6)			5.05	1.05	−0.97	1.76	5.69	0.4	0.11	0.67	−4.387	62	0.000
Similarities (TS/36)			**22.33**	**6.68**	**−0.38**	**0.98**	**28.09**	**2.95**	**0.73**	**0.6**	**−7.032**	**58**	**0.000**
Cognitive estimation (TS/4)			3.51	0.56	−3.27	3.89	3.99	0.06	0.05	0.45	−5.291	38	0.000
BEDSIDE TESTS OF OVERALL COGNITIVE FUNCTION													
MMSE (TS/30)	0.480	0.621	28.7	1.25	−0.05	0.78	28.46	2.86	−0.26	1.87	0.156	34	0.439
Planning (TS/2)			1.92	0.27	n.a.	n.a.	2	0	n.a.	n.a.	−1.781	37	0.042
ATTENTION AND VIGILANCE TESTS													
DSF (TS/16)	87.948	0.000	9.94	2.38	−0.08	0.95	11.79	1.82	0.47	0.51	−4.698	60	0.000
Longest DSF (TS/9)			**6.25**	**1.19**	**−0.77**	**0.91**	**7.29**	**0.91**	**0.02**	**0.69**	**−5.7**	**62**	**0.000**
Vigilance (TS/1)			0.91	0.29	−0.23	1.45	1	0	0.17	0	−1.776	41	0.042
FRSBE													
Total score (self rating) (TS/255)	24.517	0.000	99.19	23.71	1.21	0.95	73.69	9.11	−0.23	0.67	9.908	54	0.000
Apathy (self rating) (TS/85)			31.95	8.95	1.2	1.12	22.15	3.16	−0.22	0.67	7.985	54	0.000
Disinhibition (self rating) (TS/85)			29.4	8.5	0.64	1.24	23.89	3.42	0.03	0.81	3.567	54	0.001
Dysexecutive (self rating) (TS/85)			39.79	9.63	1.16	1.01	27.61	4.24	−0.27	0.7	8.823	54	0.000
Total score (family rating) (TS/255)			98.02	29.66	1.13	1.24	73.21	11.08	0.06	0.94	5.465	38	0.000
Apathy (family rating) (TS/85)			32.37	9.92	1.35	1.07	22.14	3.77	0.07	0.63	6.731	38	0.000
Disinhibition (family rating) (TS/85)			27.41	11.4	0.51	1.36	22	2.65	0.06	0.68	2.442	38	0.010
Dysexecutive (family rating) (TS/85)			39.73	12.68	1.06	1.22	29.32	6.28	0.28	0.95	4.18	38	0.000
SOCIAL COMMUNICATION DISORDERS CHECKLIST													
Total (TS/24)	n.a.	n.a.	6.39	5.77	0.88	1.45	2.79	2.39	−0.03	0.6	4.086	39	0.000
CEREBELLAR NEUROPSYCHIATRIC SCALE													
Social skill negative (TS/12)	5.329	0.000	2.08	2.30	0.80	1.54	0.79	0.89	−0.06	0.60	3.138	38	0.002
Social skill positive (TS/12)			3.08	2.49	1.36	1.83	1.32	1.10	0.07	0.81	3.842	38	0.000
Emotion regulation negative (TS/12)			3.40	2.48	1.85	1.91	0.97	1.36	−0.02	1.05	5.327	39	0.000
Emotion regulation positive (TS/12)			3.18	2.40	1.52	2.02	1.54	0.80	0.14	0.67	3.982	39	0.000
Autism spectrum negative (TS/6)			1.72	1.39	1.41	1.66	0.61	0.62	0.09	0.74	4.713	38	0.000
Autism spectrum positive (TS/6)			0.69	0.89	0.43	1.11	0.44	0.62	0.11	0.77	1.241	35	0.112

(continued)

Table 2 Continued

	Hotelling's T square F	Hotelling's T square P	Patients				Controls				One tailed paired t-test		
			Raw		z		Raw		z		t	df	p
			Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Psychosis spectrum negative (TS/9)			2.28	2.32	1.57	2.16	0.62	1.03	0.02	0.96	4.328	38	0.000
Psychosis spectrum positive (TS/9)			0.87	1.13	2.63	3.81	0.19	0.30	0.33	1.03	3.6	38	0.001
Attention spectrum negative (TS/12)			4.37	3.39	0.78	1.53	3.69	2.24	0.47	1.01	1.076	42	0.144
Attention spectrum positive (TS/12)			3.40	2.31	0.44	1.22	2.86	1.60	0.16	0.84	1.215	42	0.116

Multivariate analysis of the difference in means of each measure between patient groups and controls using Hotelling's t-square test followed by Student's *t*-tests (Hotelling, 1931). Notice that all test domains revealed significant Hotelling's *F*-values except for short bedside tests of cognitive function (MMSE). Tests that were included in the CCAS/Schmahmann scale are highlighted in bold.
n.a. = not available for statistical reasons; TC = total correct responses; TM = total number of mistakes; TS/x = total score out of a maximum score of x.

patients passed selected MoCA tests when MoCA cut-offs were applied but were impaired compared to controls when the tests were administered as designed and normed on standard tests. This is exemplified by the full Trails B minus Trails A test, and by the digit span task where patients exceeded MoCA normal thresholds (five digits forwards, three backwards) but were significantly impaired compared to controls with more rigorous tests (Table 2).

Confirmation of CCAS in cerebellar patients

Patients demonstrated executive, linguistic, visual spatial and affective impairments, the defining characteristics of CCAS.

Executive function

Standard neuropsychological testing (WAIS-IV; Wechsler, 2008) revealed that cerebellar patients were impaired compared to controls on Trails A ($P < 0.001$) and Trails B ($P < 0.001$). Trails B produced more pronounced deficits than Trails A (Trails B – Trails A, $P = 0.017$) indicating difficulties with cognitive set shifting. Patients experienced impaired verbal cognitive set shifting as measured by category switching tasks: the fruit-furniture naming test in the D-KEFS (Delis *et al.*, 2001) showed lower accuracy ($P < 0.001$) and more set loss errors ($P < 0.048$), as did letter number sequencing with more set loss errors ($P < 0.024$) and slowed overall cognitive processing time ($P < 0.001$).

The letter number sequencing test also evaluates verbal working memory. Deficits in verbal working memory were further substantiated by the standard version of the digit span task (WAIS-IV) including impairments on the forward digit span, a measure of attention, [Digit Span Forwards (DSF), $P < 0.001$] and even more affected on the reverse digit span, a measure of verbal working memory [Digit Span Backwards (DSB), $P < 0.001$] (Wechsler, 2008).

The go/no-go task was impaired because of commission errors, indicating deficits with sustained attention as well as impulse control and disinhibition ($P < 0.001$).

Language

Deficits in patients versus controls were identified on phonemic and semantic fluency tests (D-KEFS test; both $P < 0.001$). Phonemic fluency was more impaired than semantic ($P < 0.001$); controls provided an average of 4.3 more correct phonemic fluency answers than patients. Cerebellar patients were also impaired on pseudo-word decoding [Wechsler Individual Achievement Test; second edition (WIAT-II); $P < 0.001$] and the verb for noun generation task (Fiez, 1996; $P < 0.001$).

Visual-spatial function

Judgement of line orientation (JLO; Benton *et al.*, 1983) was impaired ($P = 0.001$), as was the draw a clock test

Table 3 Validation cohort: patient diagnoses and demographic features

Disease entity	Patients *n*	Gender (F/M)	Age (years, mean)	Education (years, mean)
Isolated cerebellar pathology				
Right cerebellar infarction s/p meningioma resection	1	F	68	16
Spontaneous large R > L and midline cerebellar haemorrhage	1	F	30	18
Ischaemic cerebellar infarction–L anterior lobe and lobule VI; R hemispheric lobules VI and VII; L. paramedian pons	1	M	47	18
Midline and left cerebellar hemisphere infarction s/p partial cerebellar resection	1	F	59	16
Midline and bilateral paramedian cerebellar encephalomalacia s/p pineal gland resection	1	M	42	18
Schizoaffective disorder exacerbated by L-PICA infarction	1	M	32	16
Cerebellar AVM with L-cerebellar haemorrhage	1	M	62	16
L-PICA stroke	1	M	61	12
Bilateral PICA stroke	1	M	65	16
Residual features of remote rhombencephalitis	1	F	56	14
SCA6	6	2F/4M	68.5	16.5
SCA6 and 8 (CAG expansions in both)	1	F	69.1	16
SCA8	1	M	47	18
SCA28	1	F	53	12
Autosomal dominant cerebellar ataxia, gene negative	2	1F/1M	53.5	16.5
ARCA-1	2	1F/1M	43.5	15
Complex cerebro-cerebellar pathology				
SCA1	4	1F/3M	42	16.5
SCA2	1	F	49	16
SCA3	3	2F/1M	55.3	14
DRPLA	1	M	61	18
Fragile X tremor associated ataxia syndrome	1	M	75	12
SCA and sensory neuropathy/neuronopathy	1	M	67	18
Spastic ataxia	1	M	54	12
Gordon Holmes syndrome	1	M	31	12
Progressive ataxia with palatal tremor	1	F	69	18
Sagging brain syndrome	1	F	53	16
MSA-C	1	M	56	12

Thirty-nine patients not previously tested were investigated. ARCA-1 = autosomal recessive cerebellar ataxia type 1; AVM = arteriovenous malformation; DRPLA = dentatorubro pallidoluysian atrophy; L = left; MSA-C = multiple system atrophy of the cerebellar type; PICA = posterior inferior cerebellar artery; R = right; s/p = status post; SCA = spinocerebellar ataxia.

($P = 0.002$) (Freedman *et al.*, 1994) and copy a cube task ($P < 0.001$) (Kokmen *et al.*, 1987). No significant differences were found between patients and controls on the MMSE copy a pentagon task (Folstein *et al.*, 1975), or the Luria diagram copy (Luria, 1966).

Abstract reasoning

Cognitive estimation tasks were intact (e.g. 'How tall is the empire state building?'; Macpherson *et al.*, 2014), but patients were impaired on the similarities task of WAIS-IV (Wechsler, 2008) ($P < 0.001$), and on verbal addition and subtraction tasks (both $P < 0.001$). Addition and subtraction both require working memory, which was impaired.

Behaviour and affect

Neuropsychiatric symptoms measured by a standard assessment of executive behavioural dysfunction (FRSBE) (Grace *et al.*, 1999) revealed that patients scored higher than controls on apathy, executive dysfunction and disinhibition (all $P < 0.001$). Patient self-report was no different than family member ratings. Neuropsychiatric behaviours evaluated with the CNRS (Schmahmann *et al.*, 2007) revealed that family members reported difficulties with emotional control ($P < 0.001$), autism spectrum symptoms ($P < 0.001$), psychosis spectrum symptoms ($P < 0.001$) and deficient social skills ($P = 0.002$). Patients were also impaired on a questionnaire of social skills and communication (SCDC; Skuse *et al.*, 1997).

Verbal memory

Cerebellar patients were not impaired with respect to controls in their ability to learn five words on the MoCA episodic memory test ($P = 0.13$), but they showed deficits on delayed recall ($P < 0.001$) and required category cues or multiple choice to retrieve the majority of the words. No patient in the exploratory cohort failed to retrieve learned words from multiple choice. Verbal associative learning measured by verbal paired associates (VPA-I and VPA-II) was impaired: patients had difficulty learning word pairs ($P < 0.001$) and with delayed recall (VPA-II; $P < 0.001$), and their learning slope between the four repetitions of the word pairs was impaired ($P < 0.001$).

Complex versus isolated degeneration versus isolated injury

There were no significant differences in performance between patients with complex or isolated cerebellar pathology (isolated cerebellar disease, isolated cerebellar injury) with the exception of WAIS-IV similarities, where ANOVA F between complex cerebrocerebellar disease/isolated cerebellar disease/isolated cerebellar injury was significant ($F = 4.513$; $P = 0.015$). Independent samples t-test showed that patients with complex cerebrocerebellar disease had lower scores on similarities than isolated cerebellar and isolated injury disease patients.

Cognitive performance and cerebellar ataxia scores

We analysed whether cognitive performance correlated with motor disability in patients with cerebellar disease as measured by the BARS total score, 25-foot walk and 9HPT. There was no correlation between cognitive domains and BARS scores. Without Bonferroni correction for multiple comparisons, scattered low level correlations ($r \leqslant -0.2$) reached significance between some cognitive tests and 9HPT performance and 25-foot walk (Supplementary Table 6). As expected, motor tests correlated with each other: BARS – Pegboard (dominant hand) ($r = 0.817$, $P < 0.001$, $n = 46$), BARS – 25-foot walk ($r = 0.479$, $P = 0.001$, $n = 43$), and 25-foot walk – Pegboard (dominant hand) ($r = 0.391$, $P = 0.003$, $n = 56$) (Cohen, 1997).

Development of the cerebellar cognitive affective/Schmahmann syndrome scale

The results were analysed to delineate a brief set of cognitive tests sufficiently sensitive to detect the presence of CCAS and selective enough to differentiate between cerebellar patients and controls.

Excluding MMSE total score, MoCA total score and the motor tests, performance was analysed on 34 tests, a total of 70 measures (Table 2), e.g. go/no-go total score, go/no-go omission mistakes, and go/no-go commission mistakes. Eight measures failed to show significant differences between patients and controls and were excluded from further analysis. These were: pentagon, word immediate recall, repetition errors in verbal fluency task, word repetition, omission errors in the go/no-go test, CNRS autism overshoot, and CNRS attention undershoot and overshoot.

Of the remaining 62 measures, 13 were excluded because absolute value difference was not sufficient to permit derivation of a diagnostic cut-off, even though the difference between patient and control mean raw scores was significant. These were: star draw, clock draw, MoCA animal naming, ideational praxis (planning), vigilance (letter A test), production of derived words, cognitive estimation, letter number sequencing, months backwards, oral sentence production test, word stem completion, addition and subtraction.

The remaining 49 measures were ranked for difference in z-score means between patients and controls (Supplementary Table 7). When we applied the *a priori* hypothesis that the scale should capture the defining cognitive and affective domains of CCAS (Table 4), we selected the following measures with the highest position in the z-score ranking: verb for noun, semantic fluency, category fluency accuracy, category fluency set loss, DSB, longest DSB, DSF, longest DSF, Trails B minus Trails A, verbal recall, CNRS psychosis overshoot, CNRS autism undershoot, CNRS psychosis undershoot, CNRS emotion undershoot, go/no-go, subtraction and cube.

Some of these were inappropriately lengthy for a short bedside test and were excluded from the CCAS scale. In the verb for noun test, errors were distributed across the entire set of 22 noun-verb pairs, but no single noun or cluster of nouns elicited errors more predictably than others. The entire test would have had to be administered, a time-consuming challenge for the bedside/office setting. Similar reasoning applied to the Trails A and B tests. The timed tasks of months backwards and letter-number sequencing were also excluded because of the potential impact of motor impairment on test performance.

The measures of DSB total score, DSF total score and category fluency set loss were excluded because they provided no additional information to the measures of longest DSB, longest DSF and category fluency accuracy. Phonemic fluency placed high in the ranking of z-scores (Table 4) and was included (supported by Molinari *et al.*, 1997; Leggio *et al.*, 2000; Stoodley and Schmahmann, 2009*b*). The similarities test of abstract reasoning was added after reducing the original task from 18 associated word pairs to four word pairs. These were selected based on maximizing selectivity—most patients failed these items whereas controls passed them. In the scale, we chose different words within similar semantic categories to avoid copyright infringement (WAIS-IV; Pearson).

We amended the cube-copy task by adding the requirement that the subject first draw the cube from detailed verbal instruction. As we demonstrated in a study of metalinguistics abilities, cerebellar patients have difficulty self-directing their use of syntax in a context-dependent manner with only minimal constraints (Guell *et al.*, 2015). On this basis, and consistent with the dysmetria of thought hypothesis (Schmahmann, 1991, 2010), we reasoned that cerebellar patients may similarly have more difficulty self-directing their own drawing of a cube in

Table 4 Test measures

Domain and test	Z-score difference between patients and controls	One-tailed paired *t*-test		
		t	*df*	*P*
Executive function				
Trails B (s)	7.30	−6.535	62	0.000
Go/No-go (commission mistakes) (TM)	3.26	6.55	51	0.000
Trails A (s)	3.17	−8.133	62	0.000
Go/No-go (TS/2)	1.44	−6.381	63	0.000
Category switching accuracy (TC)	1.27	−7.235	49	0.000
Letter number sequencing time (s)	0.88	3.702	45	0.001
Trails B – Trails A (s)	0.81	−2.156	76	0.017
Total D-KEFS set loss mistakes (TM)	0.40	−3.675	49	0.001
Category switching set loss mistakes (TM)	0.28	1.692	56	0.048
Working memory				
DSB (TS/16)	1.37	−9.408	59	0.000
Longest DSB (TS/8)	1.05	−8.541	61	0.000
Longest DSF (TS/9)	0.79	−5.7	62	0.000
Months backwards time (s)	0.61	2.515	46	0.008
DSF (TS/16)	0.55	−4.698	60	0.000
Verbal memory				
Word delayed recall (TS/15)	1.14	−3.987	68	0.000
Verbal paired associates-I (TS/32)	0.70	−4.354	59	0.000
Learning slope	0.70	−4.304	59	0.000
Verbal paired associates-II (TS/8)	0.68	−4.683	58	0.000
Language				
Verb for Noun (TS/17)	6.44	−8.342	49	0.000
Word Stem Completion (TS/22)	1.95	−4.272	48	0.000
Phonemic fluency (TC)	1.78	−8.434	49	0.000
Semantic fluency (TC)	1.72	−8.335	49	0.000
Pseudoword Decoding at 60 s (TS/52)	1.11	−4.153	45	0.000
Pseudoword Decoding at 30 s (TS/52)	1.00	−6.015	41	0.000
Visual-spatial ability				
Cube (TS/2)	0.81	−4.442	61	0.000
JLO (TS/15)	0.44	−3.233	58	0.001
Attention and vigilance				
Longest DSF (TS/9)	0.79	−5.7	62	0.000
DSF (TS/16)	0.55	−4.698	60	0.000
Abstract reasoning				
Similarities (TS/36)	1.11	−7.032	58	0.000
Affect				
CNRS Psychosis spectrum positive (TS)	2.30	3.6	38	0.001
CNRS Emotion regulation negative (TS)	1.88	5.327	39	0.000
CNRS Psychosis spectrum negative (TS)	1.55	4.328	38	0.000
FRSBE Total score (self rating) (TS/255)	1.44	9.908	54	0.000
FRSBE Dysexecutive (self rating) (TS/85)	1.43	8.823	54	0.000
FRSBE Apathy (self rating) (TS/85)	1.42	7.985	54	0.000
CNRS Emotion regulation positive (TS)	1.38	3.982	39	0.000
CNRS Autism spectrum negative (TS)	1.31	4.713	38	0.000
CNRS Social skill positive (TS)	1.29	3.842	38	0.000
FRSBE Apathy (family rating) (TS/85)	1.28	6.731	38	0.000
FRSBE Total score (family rating) (TS/255)	1.07	5.465	38	0.000
SCDC Total (TS/24)	0.91	4.086	39	0.000
CNRS Social skill negative (TS)	0.86	3.138	38	0.002
Dysexecutive (family rating) (TS/85)	0.78	4.18	38	0.000
FRSBE Disinhibition (self rating) (TS/85)	0.61	3.567	54	0.001
FRSBE Disinhibition (family rating) (TS/85)	0.45	2.442	38	0.010

Test measures are ranked by descending order for difference in z-score means between patients and controls within each of the major CCAS domains (*a priori* requirement that the CCAS scale tests each domain).

TC = total correct; TM = total number of mistakes; TS = total score.

response to verbal instruction than they would when copying a cube that is a more constrained and visually-guided task. In the validation cohort of 39 patients, cube draw in this verbal instruction condition was impaired in 19 (49%); of these, five were able to copy the cube correctly (Fig. 3).

The original description of CCAS included observations by the examiner, or report by caregivers, of changes in comportment, mood, affect and social behaviour as well as performances on bedside and neuropsychological tests. In the present analysis, CNRS measures were among the most sensitive discriminators between patients and controls. To meet the *a priori* requirement that the CCAS scale reflect the core aspects of the syndrome, we added a component that addresses cerebellar neuropsychiatry. Unlike the objective scoring criteria for the other tests in the scale, the resulting item is a clinical judgement by the examiner that takes into consideration the observations by the caregiver. This adds a clinically meaningful, albeit qualitative, screening assessment of the neurobehavioural/affective aspects of CCAS.

For each test item within the scale, there was a threshold score for the performance that distinguished patients from controls. This score was the diagnostic cut-off, used to determine pass/fail for each item. Diagnostic cut-offs were derived from the exploratory cohort and validated in the validation cohort. As exemplified by semantic fluency (Fig. 1), few controls scored $\leqslant 15$ animals in 1 min (five in the exploratory cohort, 0 in the validation cohort), whereas 35 patients provided $\leqslant 15$ animals (24 in the exploratory cohort, 11 in the validation cohort). We focused on selectivity (to prevent diagnosing a control person as a patient) rather than sensitivity (identifying all the patients), to prevent false positives. This is reflected in the designation of 'possible', 'probable', and 'definite' CCAS in which the selectivity goes up but the sensitivity goes down as the diagnosis becomes more firmly established (Table 5). Patients scored a mean of 6.25 on the DSF span length, but we chose 5 as a passing number/cut-off (as in MoCA) because a cut-off of 6 produced a higher false positive rate in controls who scored an average of 7.29. Threshold determined for success on the DSB span length is four digits, one digit more than on the MoCA. Patients scored a mean of 4.25 digits whereas controls provided an average of 6.25 digits backwards (Fig. 1).

This resulting 10-item battery is the cerebellar cognitive affective/Schmahmann syndrome scale, shown in Fig. 2. It measures semantic fluency, phonemic fluency, category switching, DSF, DSB, cube draw and cube copy, delayed verbal recall, similarities, go/no-go, and assessment of neuropsychiatric domains. It takes <10 min to administer to a healthy control, and 12–15 min for a patient with cerebellar dysfunction.

Each test within the scale has a threshold score allowing a pass/fail determination that differentiates cerebellar patients from controls. Table 5 shows the performance of patients and controls determined by cut-offs for the nine cognitive test items on the CCAS scale (excluding the Affect component).

We reasoned that total raw score for the scale (the sum of the raw scores of all the subtests) would increase granularity in scoring and allow for more nuanced detection of changes over time in individual patients. To do this we needed an upper limit of the raw score for some measures because they would potentially have undue weight on the total score. We set the maximum possible score as 1 SD above the mean for the performance of controls on tests of semantic fluency, phonemic fluency, category switching, and longest digit span forwards. For the other tests, the maximum score is a perfect score for that test (cube, verbal recall, similarities, go/no-go). The Affect denominator was kept low to avoid skewing results with subjective data. Neuropsychiatric features within CCAS may be assessed more directly and in greater detail by the CNRS.

With these criteria, a diagnosis of CCAS in the large exploratory cohort based on a single failed test yields a sensitivity of 85% but selectivity of 74%—an unacceptably high false positive rate of 26%. Diagnosis of CCAS based on two failed tests yields a sensitivity of 58.3% and selectivity rate 94.4%. Failure on three tests translates to a sensitivity of 48.3% and selectivity 100%, i.e. no control subject failed three tests. We therefore chose to consider one failed test as a diagnosis of possible CCAS, two failed tests as probable CCAS, and three failed tests as definite CCAS (Table 5).

Validation of the cerebellar cognitive affective/Schmahmann syndrome scale

The scale was administered in a prospective manner to a validation cohort of 39 new patients with cerebellar disorders who were not part of the original exploratory cohort (Table 3). Of these, 23 were isolated cerebellar disorders (acquired or hereditary), and 16 were complex cerebrocerebellar disorders. These were compared with 55 healthy controls. The control cohort (40.43 ± 16.24 years) was younger than the patients (55.01 ± 12.48 years; two-tailed P-value < 0.001). In the controls, there were no significant correlations between age and test scores with the single exception of verbal recall (Pearson's $r = -0.438$, one tailed P-value < 0.001). There was no difference in educational level between patients 15.64 ± 2.07 years and controls 16.28 ± 1.16 years; two-tailed P-value = 0.08).

The sensitivity and selectivity of the CCAS scale in the validation cohort of cerebellar patients and healthy controls was comparable or slightly improved compared to the results in the exploratory cohort. A diagnosis of possible CCAS (one test failed) achieved 95% sensitivity and 78% selectivity, probable CCAS (two tests failed) 82% sensitivity and 93% selectivity, and definite CCAS (three or more tests failed) achieved 46% sensitivity and 100% selectivity.

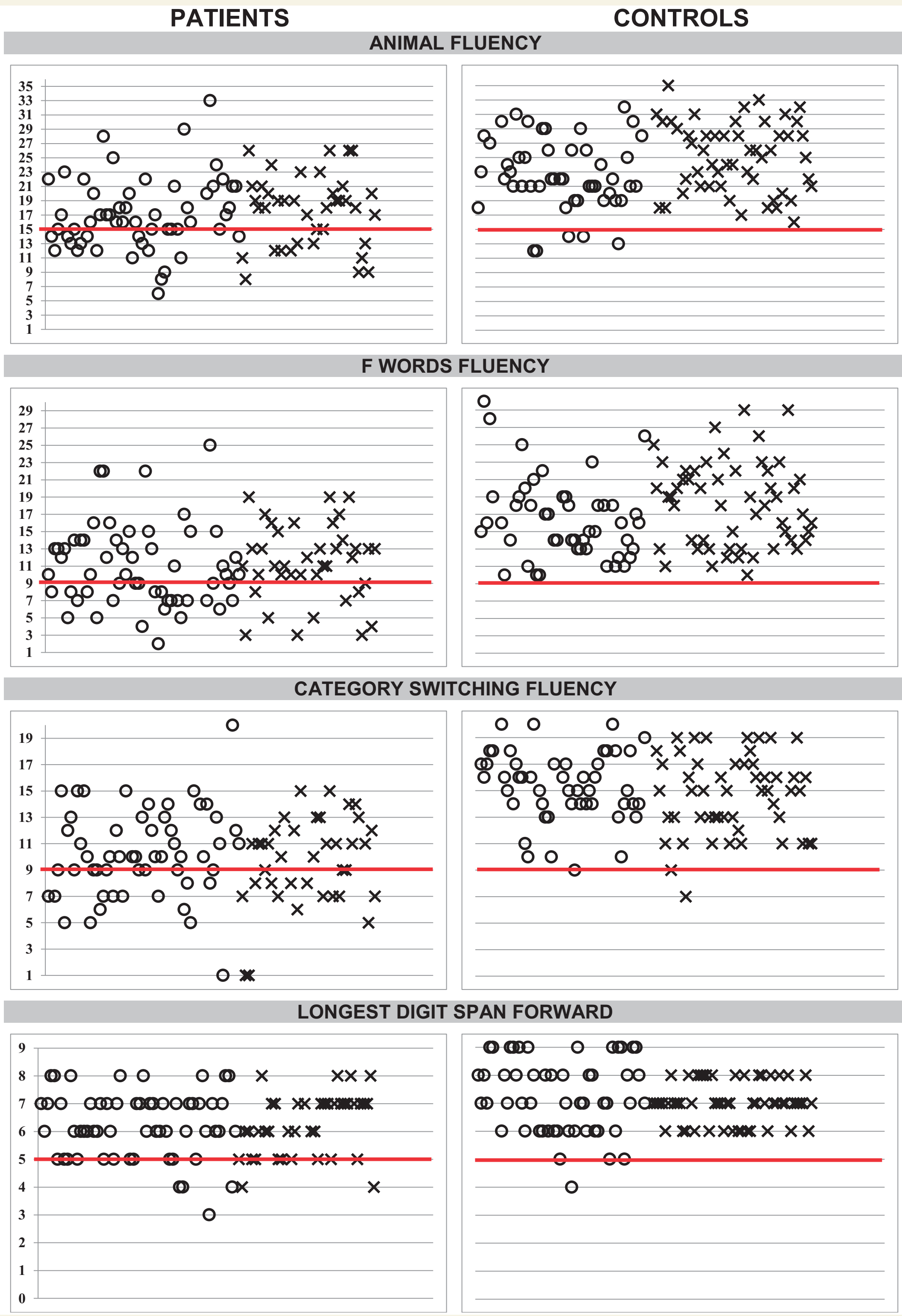


Figure 1 Scatterplots of performance of patients and controls on cognitive tests in the CCAS/Schmahmann scale. Bold line indicates the threshold value (the cut-off) determining that performance is impaired. Circles = exploratory cohort, crosses = validation cohort. *Y*-axis represents total raw scores.

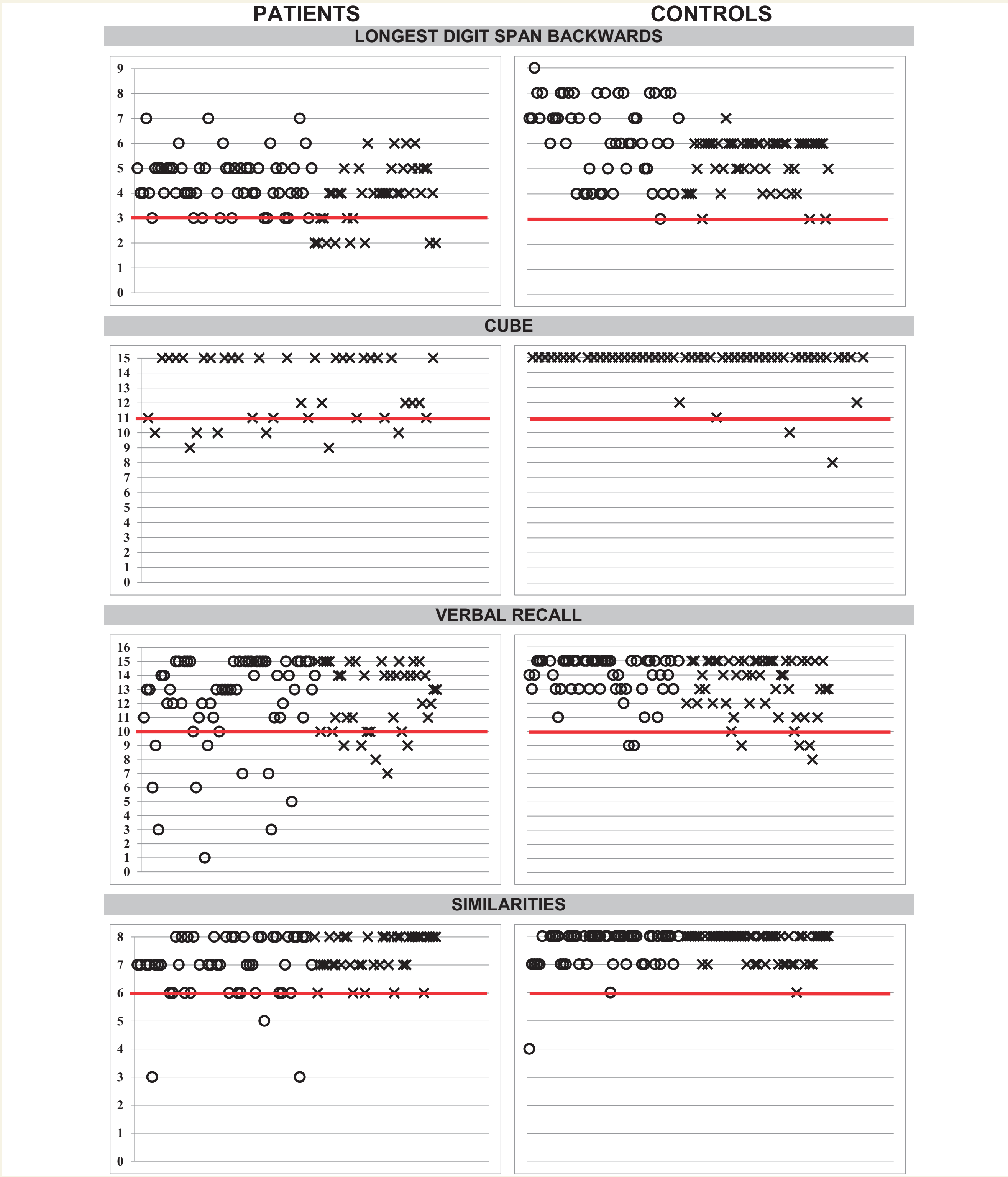


Figure 1 Continued.

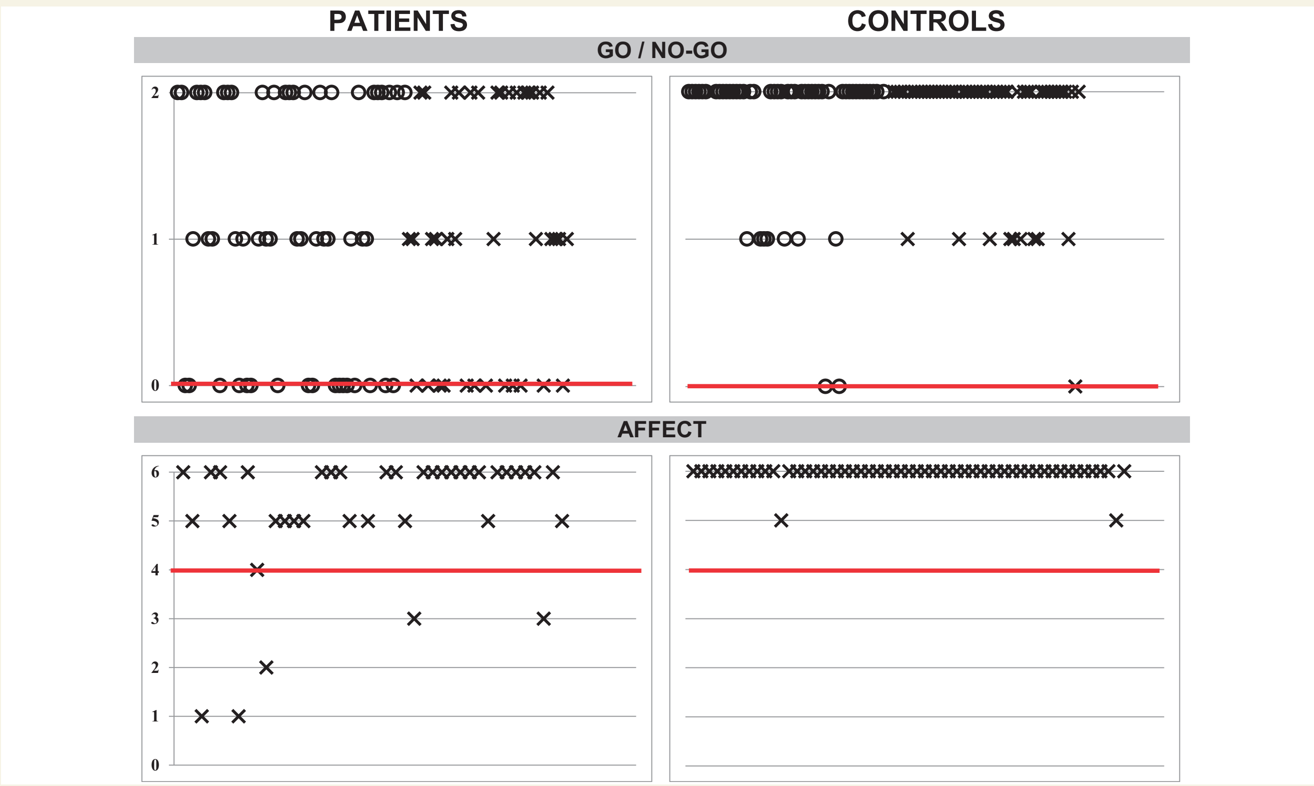


Figure 1 Continued.

Table 5 Performance on subtests of the CCAS/Schmahmann scale by patients and controls in the exploratory and validation cohorts; and sensitivity and selectivity of the scale according to possible, probable and definite criteria

Test	Cut-off (raw score)	Patients diagnosed as patients; exploratory cohort (%)	Patients diagnosed as patients; validation cohort (%)	Controls diagnosed as controls; exploratory cohort (%)	Controls diagnosed as controls; validation cohort (%)
Animal fluency	⩽15	24/56 (43)	13/39 (33)	45/50 (90)	55/55 (100)
F word fluency	⩽9	25/56 (45)	10/39 (26)	50/50 (100)	55/55 (100)
Category switching	⩽9	23/55 (42)	18/39 (46)	49/50 (98)	53/55 (96)
LDSF	⩽5	15/58 (26)	11/39 (28)	49/53 (92)	55/55 (100)
LDSB	⩽3	10/57 (18)	12/39 (31)	52/53 (98)	52/55 (93)
Cube	⩽11	8/56 (14)	14/39 (36)	53/53 (100)	51/54 (94)
Verbal recall	⩽10	12/56 (21)	10/39 (26)	51/53 (96)	47/53 (89)
Similarities	⩽6	14/50 (28)	5/39 (13)	49/51 (96)	54/55 (98)
Go/no-go	=0	17/56 (30)	12/39 (31)	51/53 (96)	54/55 (98)
CCAS/Schmahmann scale		**Sensitivity (%)**		**Selectivity (%)**	
		Exploratory cohort	**Validation cohort**	**Exploratory cohort**	**Validation cohort**
One test fail (Possible CCAS)		85	95	74	78
Two tests fail (Probable CCAS)		58	82	94	93
Three tests fail (Definite CCAS)		48	46	100	100

LDSB = longest DSB; LDSF = longest DSF.

Cronbach's alpha for the CCAS scale administered to the validation cohort was 0.59, reflecting only modest internal consistency. This means that patient performance on any single item in the scale did not predict performance on other items within the scale, and therefore the items within the scale are necessary, and not redundant.

As in the exploratory cohort, the patient validation cohort was quite heterogeneous in terms of diagnosis; 22

CEREBELLAR COGNITIVE AFFECTIVE / SCHMAHMANN SYNDROME SCALE (CCAS-Scale) VERSION 1A.

NAME:
ID#
DATE
DOB:
Education (Yrs)

Test	Instructions	RAW SCORE	PASS=0 FAIL=1
SEMANTIC FLUENCY	Score = total correct words (up to a maximum of 26 words). Fail if Score 15 or less. *(Use space bottom right for notation).* Please name as many animals or living creatures as you can in one minute	/26	
PHONEMIC FLUENCY	Score = total correct words (up to a maximum of 19 words). Fail if Score 9 or less. *(Use space bottom right for notation).* Please name as many words as you can in one minute that start with the letter F. Do not use names of people or places or repeat the same word in different forms.	/19	
CATEGORY SWITCHING	Score = total number of correct alternating words (up to a maximum of 15 alternations). Repetitions or set loss errors are not scored. Fail if Score 9 or less. *(Use space bottom right for notation).* Please name a type of vegetable and then a type of profession or job, and then another vegetable and another profession, and so on, switching between the two lists. Name as many as you can in one minute.	/15	
VERBAL REGISTRATION	This test is not scored. (The need for 4 attempts to learn 5 words raises concern for cerebral involvement). I am going to read you a list of words which I would like you to learn. Please repeat these words. I am going to ask you to give them back in a few minutes. *(Read 5 words at rate of 1 / second. Subject repeats them once, then repeats them again. Repeat trials until subject recalls all 5 words. Stop after 4 attempts.)*		

	[Flower]	[Robert]	[Courage]	[Speak]	[Yellow]
1st attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
2nd attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
3rd attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
4th attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]

Test	Instructions	RAW SCORE	PASS=0 FAIL=1
DIGIT SPAN FORWARD	Score = maximum string of numbers correctly repeated. Fail if Score 5 or less. I am going to read you some numbers. Please repeat them in exactly the same order *(Read aloud at a rate of 1 per second. Start with * and administer previous items if subject fails to repeat *).* 5-9 [ ] 4-8-7-0 * [ ] 3-0-1-2-6-4 [ ] 2-0-5-6-9-7-3-8 [ ] 2-1-3 [ ] 1-6-9-2-5 [ ] 7-3-1-9-8-4-6 [ ]	/8	
DIGIT SPAN BACKWARD	Score = maximum string of numbers correctly repeated. Fail if Score 3 or less. Inability to reverse 2 digits scores 0. Now please say these numbers backwards, in reverse order. *(Give example, then start with *).* (e.g., 5-8 = 8-5) *6-1 [ ] 3-8-2 [ ] 4-7-0-9 [ ] 6-5-2-8-1 [ ] 5-9-0-3-7-4 [ ]	/6	
CUBE (DRAW)	Score = 15 points if 12 lines present and diagram is 3-dimensional. If 12 lines not present or the diagram is not 3 dimensional, administer "CUBE (COPY)". Please draw a cube – a six-sided box, make it transparent or see-through. *(Use space bottom left).*		
CUBE (COPY)	Score = 12 points, 1 for each line. Deduct 1 point if not 3-D, 1 point for each line not drawn, 1 point for each additional line >12. Fail if Score 11 or less. Please copy the cube shown on PAGE 2. *(Neatness not scored).*	/15	

Draw cube here.

Notation:

Semantic Fluency	Phonemic Fluency	Category switching

Figure 2 The cerebellar cognitive affective/Schmahmann syndrome scale (Version 1A). See Supplementary material for administration and scoring instructions, and Versions 1B, 1C, and 1D that have different test items within each domain to facilitate test-rest reliability.

(continued)

VERBAL RECALL Spontaneous = 3 points per word, category = 2 points , multiple choice = 1 point. Score = total points. Fail if Score 10 or less. Inability to recall more than 1 word from multiple choice raises concern for cerebral involvement. **RAW SCORE** **PASS=0 FAIL=1**

What were the words I asked you to learn earlier? *(Subject recalls the words learned previously. Use cues and multiple choice alternatives bottom left if needed).*

	[Flower]	[Robert]	[Courage]	[Speak]	[Yellow]
Spontaneous recall:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with category cue:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with multiple choice:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]

/15

SIMILARITIES Correct answer (conceptual) = 2 points, partial answer (concrete) = 1 point, incorrect answer / no answer = 0 points. Score = total points. Fail if Score 6 or less. Key-bottom right.

How are the following words alike; what is the same about them? (*Provide example, then test items).*

(e.g., Ball/Moon = Round) 1.Nose/Ear [__/2] 2. Sheep/Elephant [__/2] 3. Lake/River [__/2] 4. Airplane/Motorcycle [__/2]

/8

GO NO-GO 2 points for no errors, 1 point for one error, 0 points for two or more errors. Score = total points. Fail if Score 0.

I am going to tap the table. When I tap once, please raise your finger then put it back down again. When I tap twice, don't do anything. *(Give an example of each condition to make sure subject understands).*

1 – 1 – 1 – 2 – 2 – 1 – 2 – 2 – 2 – 1 – 2 – 1 – 2 - 1

/2

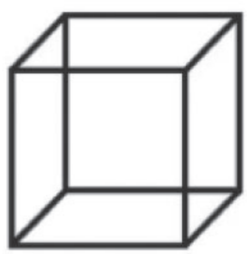
AFFECT Score 6 points if none are present. Subtract 1 for each item present. Fail if Score 4 or less. *(Rater assesses if the following are present, incorporating input from patient and/or caregiver)*

[ ] Difficulty with focusing attention or mental flexibility
[ ] Emotionally labile, incongruous emotions, appears hopeless or depressed
[ ] Shows easy sensory overload or avoidant behaviors
[ ] Expresses illogical thoughts or paranoia
[ ] Lacks empathy, is apathetic, or has blunted affect
[ ] Angry or aggressive, irritable, oppositional, difficulty with social cues and social boundaries

/6

TOTAL SCORE /120 /10

Calculate total raw score (1st column) and total number of failed tests (2nd column).
1 failed test = Possible CCAS; 2 failed tests = Probable CCAS; 3 or more failed tests = Definite CCAS



Copy the cube here.

CUES AND MULTIPLE CHOICE ITEMS FOR VERBAL RECALL TEST					
Test word	**Flower**	**Robert**	**Courage**	**Speak**	**Yellow**
Cue	Grows in the garden	Boy's name	Trait or virtue	Way of communicating	Color
Multiple choice items	Tree	Stephen	Bravery	Speak	Red
	Bush	Michael	Courage	Talk	Green
	Flower	Joseph	Honesty	Sing	Blue
	Grass	Robert	Patience	Shout	Yellow

SIMILARITIES	Correct conceptual answers (examples)	Partial correct / concrete answers (examples)
Nose/Ear	Sense organs	Face, body part
Sheep/Elephant	Mammals, animals	Legs, tails
Lake/River	Bodies of water	Wet, cold, swim
Airplane/Motorcycle	Vehicles, transportation	Use fuel, ride them

Hoche, Guell, Vangel, Sherman, Schmahmann
Ataxia Unit, Cognitive Behavioral Neurology Unit, Schmahmann Laboratory for Neuroanatomy and Cerebellar Neurobiology, Department of Neurology, Massachusetts General Hospital.

Figure 2 Continued.

of 39 patients had diagnoses shared by others (Table 3). Further, the distribution of failing scores across the scale was random, with no consistent pattern identifiable. Only three pairs of patients failed the same two tests, and each had a different diagnosis. We used logistic regression to assess whether disease duration is associated with a pattern of test failure, and found a significant association only for phonemic fluency ($P = 0.02$). Logistic regression applied to

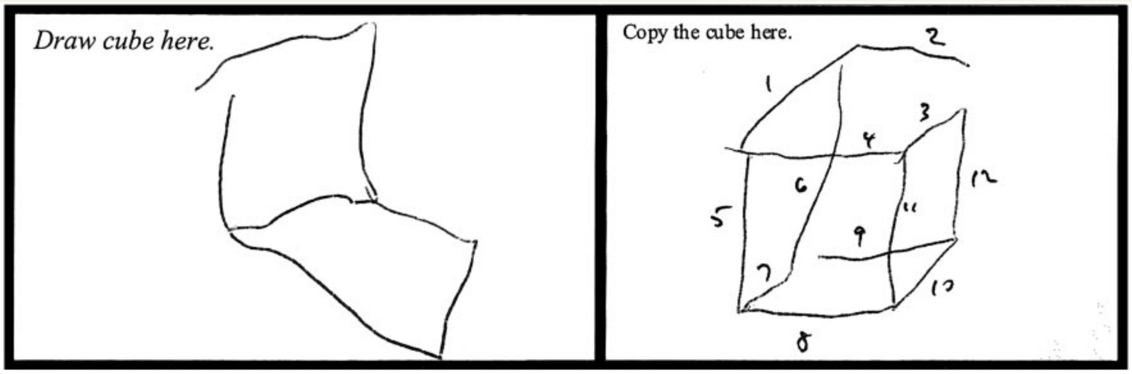


Figure 3 Patient performance with verbal instruction to draw a cube (*left*) and to copy a cube (*right*).

the performance across the 10 tests on the scale showed no association ($P > 0.09$) between the number of failures for any single test and isolated cerebellar ($n = 23$) versus complex cerebrocerebellar ($n = 16$) condition. Total BARS score correlated with phonemic fluency (Pearson's r = −0.45, two tailed $P < 0.01$) and with affect (r = 0.57, $P < 0.001$).

Discussion

This study reaffirms that executive, linguistic, visual spatial and affective/neuropsychiatric impairments characterize the disturbances of higher function in patients with cerebellar injury—CCAS/Schmahmann's syndrome (Schmahmann and Sherman, 1997, 1998; Levisohn *et al.*, 2000; Schmahmann *et al.*, 2007; Manto and Mariën, 2015).

Executive function

As originally described, executive function impairments in patients with focal cerebellar injury included deficient planning, abstract reasoning, and working memory, with impaired motor or ideational set-shifting, perseveration of actions or drawings, and decreased verbal fluency sometimes with telegraphic speech so severe as to resemble mutism (Schmahmann and Sherman, 1998). Following cerebellar tumour resection children demonstrated deficits in planning and sequencing, impaired digit span, perseveration, and difficulties establishing set (Levisohn *et al.*, 2000).

In the present study, prominent deficits were noted on DSF, DSB, Trails B, and D-KEFS category switching. Deficits were also found for commission mistakes on the go/no-go task, and letter number sequencing total score and vigilance (Table 2). These cognitive tests tap executive functions including working memory, mental flexibility, problem-solving strategies, multitasking, planning, sequencing, and self-organizing. Impairments on these tests are associated with clinical deficits including concrete thinking and perseveration (Botez *et al.*, 1989; Schmahmann and Sherman, 1997, 1998; Levisohn *et al.*, 2000; Ravizza *et al.*, 2006; Leggio *et al.*, 2011; reviewed in Koziol *et al.*, 2014). Working memory deficits that have been widely reported in cerebellar patients (Schmahmann and Sherman, 1998; Justus *et al.*, 2005; Ravizza *et al.*, 2006) depend on a network of frontal and parietal cortical regions as well as subcortical structures (Rowe *et al.*, 2000). It has been proposed that cerebellar patients are impaired on working memory tasks because of deficient silent rehearsal of verbal information (Desmond *et al.*, 1997; Chen and Desmond, 2005; Mariën *et al.*, 2014). Diminished attentional resources may also contribute to working memory impairments (Purcell *et al.*, 1998; Klingberg *et al.*, 2002; Egeland *et al.*, 2003).

Linguistic function

The language deficits in the original report (Schmahmann and Sherman, 1998) included dysprosodia, agrammatism, anomia and impaired syntax, in addition to the deficits in verbal fluency, telegraphic speech, and mutism. Language impairments in children following cerebellar tumour resection were characterized by expressive language deficits, word-finding difficulties evident in spontaneous conversation and testing, and mutism in those with damage to the vermis (Levisohn *et al.*, 2000). Subsequent insights into the modulatory role of the cerebellum in language include the contribution of the cerebellum to speech and language perception, motor speech planning, syntax processing, and the dynamics of language production, reading and writing (Mariën *et al.*, 2014). Phonological and semantic verbal fluency tasks and verbal working memory tests also tap executive function, but these tests rely heavily on verbal output and therefore reflect the integrity of language processing as well.

Here we demonstrate deficits in oral word production (verb for noun task) (Fiez, 1996; Stoodley *et al.*, 2012), syntax processing (production of derived words), oral sentence production (Justus, 2004; Michael and Kenneth, 2015), and phonological processing (pseudoword decoding task) (Stoodley, 2015). Phonemic (letter) and semantic fluency (category naming) were also impaired, phonemic more than semantic, as noted previously (Silveri *et al.*, 1994;

Molinari *et al.*, 1997; Schmahmann and Sherman, 1997, 1998; Leggio *et al.*, 2000; Levisohn *et al.*, 2000; Mariën *et al.*, 2001, 2014; Gottwald *et al.*, 2003; Brandt *et al.*, 2004; Richter *et al.*, 2007; Stoodley and Schmahmann, 2009*b*; Peterburs *et al.*, 2010; Schweizer *et al.*, 2010; Tedesco *et al.*, 2011; Arasanz *et al.*, 2012; Mariën and Beaton, 2014). Cerebellar patients could name the three animals on the MoCA semantic memory/knowledge task, but in comparison to controls they were impaired on the D-KEFS category fluency task in which they needed to generate animals and boys' names. Deficits on the semantic fluency task likely reflect dysfunctional executive retrieval of semantic knowledge subserved by prefrontal cerebrocerebellar circuits rather than a primary storage defect associated with medial temporal lobe pathology. Thus, naming tasks may distinguish patients with pathology of the temporal lobe in whom animal naming may be impaired, from patients with disruption of prefrontal cortices or associated cerebrocerebellar circuitry in whom the pictured animal naming task, with its minimal executive retrieval demand, is intact.

Metalinguistic deficits are noted in cerebellar patients, manifesting as impaired understanding of metaphor, ambiguity, and inference, and generation of grammatically and syntactically correct sentences according to context (Guell *et al.*, 2015), but we did not evaluate this task in the present cohort.

Visual spatial function

Deficits in spatial cognition in the original study were demonstrated when patients attempted to draw or copy a diagram. The approach to the drawing was not sequentially ordered, and the conceptualization of the figures was disorganized. Some patients demonstrated simultanagnosia (Schmahmann and Sherman, 1998). Children post-tumour resection also showed deficits in visual-spatial functions, including marked fragmentation of a complex figure copy (Levisohn *et al.*, 2000), a phenomenon observed subsequently in children with ataxia telangiectasia (Hoche *et al.*, 2014, 2016*a*).

In the present study patients were impaired on JLO (Benton *et al.*, 1983), draw a clock (Freedman *et al.*, 1994), and the copy a cube task (Kokmen *et al.*, 1987). In contrast, no difference between patients and controls was found on the ability to copy intersecting pentagons (in the MMSE) and a triangle. The distinction between intact performance on the 2D tasks versus impaired 3D copy and JLO may be explained by damage to the cerebellar posterior lobe, which is linked with cerebral posterior parietal association cortices (Schmahmann and Pandya, 1989) concerned with internal representations of spatial maps, and with the dorsal premotor cortices (Middleton and Strick, 1994; Schmahmann and Pandya, 1995, 1997) concerned with motor imagery (Guillot and Collet, 2010). Both these cerebral cortical areas are involved in spatial transformation and mental rotation tasks (Gerardin *et al.*, 2000; Cengiz and Boran, 2016).

Memory and learning

Cerebellar-based memory impairments defined in the 1998 study included working memory, and efficiency of retrieval of previously learned information. This pointed to a cerebellar role in the executive control of memory. Later imaging studies suggested this was related to the cerebellar contribution to search functions, rather than storage of information (Desmond *et al.*, 1997; Marvel and Desmond, 2010). These findings are consistent with anatomical studies in monkey of prefrontal cerebrocerebellar connections (Schmahmann and Pandya, 1995, 1997; Kelly and Strick, 2003) and resting state functional connectivity using MRI in humans showing representation in the cerebellum of the frontoparietal and default mode networks (Habas *et al.*, 2009; O'Reilly *et al.*, 2010; Buckner *et al.*, 2011).

Here we show that episodic memory impairments in cerebellar patients are similar to those in patients with prefrontal dysfunction, namely, deficits in retrieval and associative learning (Preston and Eichenbaum, 2013). A standard test of verbal associative learning (VPA-I and VPA-II) revealed deficits on immediate and delayed recall of associated word pairs. The learning slope between the four repetitions of the associated word pairs was also impaired. This is consistent with the observation that the cerebellum participates in the acquisition of cognitive associations and associative learning (Gerwig *et al.*, 2007; Sacchetti *et al.*, 2009; Thompson and Steinmetz, 2009; Timmann *et al.*, 2010; Cheng *et al.*, 2014). Whether the discrepancy between relatively preserved five-word recall and the impaired associative learning reflects deficient encoding or impaired retrieval of the fully encoded verbal pairs remains to be determined.

Our clinical experience with patients in the late stages of disease known to involve cerebral hemispheres as well as cerebellum e.g. SCA2 (Koeppen, 2002; Seidel *et al.*, 2012), Gordon Holmes syndrome (Seminara *et al.*, 2002; Margolin *et al.*, 2013; Santens *et al.*, 2015), and fragile X tremor ataxia syndrome (Hagerman *et al.*, 2001; Santens *et al.*, 2015) is that they develop episodic memory loss that is not seen in CCAS. This conclusion is supported by our finding that patients with these diagnoses in the validation cohort (SCA2, FAXTAS, Gordon Holmes syndrome) failed the memory test in the scale; these were the only patients of the 116 in both the exploratory and validation cohorts who were unable to recall words from a multiple-choice list (data not shown). Thus, whereas the executive aspects of memory (speed and accuracy of retrieval) appear to be under the influence of the cerebellum, storage of declarative memories appears to escape cerebellar influence. From this perspective, in a patient with cerebellar disease, memory loss (inability to recall words from multiple choice) should be regarded as a red flag pointing to a non-cerebellar basis of the memory impairment.

Neuropsychiatry of the cerebellum

The present findings are harmonious with our previous report that cerebellar patients experience deficits in attentional control, emotional control, autism spectrum symptoms, psychosis spectrum symptoms, and deficient social skills (Schmahmann *et al.*, 2007). These results are also in line with scores on the CNRS in a study of social cognition in cerebellar patients showing impairments on assessments of emotion control, autism spectrum behaviours, psychosis spectrum symptoms and social skills (Hoche *et al.*, 2016*b*). Further, they are consistent with the observations from the FRSBE, a standard assessment of executive behavioural dysfunction (Grace *et al.*, 1999), in which family members and patients reported apathy and disinhibition.

Cerebellar versus cerebrocerebellar contribution to cognitive function

Group-wise analysis revealed no differences in performance of patients with isolated cerebellar disease, injury, or complex cerebrocerebellar disease pathology on any of the neuropsychological tests administered, with the exception of similarities. This indicates that cerebellar disease alone is sufficient to produce CCAS. This interesting result speaks to the role of cerebellum in executive, visual spatial, linguistic and affective behaviours that characterize CCAS. It remains to be determined how cerebral hemisphere involvement in addition to cerebellar dysfunction affects these cognitive and neuropsychiatric domains. The CCAS scale will be helpful in that regard, supplemented by the additional tests defined here that when administered in the neuropsychology laboratory can detect CCAS. We draw attention again to the observation that impairment of declarative memory, with difficulty recalling words even from multiple choice, is a 'red flag' for cerebral hemisphere involvement because this is not part of the core constellation of CCAS. The heterogeneity and large number of patients in this study ($n = 116$, 77 exploratory and 39 validation) serves as the basis for these conclusions, and it will be important to explore this further with larger groups of patients and a wide range of cerebellar and cerebrocerebellar disorders.

MMSE and MoCA

Despite the facts that cerebellar patients failed many standard neuropsychological and experimental tests, and were significantly different than control subjects on MoCA total score, they performed within the published normal ranges on both the MMSE and the MoCA. This may be explained by the fact that MMSE and MoCA contain many test items that are insensitive to those cognitive functions that are compromised in cerebellar patients. This also masks the finding that the MoCA subtests with which patients struggled tap the same domains that were impaired on neuropsychological tests in the exploratory cohort, and on the CCAS scale in the validation cohort. The MoCA domains that were impaired included trail making, clock draw, visual spatial domain, reverse digit span, subtraction, phonemic fluency, language, abstract reasoning, and delayed recall. These deficits on MoCA subtests are lost in the summation of the total score. MoCA was therefore inadequate to detect CCAS in cerebellar patients for three reasons: (i) the individual MoCA cut-offs are too lenient (e.g. digit span backwards); (ii) some tests are mini versions of the original test design (e.g. Trails) and are not sufficiently sensitive in this population for the mental flexibility that this test assesses; and (iii) errors in critical cognitive skills are hidden in the total MoCA score, overwhelmed by preserved performance on tasks spared in patients whose lesions are confined to the cerebellum.

Cognitive performance does not correlate with motor deficit

The tests that rate the severity of motor ataxia correlated with each other. Correlations were strong between BARS and the 9HPT, while the 25-foot timed walk had modest correlations with BARS and with the 9HPT.

In contrast, in the exploratory cohort none of the CCAS domains correlated with total BARS score. A small number of items of the CCAS scale had low level correlations with 25-foot timed walk and 9HPT performance. In the validation cohort, total BARS score correlated only with phonemic fluency (a shorter version of the test than was administered to the exploratory cohort), and with affect, which was not measured in the same way in the exploratory cohort. This motor-cognitive relationship, or lack thereof, will need to be explored in future studies using the new scale in larger cohorts, but it underscores the motor-cognitive dichotomy in cerebellum, in which the sensorimotor cerebellum is represented in the anterior lobe and lobule VIII, and the cognitive cerebellum in the massively expanded posterior lobe (lobules VI, VII and probably lobule IX). Some correlations are to be expected, given the different patterns of pathology in many of our cases, and this likely reflects involvement by the disease process of cerebellar areas engaged in these motor or cognitive/emotional behaviours. The existence of functional topography of different domains of cognition within the cerebellum (e.g. Stoodley and Schmahmann, 2009*a*, *b*; Schmahmann, 2010) is directly relevant to the development of the CCAS/Schmahmann scale. The internal consistency of the scale as measured by Cronbach alpha is modest, indicating that no single test, or aggregation of tests, can fully predict performance on the scale as a whole. This reflects the observation that different parts of the cerebellum are engaged in different cognitive and affective processes. It is not mandatory that all features of CCAS (executive, linguistic, visual spatial, affective), manifest in every patient with damage localized to the cognitive/limbic cerebellum. This is determined, in large part, by the precise location of the lesion, a well-established principle in neurology in general, and behavioural neurology/neuropsychiatry in particular.

Development of the CCAS/ Schmahmann scale

We derived a subset of tests sensitive to the presence of CCAS in cerebellar patients that distinguished between cerebellar patients and healthy controls, and which is brief enough to be useful in the clinic or bedside setting. When ranking all tests administered to the exploratory cohort for their difference in performance between patients and controls, the results were weighted towards executive and language functions, consistent with the original observations that executive function impairment was a prominent feature of CCAS, followed by language, visual spatial and affective changes (Schmahmann and Sherman, 1998). Similarly, we confirm previous reports (Schmahmann and Sherman, 1998; Schmahmann *et al*., 2007; Garrard *et al*., 2008; Sokolovsky *et al*., 2010; Hoche *et al*., 2016*b*) that adults with cerebellar lesions show emotional dysregulation, difficulties with social skills and psychosis spectrum behaviours, but not autism spectrum behaviours that are more evident in children.

In developing the CCAS scale we did not include some tests that reached significance in the exploratory cohort. The omission of these tests did not alter the sensitivity or selectivity of the resulting scale, as confirmed in Table 2 and Supplementary Table 7. The brief tests included in the scale all had high sensitivity and selectivity, and were essentially interchangeable with the longer tests that were not practical for the screening instrument.

To screen for the CCAS pattern in each individual patient with cerebellar injury in a bedside setting, the scale was developed using the *a priori* hypothesis that all characteristics of CCAS should be represented. We eliminated some tests either because they take too long to administer in an office or bed-side encounter (e.g. the full Trails test, or all the words of the verb-for-noun task), or because the absolute value difference between patients and controls was too small to be useful in that setting.

The resulting cerebellar cognitive affective/Schmahmann syndrome scale (Fig. 1) has three defining components:

(i) A pass/fail diagnostic cut-off score for each test within the scale. To our knowledge this feature is unique, and the first time this approach has been introduced into any screening cognitive instrument.
(ii) A pass/fail for the scale as a whole, which determines the likelihood that the subject has CCAS or not, and provides evidence supporting the stratification into possible, probable, or definite CCAS.
(iii) The scale total raw score facilitates a more granular analysis of patient performance. Note that the range of passing scores on the scale extends from 82 (sum of minimum passing scores for each item on the scale) to 120 (sum of maximum scores for each item as described above). A patient can have definite CCAS (three failed test items) with a total raw score that falls in the 82–120 range. The total score does not determine whether a patient has CCAS or not, but it does provide additional quantitative detail of a patient's performance in each domain that can be used for longitudinal follow-up. Thus, for example, a subject may fail the semantic fluency task by producing 15 words or less, but this could decline further, reflecting deterioration. Alternatively, a subject could fail this task by producing only a few words (e.g. five or six), but improve over time as they recover, but still failing the task by not reaching the required 15 words. One could also pass the test with 25 words, and then decline over time to 16 words, but still pass that aspect of the test—this fine-tuning of the scale with the raw score is a potentially powerful tool for the clinician following a patient over time.

The patient populations in both the exploratory and validations cohorts were remarkably heterogeneous, underscoring the suitability of the new scale for a general population of cerebellar patients. The scale has the potential to be a powerful screening and evaluation instrument to determine the presence of CCAS in an individual patient accurately, efficiently and in a validated manner, allowing for monitoring over time of cognitive changes, emergence of novel deficits in previously unaffected domains, and improvement reflecting recovery from injury or improvement with therapy.

Administration and Scoring Instructions for the scale can be found in the Supplementary material.

Alternative versions of the scale

We developed new normative data on relevant test items for versions 1B, 1C, and 1D of the scale to avoid practice effects in subsequent administrations (Supplementary Table 9 and Supplementary material). Versions 1B, 1C and 1D have not been tested in other validation cohorts, but the approach taken to develop them was rigorous. All verbal fluency items used in the retest versions (semantic, phonemic, and category switching), and words used in the memory test and in the similarities test, were developed and refined in healthy controls. We used words within the same semantic categories, and we matched frequency of word usage according to published guidelines (Brysbaert and New, 2009). For phonemic fluency we selected alternative letters that have the same frequency of usage in the English language. Using a randomizer, we scrambled the numbers in the digit span forwards and backwards tasks, and the order of stimuli in the go/no-go task. Items not changed in the retest versions were Question 10 (neuropsychiatry), and the cube-draw condition, which requires that the diagram be explained to the subject verbally, before they are asked to copy the diagram if they are unable to provide an accurate drawing from their own concept of how a cube should look. These alternative retest versions of the scale (Versions 1B, 1C and 1D) will need to be evaluated in future prospective studies to determine if they are equivalent to the original version (1A), but the care with which these versions were developed predisposes them to a high degree of reproducibility.

Additional neuropsychological tests useful for detection of CCAS

There are eight tests that distinguished cerebellar patients from controls but which were not included in the CCAS scale. This set, derived from the 17 top-ranked tests minus the nine cognitive tests included in the scale, may be useful for exploration of CCAS when administered by trained personnel in neuropsychology laboratories. These are: Trails B in relation to Trails A, verbal paired associates I and II (VPA), verb for noun, pseudoword decoding, JLO, full similarities (WAIS-IV), FRSBE, and SCDC.

Limitations

The CCAS scale was derived from an adult cohort with known disease of the cerebellum. A paediatric version of the CCAS scale is in development but not yet finalized. Our exploratory cohort included mostly patients with degenerative disorders and a relatively small number of patients (nine) with focal cerebellar lesions. The validation cohort added nine more patients with focal cerebellar injury (haemorrhage, stroke, tumour), but these numbers are insufficient to perform definitive correlations between structure and cognitive function. Such analyses have recently been performed in cerebellar stroke patients (Stoodley *et al*., 2016), and further studies of this type are needed to provide deeper insights into cerebrocerebellar anatomical and cognitive networks. By providing new normative data for alternative items within each test item of the scale we facilitate repeat testing while avoiding practice effects. Future studies need to test scale Versions 1B, 1C and 1D in new healthy and disease validation cohorts. It remains to be shown in future studies whether the CCAS/Schmahmann scale, alone or in conjunction with the CNRS, can detect a cerebellar contribution to cognitive decline and neuropsychiatric manifestations in a broader set of neurology and psychiatry patients.

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Supplementary material

Supplementary material is available at *Brain* online.

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SUPPLEMENTARY DOCUMENTS

Supplement 1
Radiographic brain images of patients evaluated in this study.

Selected brain imaging findings for the patients in this study. Representative cases are presented for each category of disease, such as the inherited ataxias and neurodegenerative disorders. For unique cases, such as hemorrhage and tumor, images from each individual's scans are shown. These are not labeled according to case number, as the data for each case are not individually presented. Images are shown in the sagittal, axial and, when available, coronal planes through the cerebellum. An axial image shows the cerebral hemisphere at the level of the thalamus, basal ganglia, cerebral hemispheric white matter and ventricles. MRI sequences were chosen that optimally reflect the findings, including high resolution T1-weighted (MPRAGE, BRAVO), T2-weighted, and fluid attenuated inversion recovery (FLAIR) sequences. In some cases in which MRI was not obtained for clinically relevant reasons, head CT is shown, with sagittal and coronal reconstructions when available. For ease of reference, the diagnosis in each case is shown below the brain images.

Supplement 2
Table of all cognitive tests administered in this study

Supplement 3
Table of domains within the Cerebellar Neuropsychiatric Scale

Supplement 4:
Table: Performance on MMSE and MoCA of patients (n=64) and controls (n=54). * = $p < .05$, ** = $p < .01$, *** $p < .001$ (student's t-test, 2-tailed, equal variances).

Supplement 5

Table: Test of correlations between subtests within the CCAS/Schmahmann Scale and BARS total score, 25-foot walk, and 9 Hole Peg Board (dominant hand) performance evaluated using Pearson r (Cohen, 1988).

Abbreviations: LDSF, longest digit span forward; LDSB longest digit span backwards.

Supplement 6

Table: Test measures ranked by descending order for difference in z-score means between patients and controls, without *a-priori* hypothesis of CCAS domain grouping.

Abbreviations: CNRS - Cerebellar Neuropsychiatric Rating Scale (Schmahmann *et al.*, 2007), FRSBE - Frontal System Behavior Scale, SCDC - Social and Communication Disorders Checklist, TC - total correct, TS - total score, TM - total number of mistakes. S – seconds. Note: Letter fluency (F, A, S letters) and Category switching fluency (animals and boy's names) were not ranked separately.

Supplement 7

Brief Ataxia Rating Scale

Supplement 8

Administration and Scoring Instructions for the CCAS/Schmahmann Scale

Supplement 9

Table of retest items used for subsequent versions of the CCAS/Schmahmann Scale

Supplement 10

The Cerebellar Cognitive Affective / Schmahmann Syndrome Scale. (Version 1B)

Supplement 11

The Cerebellar Cognitive Affective / Schmahmann Syndrome Scale. (Version 1C)

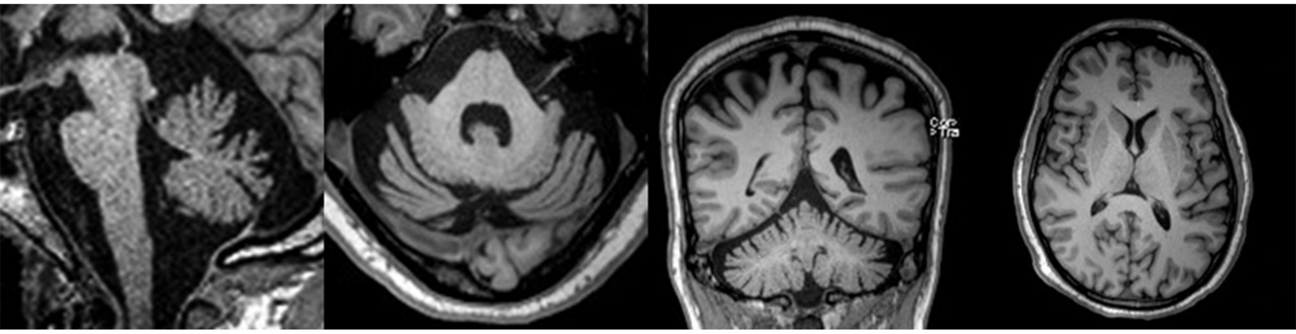
Supplement 12

The Cerebellar Cognitive Affective / Schmahmann Syndrome Scale. (Version 1D)

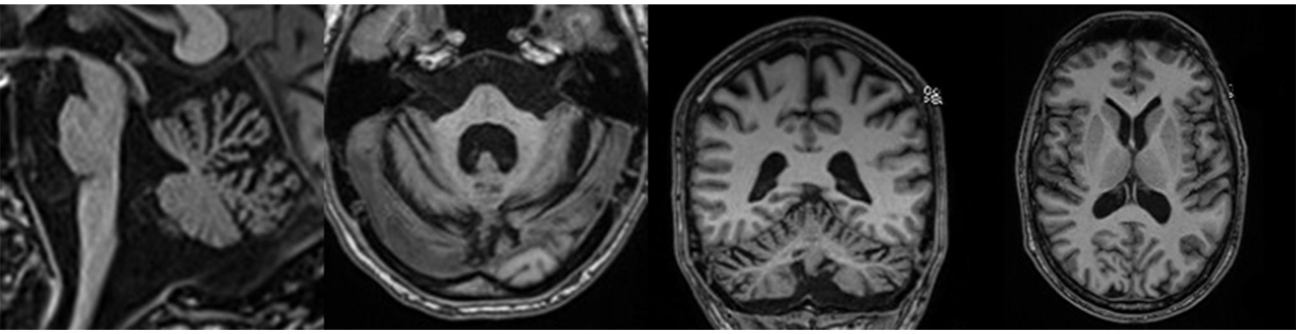
Supplement 1. Figure Legend

Selected brain imaging findings for the patients in this study. Representative cases are presented for each category of disease, such as the inherited ataxias and neurodegenerative disorders. For unique cases, such as hemorrhage and tumor, images from each individual's scans are shown. These are not labeled according to case number, as the data for each case are not individually presented. Images are shown in the sagittal, axial and, when available, coronal planes through the cerebellum. An axial image shows the cerebral hemisphere at the level of the thalamus, basal ganglia, cerebral hemispheric white matter and ventricles. MRI sequences were chosen that optimally reflect the findings, including high resolution T1-weighted (MPRAGE, BRAVO), T2-weighted, and fluid attenuated inversion recovery (FLAIR) sequences. In some cases in which MRI was not obtained for clinically relevant reasons, head CT is shown, with sagittal and coronal reconstructions when available. For ease of reference, the diagnosis in each case is shown below the brain images.

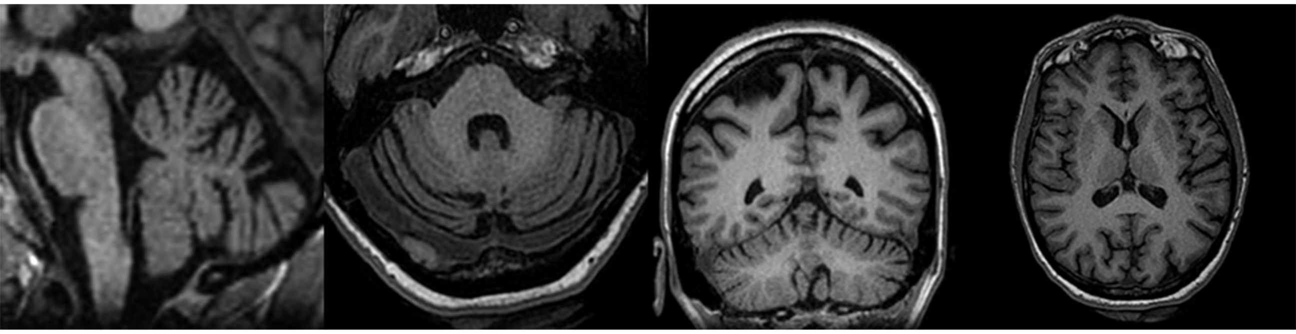
AUTOSOMAL DOMINANT ATAXIAS



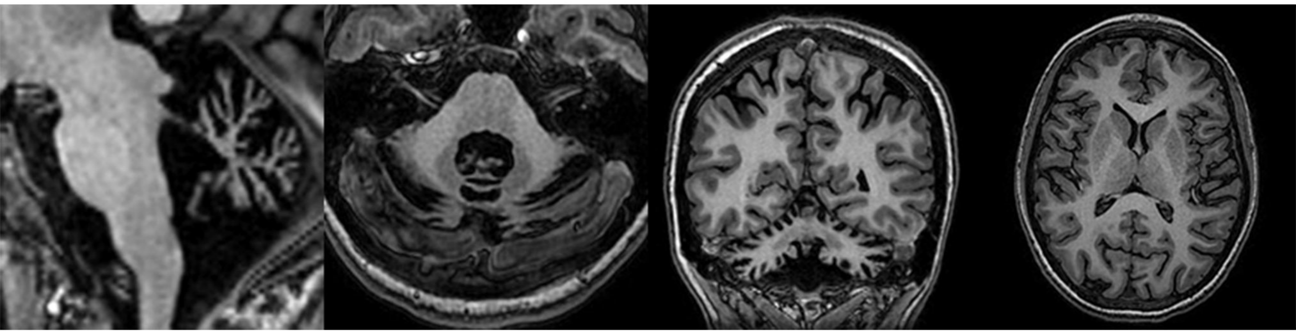
Spinocerebellar ataxia, type 1



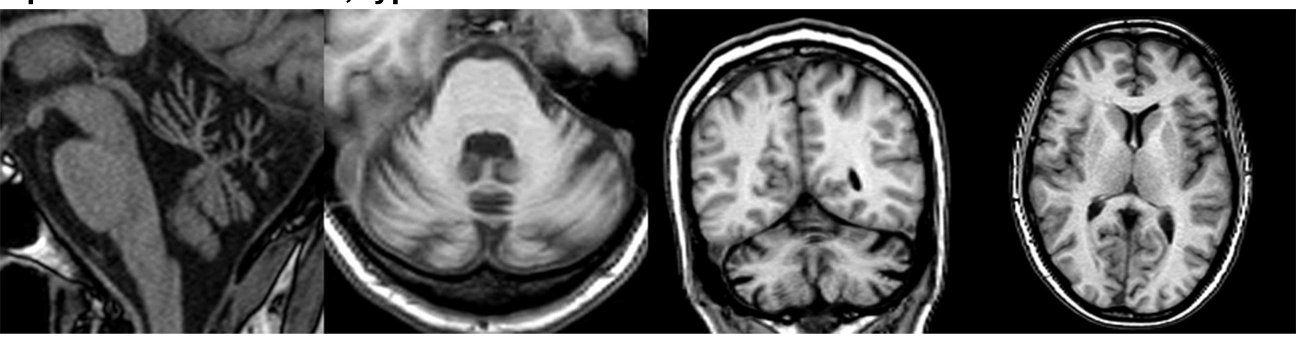
Spinocerebellar ataxia, type 2



Spinocerebellar ataxia, type 3

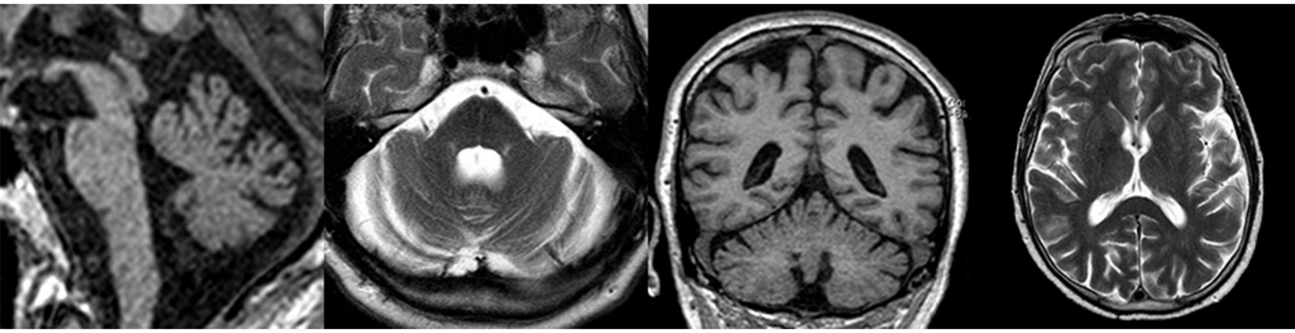


Spinocerebellar ataxia, type 5

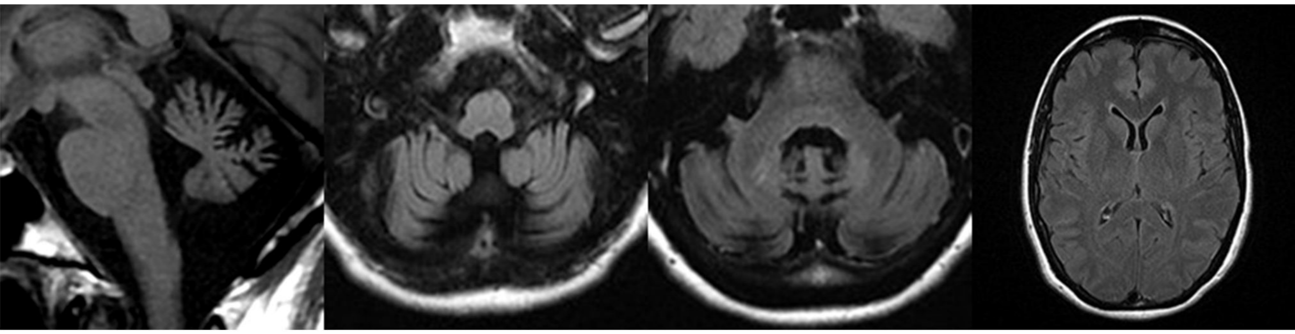


Spinocerebellar ataxia, type 6

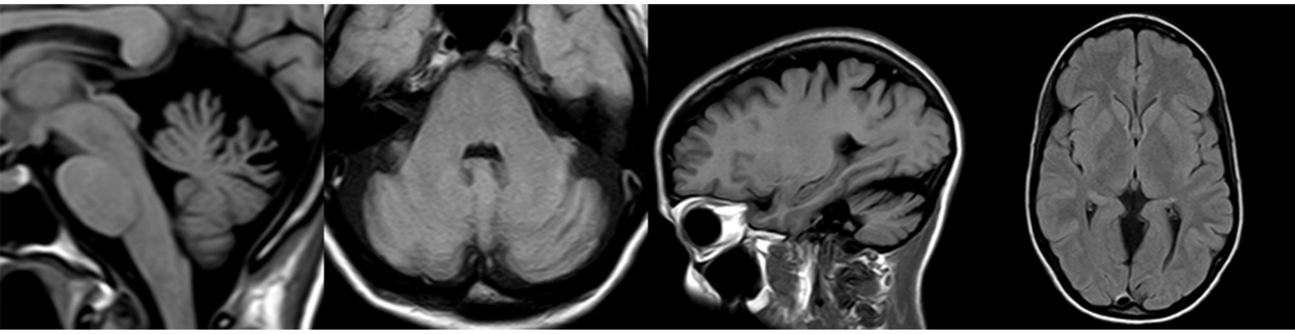
AUTOSOMAL DOMINANT ATAXIAS (continued)



Spinocerebellar ataxia, type 7



Spinocerebellar ataxia, type 8



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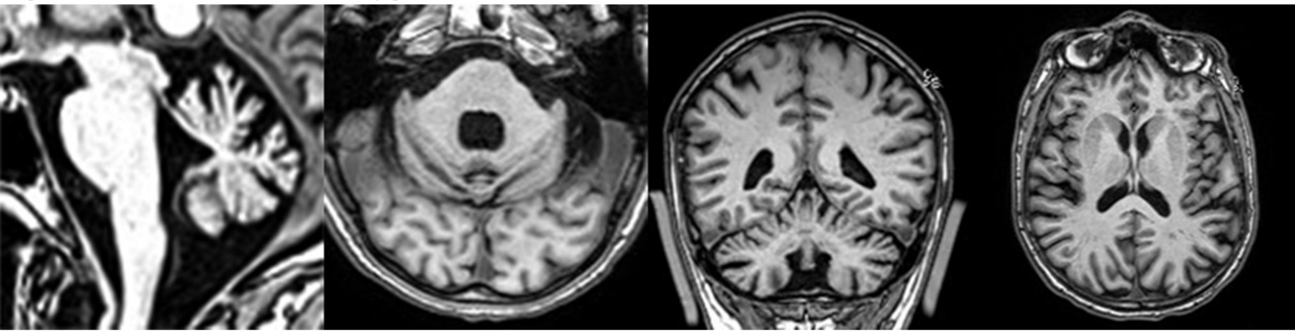
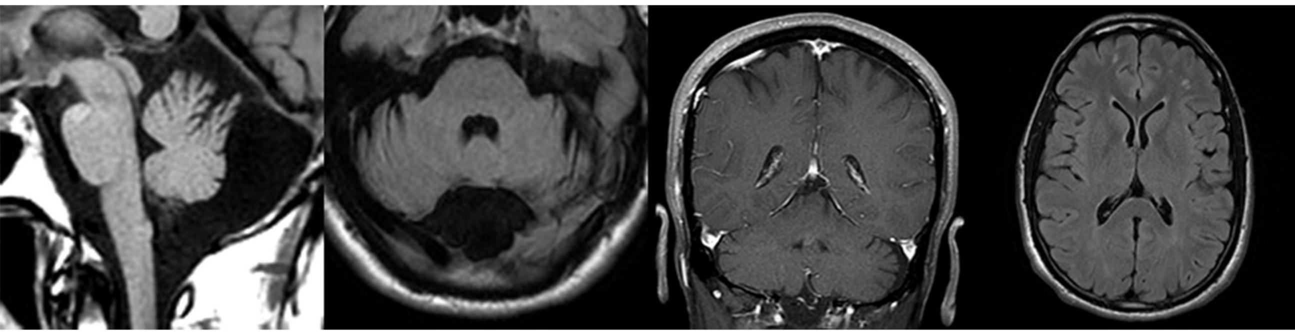
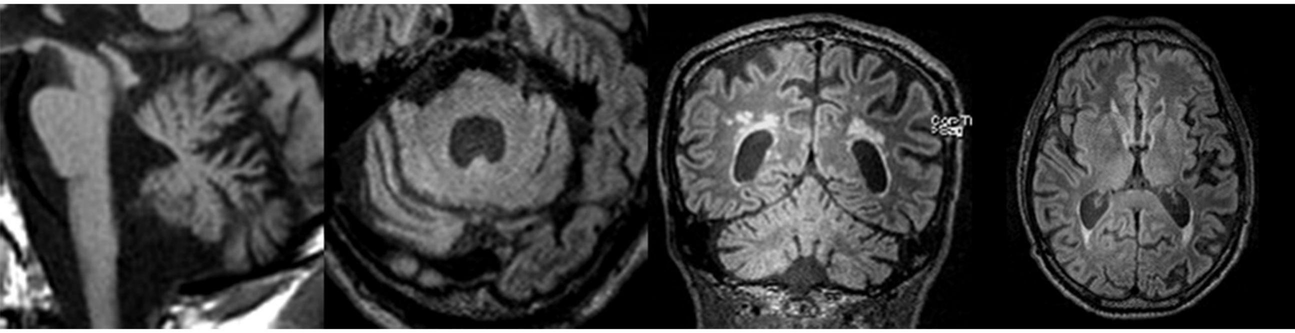


Spinocerebellar ataxia, type 28

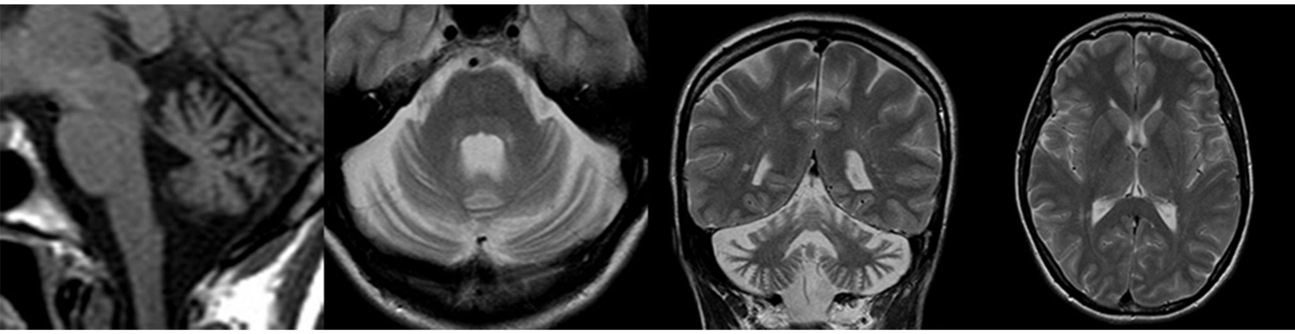


Autosomal dominant ataxia (gene not identified)

AUTOSOMAL DOMINANT ATAXIAS (continued)

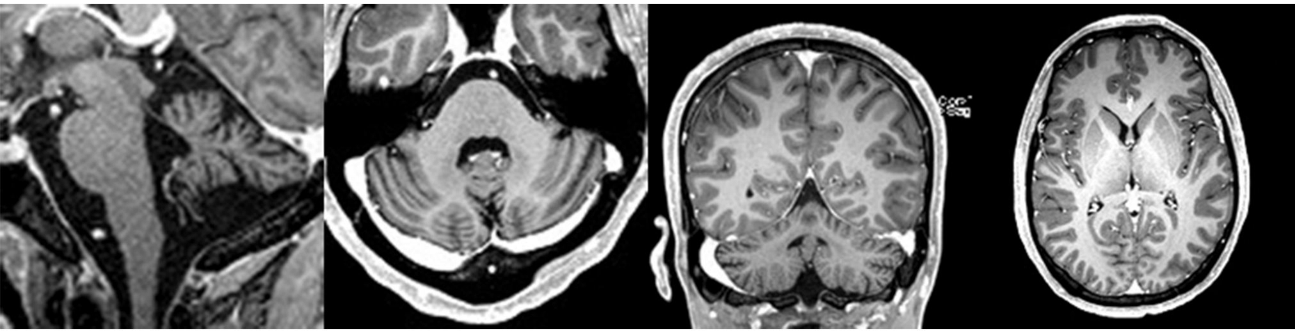


Dentatorubral-pallidoluysian atrophy (DRPLA)

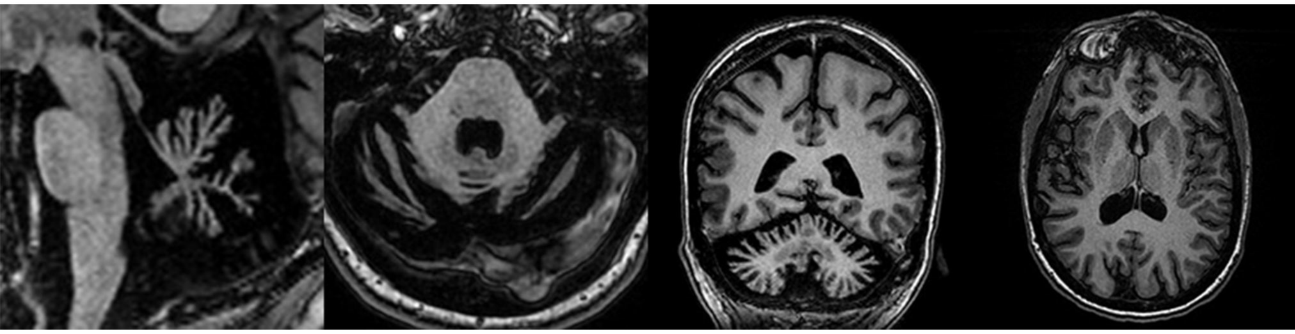


Hereditary spastic paraplegia, type 8

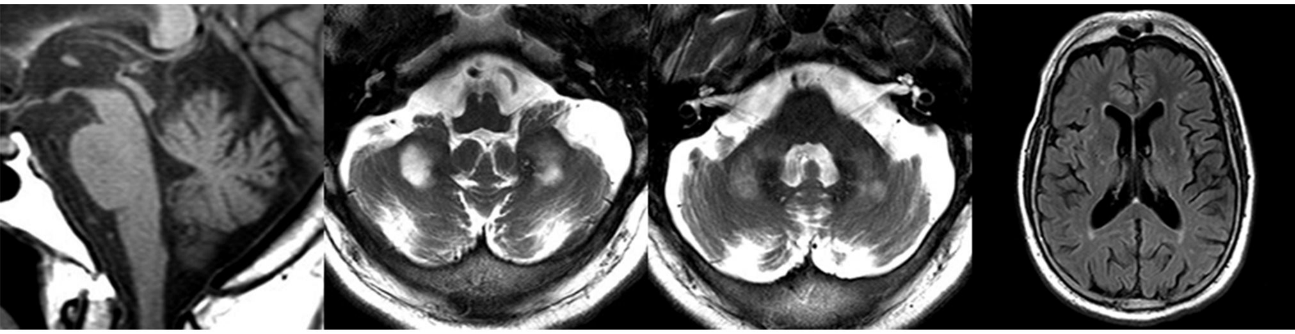
RECESSIVELY INHERITED ATAXIAS



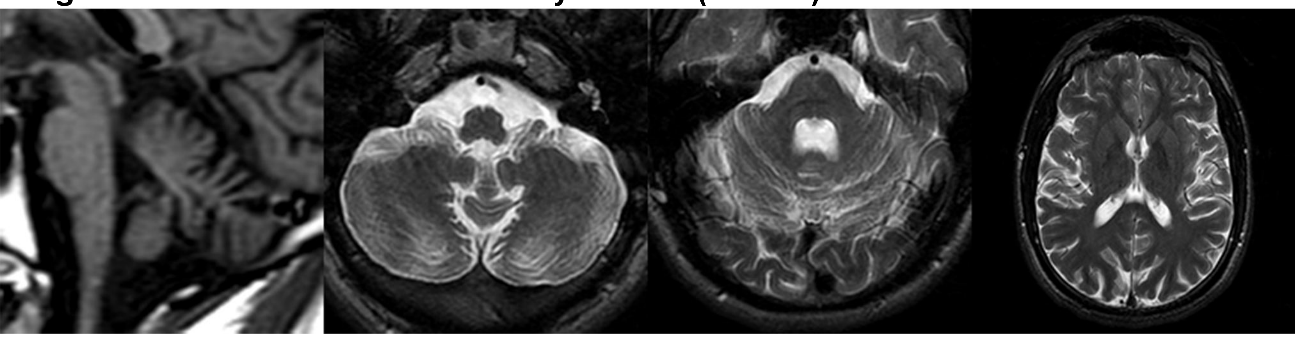
Ataxia with oculomotor apraxia, type 2 (AOA2)



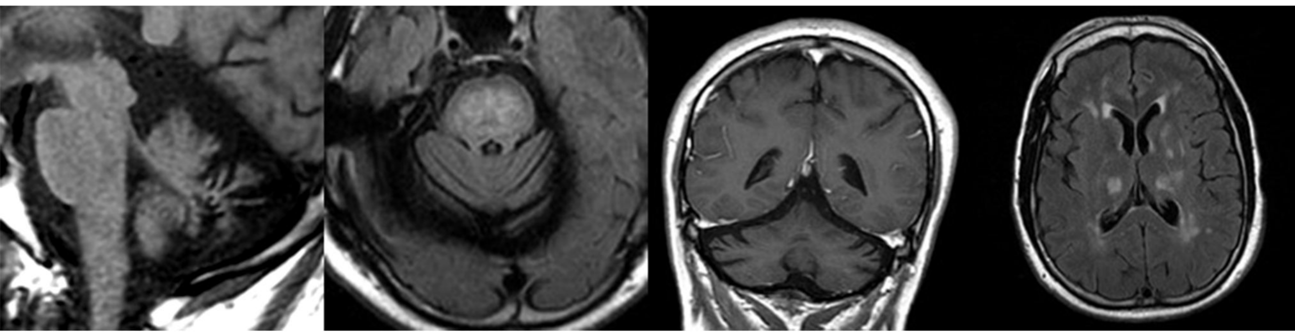
Autosomal recessive cerebellar ataxia, type 1 (ARCA1)



Fragile X-associated tremor/ataxia syndrome (FXTAS)

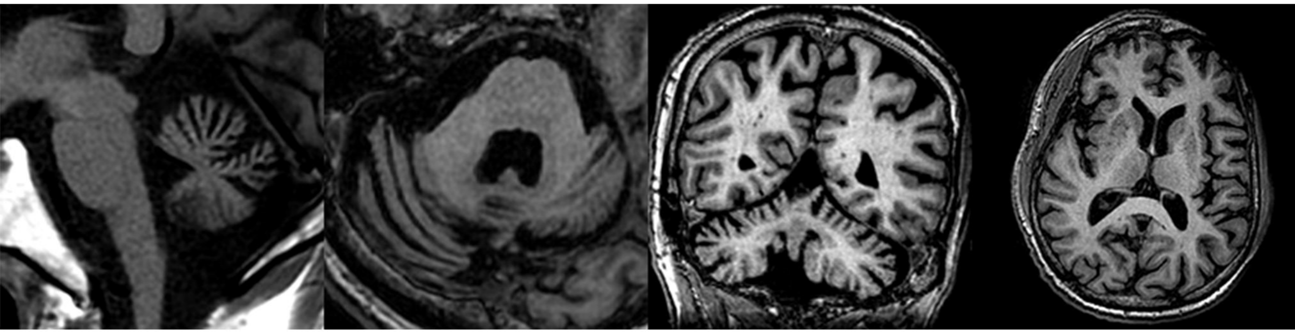


Friedreich's ataxia



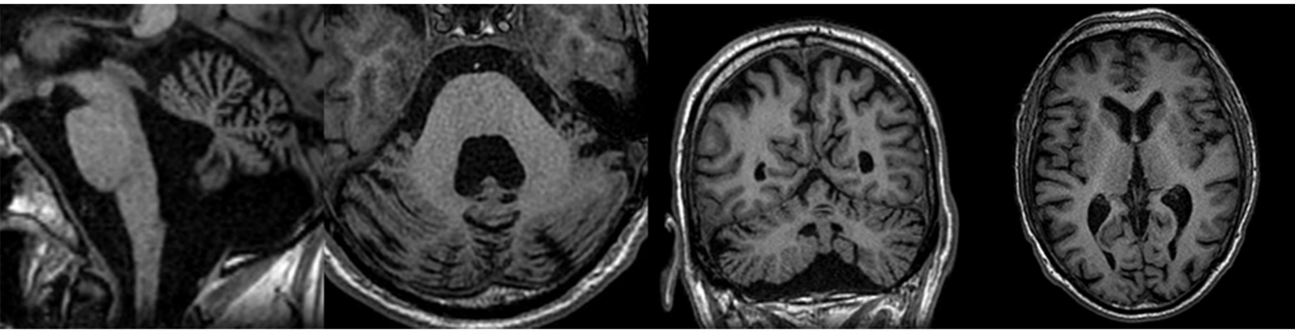
Gordon Holmes Syndrome

RECESSIVELY INHERITED ATAXIAS (continued)

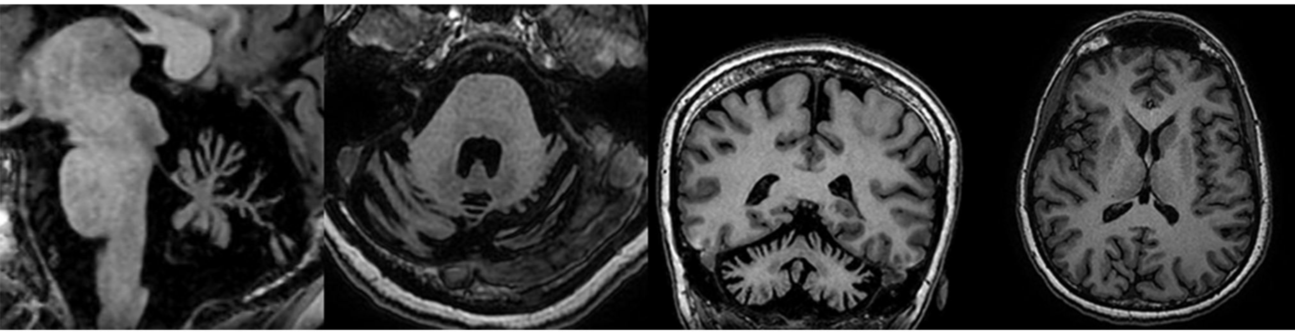


X-linked recessive ataxia

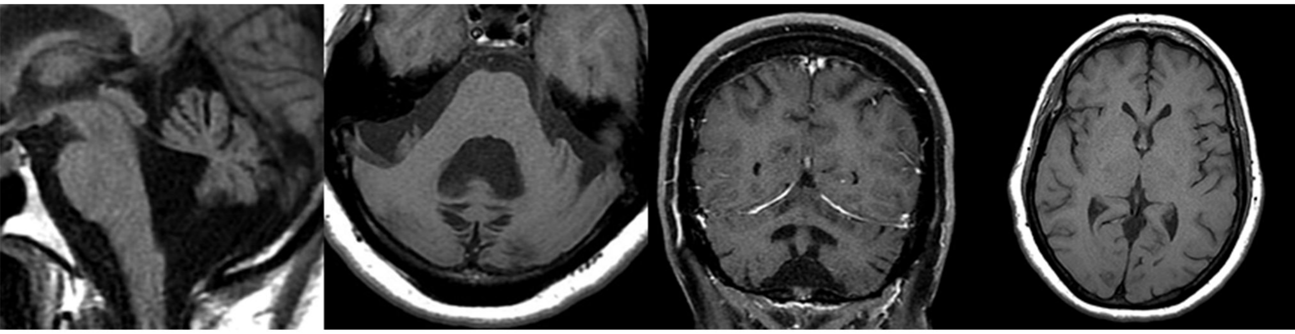
NEURODEGENERATIVE ATAXIAS



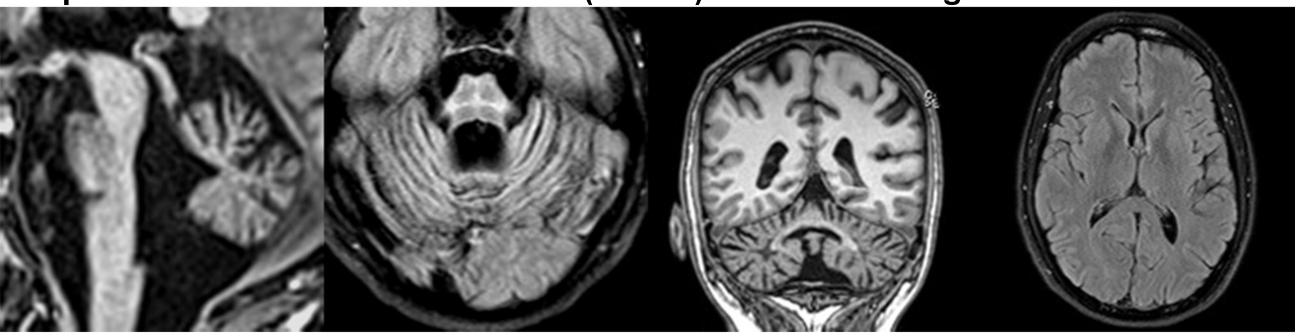
Ataxia with sensory neuropathy



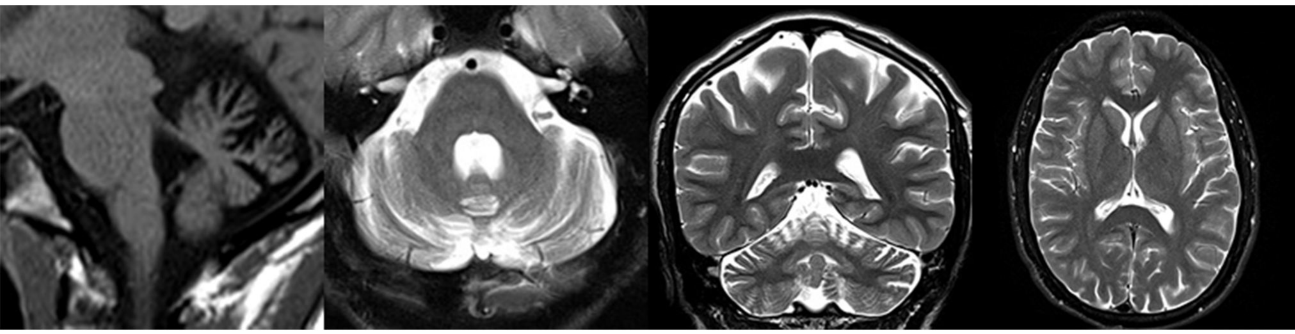
Idiopathic late onset cerebellar ataxia (ILOCA)



Idiopathic late onset cerebellar ataxia (ILOCA) with senataxin gene variant

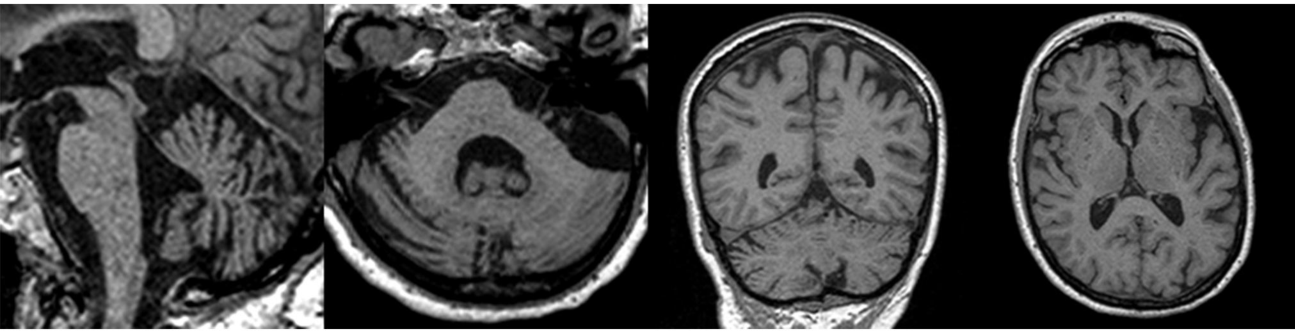


Multiple system atrophy, cerebellar type (MSA-C)

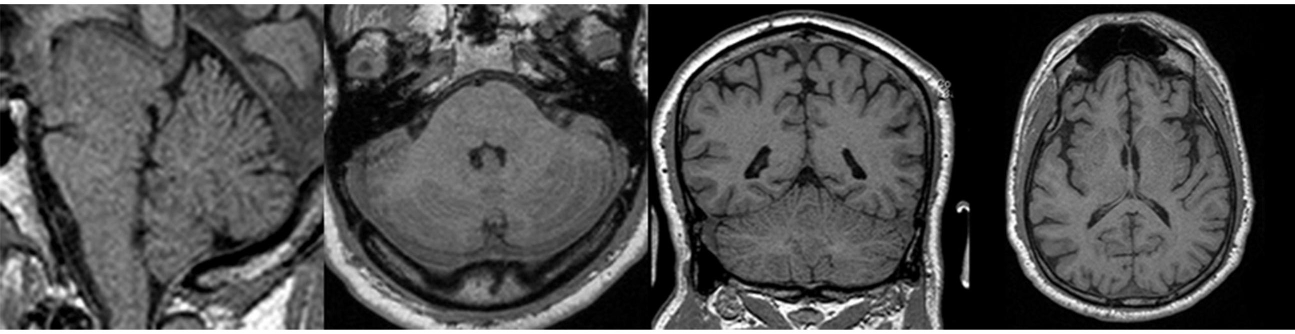


Nonprogressive cerebellar ataxia

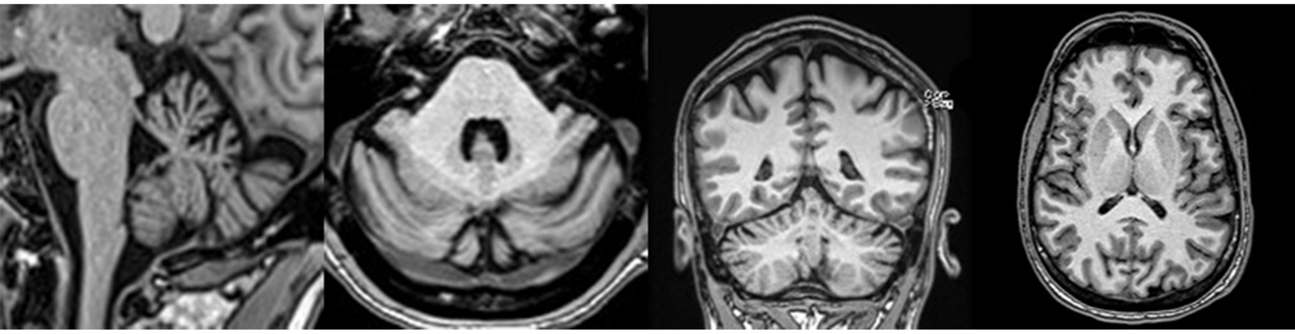
NEURODEGENERATIVE ATAXIAS (continued)



Progressive ataxia and palatal tremor (PAPT)

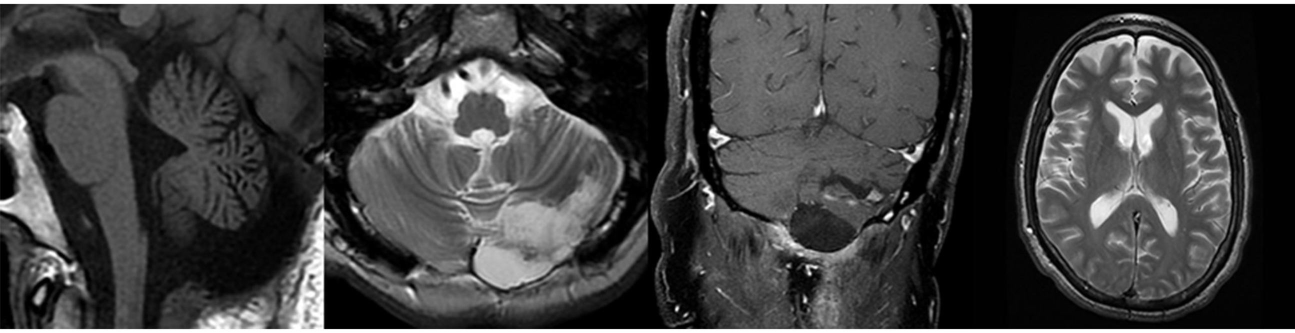


Sagging brain syndrome

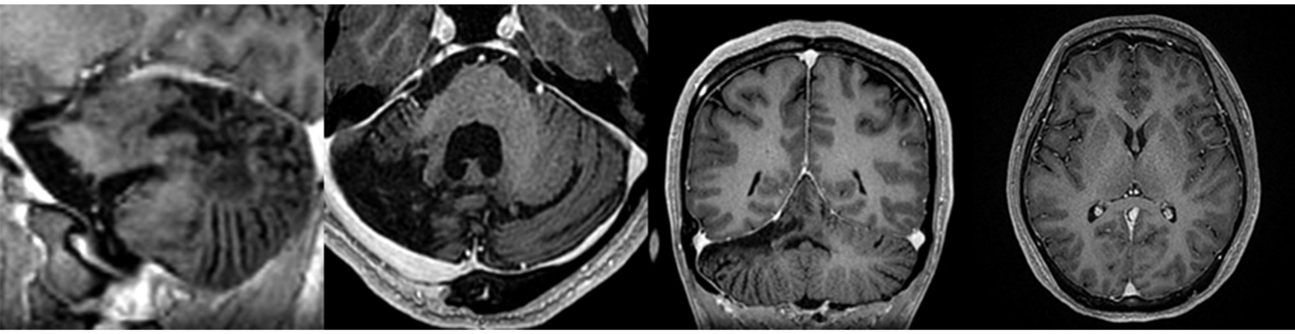


Spastic ataxia

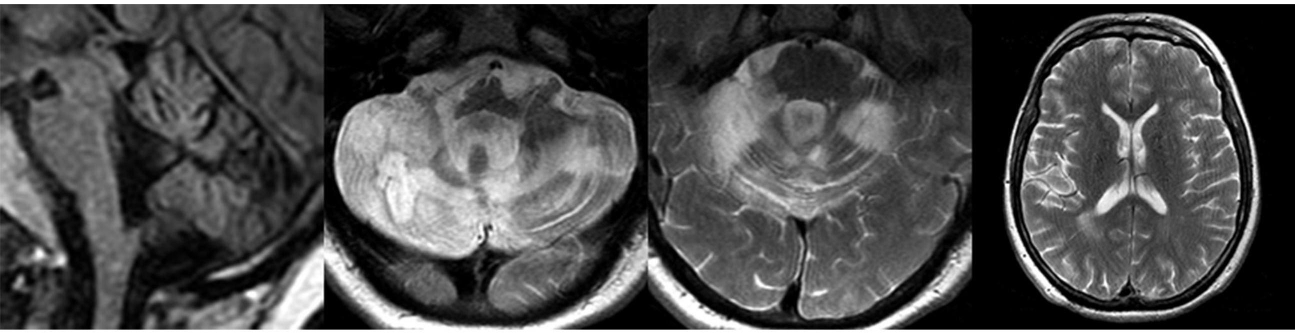
ACQUIRED CEREBELLAR DISORDERS



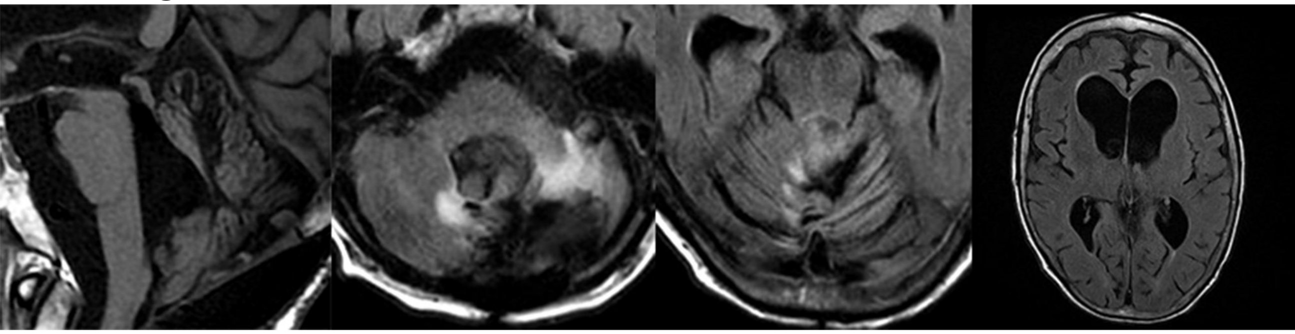
Hemorrhage



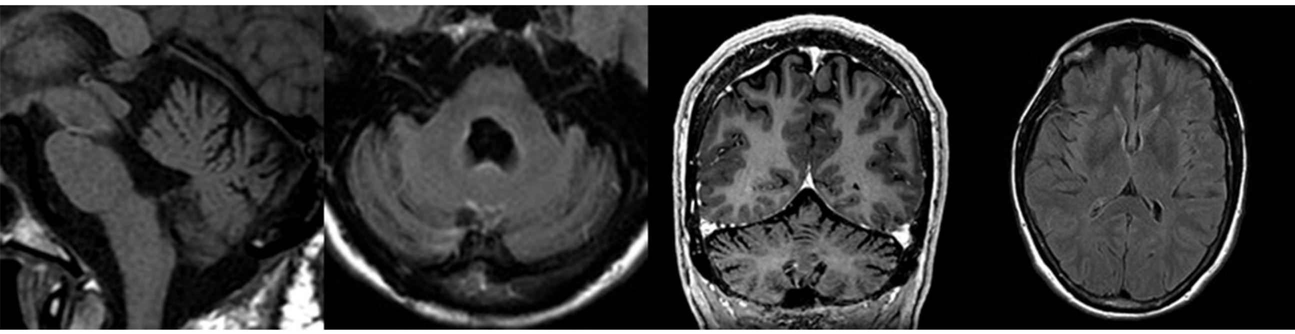
Hemorrhage



Hemorrhage

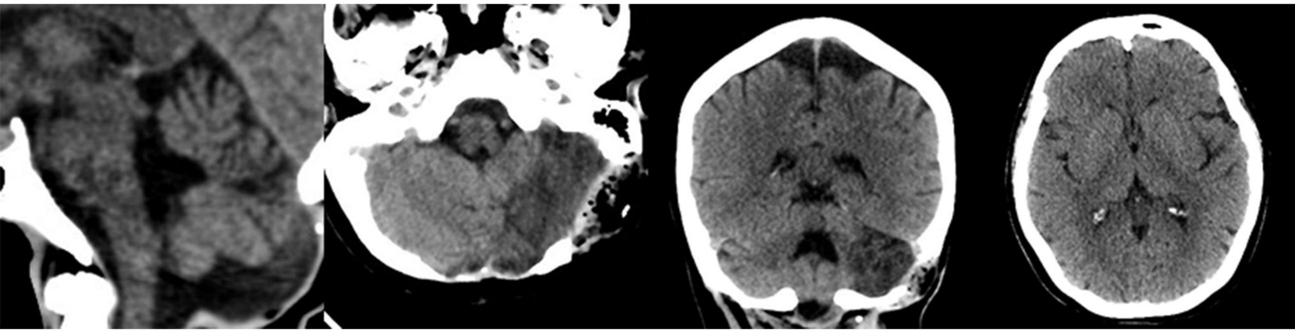


Hemorrhage

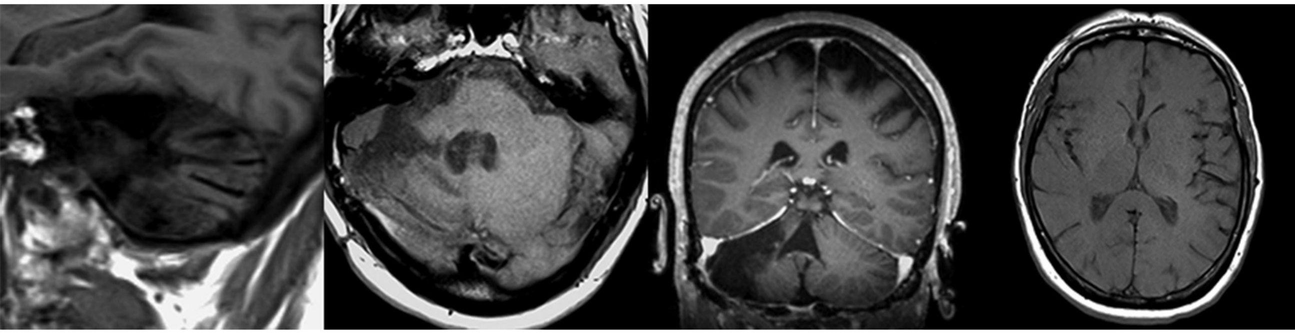


Pontine cavernoma

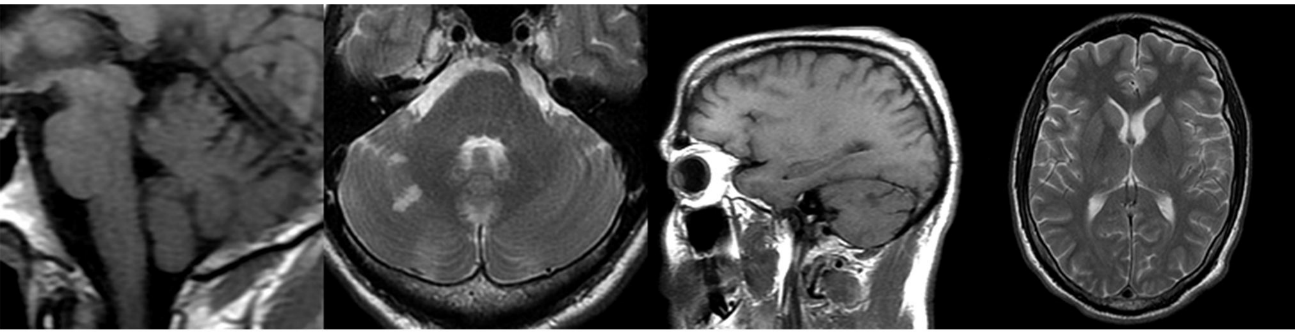
ACQUIRED CEREBELLAR DISORDERS (continued)



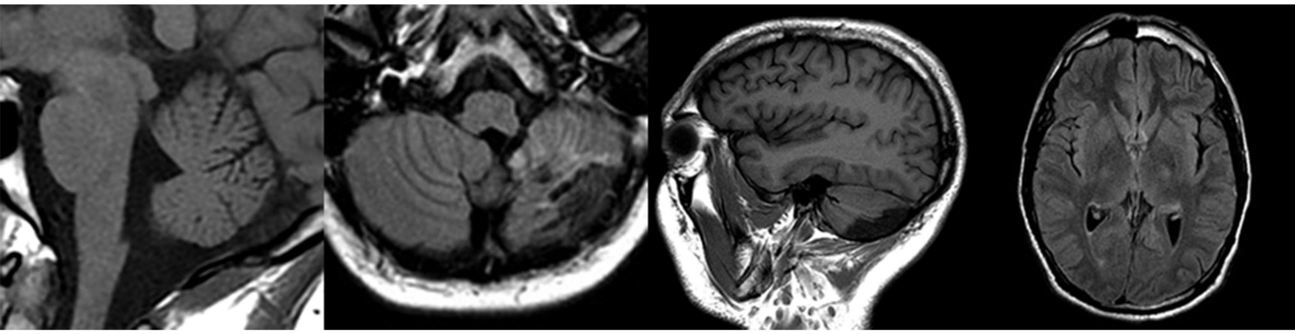
Ischemic stroke



Ischemic stroke



Ischemic stroke



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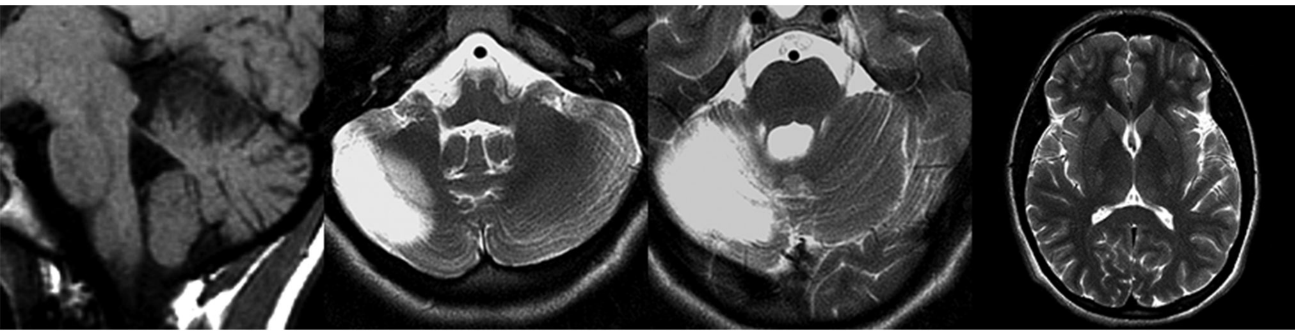
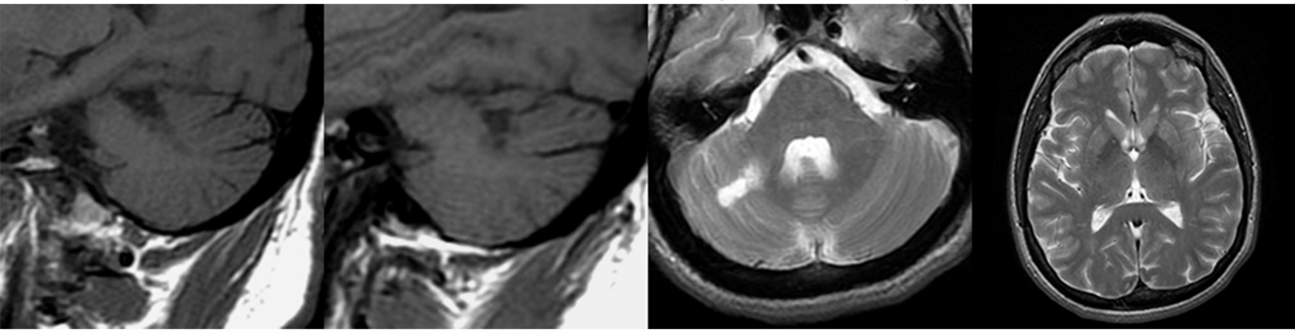
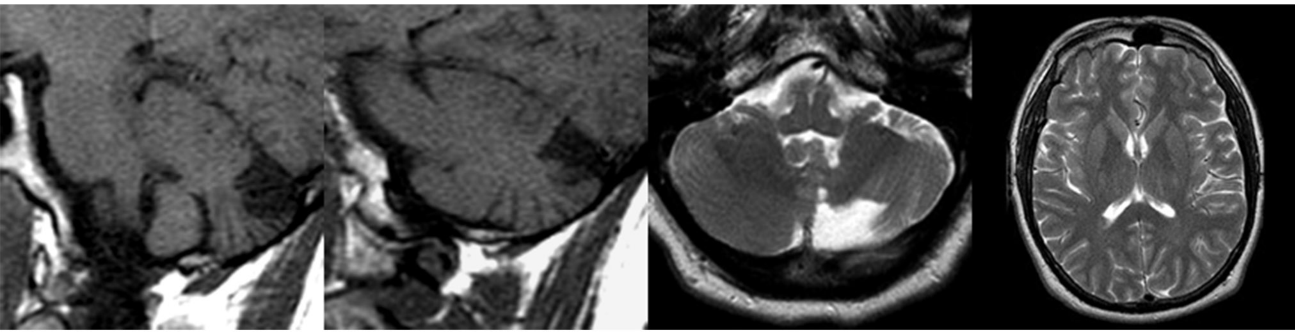


Ischemic stroke

ACQUIRED CEREBELLAR DISORDERS (continued)



Ischemic stroke



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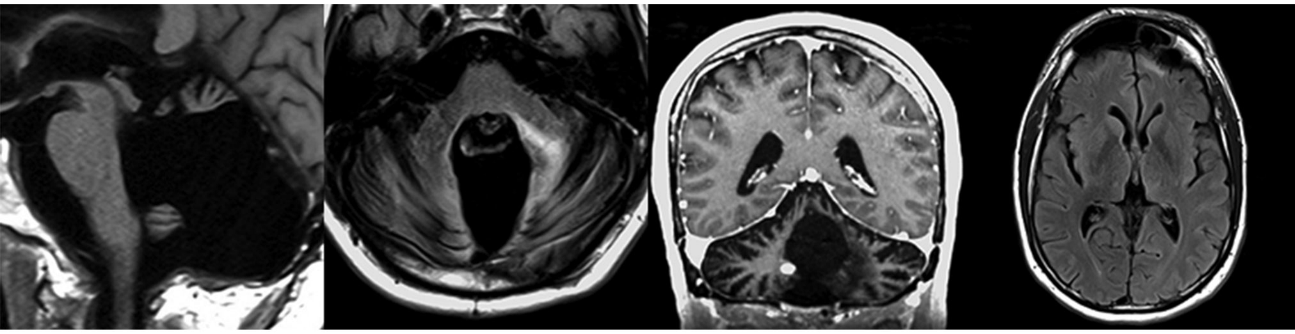
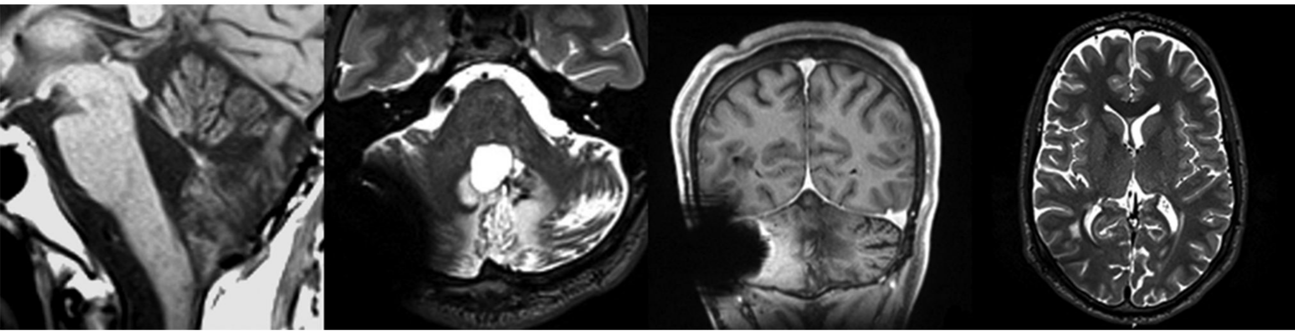
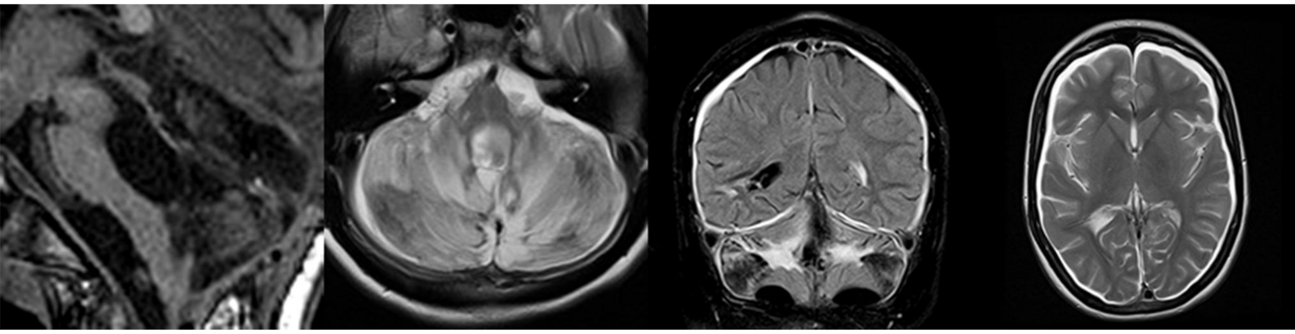


Post-tumor resection

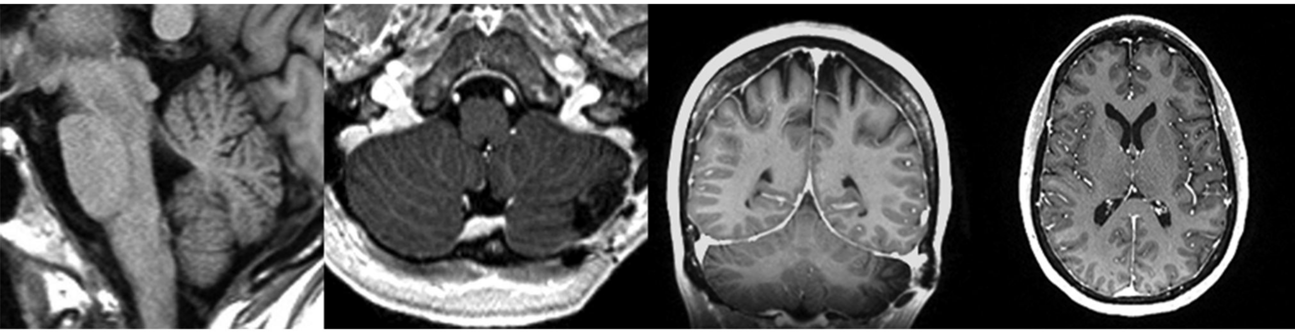


Post-tumor resection

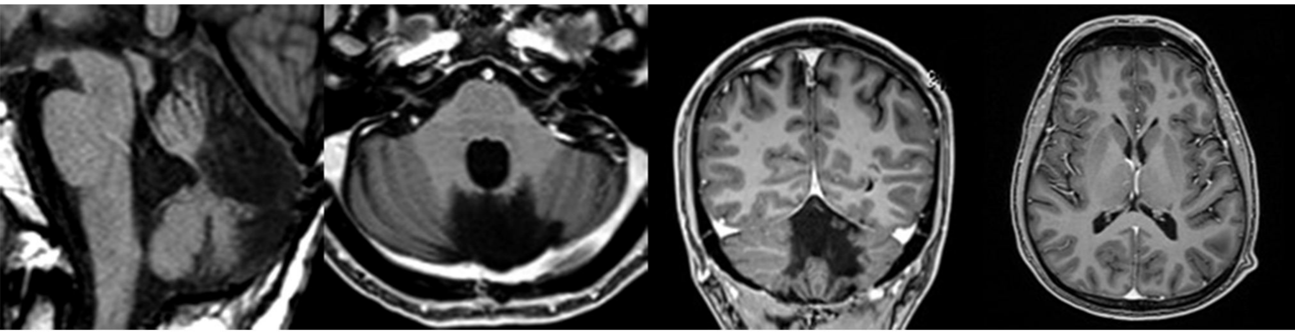


Post-tumor resection

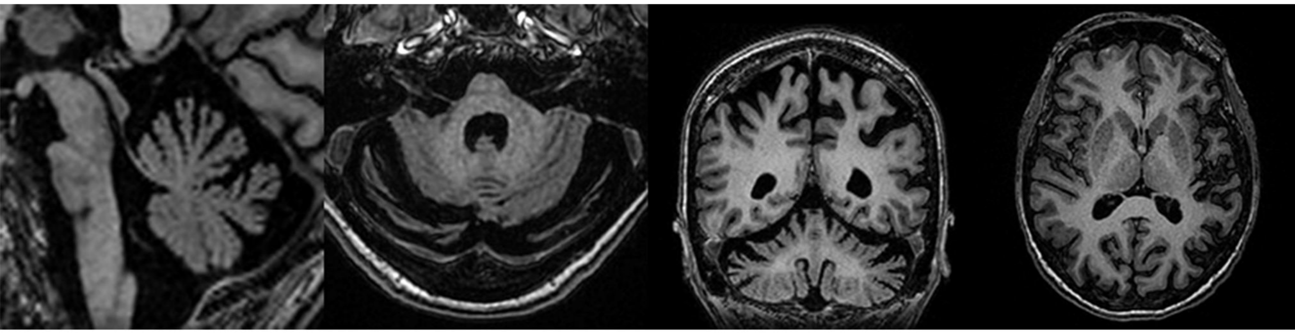
ACQUIRED CEREBELLAR DISORDERS (continued)



Post-tumor resection



Post-tumor resection



Remote rhombencephalitis

Supplement 2. Table: Neuropsychological tests, test domains and descriptions of measures

Domain and Measure	Description of Measure
Cognitive	
Overall cognitive abilities	
• Mini Mental State Examination (MMSE) (Folstein et al., 1975) • Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) • Planning (ideational praxis) (Heilman and Gonzalez Rothi, 2003)	Include measures in the domains of visual-spatial, executive, linguistic, memory, attention, abstraction and general orientation abilities.
Attention/Alertness	
Attention Span • Forward digit span (Wechsler, 2008)	Measures working memory and attention.
Alertness • Vigilance (the A test) (Sturb and Black, 1993)	Measures sustained attention.
Executive Functioning	
Working memory • Forward digit span (Wechsler, 2008) • Reversed digit span (Wechsler, 2008) • Months backwards (Shapiro et al., 1956)	Measure short term memory and the ability to hold information in mind and mentally manipulate it.
Cognitive flexibility • Letter-number sequencing (Wechsler, 2008) • Category switching (Delis et al., 2001)	Measure lexical access speed, sequencing and flexibility of thinking.
Processing speed • Trails A and B (Wechsler, 2008)	Measures psychomotor speed, visual search, sequencing and flexibility of thinking.
Inhibition • Go/no-go (Nasreddine et al., 2005)	Measures inhibitory control.
Memory	
Verbal memory • Word immediate recall • Word delayed recall • Verbal paired associates (Wechsler, 2008)	Measure short and long term memory.
Language	
Expressive Language • Production of Derived Words (Marien et al., 2014) • Oral Sentence Production (Caplan and Hanna, 1998) • Word Repetition • Verb for Noun (Fiez, 1996) • Pseudoword Decoding (Wechsler, 2008) • Word Stem Completion (Soler et al., 2015) • Naming (Nasreddine et al., 2005) • Phonemic fluency (Delis et al., 2001) • Semantic fluency (Delis et al., 2001)	Measure lexical access speed, language expression at semantic and grammatical level as well as phonetic decoding skills.

Visual Motor / Visual Spatial	
Visual Construction/Organization • Star • Pentagon (Folstein et al., 1975) • Cube (Kokmen et al., 1987) • Clock (Freedman et al., 1994)	Measure visual-construction abilities.
Visual-Perceptual • Judgment of Line Orientation (Benton et al., 1983)	Measures the ability to match the angle and orientation of lines in space.
Abstract Reasoning	
Visual/Verbal abstract Reasoning • Addition (Cohen, 1997) • Subtraction (Cohen, 1997) • Similarities (Wechsler, 2008) • Cognitive estimation (Macpherson et al., 2014)	Measure abstract concept formation, numerical reasoning ability, and the capacity to produce reasonable cognitive estimates.
Sensorimotor	
• Brief Ataxia Rating Scale (Schmahmann et al., 2009) • 9-Hole Pegboard Test (Mathiowetz et al., 1985) • 25-foot timed walk	Measure gross and fine motor ataxia.
Behavior / Emotional Regulation	
• Frontal Systems Behavior Scale (Grace et al., 1999) • Social Communication Disorders Checklist (Skuse et al., 1997) • Cerebellar Neuropsychiatric Rating Scale (Daly et al., 2016)	Measure presence of neuropsychiatric symptoms including abnormalities in attentional control, emotional control, social skills, and presence of autism spectrum and psychosis spectrum symptoms.

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	Positive (exaggerated) symptoms	Negative (diminished) symptoms
Attentional control	Inattentiveness Distractibility Hyperactivity Compulsive and ritualistic behaviors	Ruminativeness Perseveration Difficulty shifting focus of attention Obsessional thoughts
Emotional control	Impulsiveness, disinhibition Lability, unpredictability Incongruous feelings, pathological laughing/crying Anxiety, agitation, panic	Anergy, anhedonia Sadness, hopelessness Dysphoria Depression
Autism spectrum	Stereotypical behaviors Self stimulation behaviors	Avoidant behaviors, tactile defensiveness Easy sensory overload
Psychosis spectrum	Illogical thought Paranoia Hallucinations	Lack of empathy Muted affect, emotional blunting Apathy
Social skill set	Anger, aggression Irritability Overly territorial Oppositional behavior	Passivity, immaturity, childishness Difficulty with social cues and interactions Unawareness of social boundaries Overly gullible and trusting

Supplement 3. Table: Domains assessed in the Cerebellar Neuropsychiatric Rating Scale

Neuropsychiatric symptoms and signs arranged according to five major domains, each with positive / overshoot / hypermetric and negative / undershoot / hypometric features. Adapted from Table 1 in Schmahmann et al., 2007.

Supplement 4. Brief Ataxia Rating Scale (BARS) (Schmahmann et al., 2009)

BRIEF ATAXIA RATING SCALE (BARS)

Gait
0: Normal
1: Almost normal naturally, but unable to walk with feet in tandem position
2: Walking without support, but clearly abnormal and irregular
3: Walking without support but with considerable staggering; difficulties in half turn
4: Walking without support not possible; uses support of the wall for 10-meter test.
5: Walking possible only with one cane
6: Walking possible only with two canes or with a stroller
7: Walking possible only with one accompanying person
8: Walking impossible with one accompanying person (2-person assist; wheelchair)

Knee-tibia test (decomposition of movement and intention tremor)
(Left and Right scored)
0: Normal
1: Lowering of heel in continuous axis, but movement is decomposed in several phases, without real jerks, or abnormally slow
2: Lowering jerkily in the axis
3: Lowering jerkily with lateral movements
4: Lowering jerkily with extremely long lateral movements, or test impossible

LEFT
RIGHT

Finger-to-nose test (decomposition and dysmetria of arm and hand)
(Left and Right scored)
0: Normal
1: Oscillating movement of arm and/or hand without decomposition of the movement
2: Segmented movement in 2 phases and / or moderate dysmetria in reaching nose
3: Segmented movement in more than 2 phases and / or considerable dysmetria in reaching nose
4: Dysmetria preventing the patient from reaching nose

LEFT
RIGHT

Dysarthria
0: Normal
1: Mild impairment of rate / rhythm / clarity
2: Moderate impairment of rate / rhythm / clarity
3: Severely slow and dysarthric speech
4: Speech absent or unintelligible

Oculomotor abnormalities
0: Normal
1: Slightly slowed pursuit, saccadic intrusions, hypo/hypermetric saccade, nystagmus
2: Prominently slowed pursuit, saccadic intrusions, hypo/hypermetric saccade, nystagmus

TOTAL (out of 30)

TEST	PATIENTS MEAN (SD)	CONTROLS MEAN (SD)
MMSE Total Score (abnormal if <24)	**28.70 (1.25)**	**29.56 (0.72)**
MOCA Total score (abnormal if <26)	**26.45 (2.52)**	**28.77 (1.22) *** **
MOCA Sub-Scores		
Alt. Trail Making	0.80 (0.40)	0.93 (0.26) *
Cube Copy	0.73 (0.45)	0.93 (0.26) **
Clock Contour	0.93 (0.25)	1.00 (0.00)
Clock Numbers	0.96 (0.17)	1.00 (0.00)
Clock hands	0.72 (0.45)	0.94 (0.23) **
Visuospatial/Executive Total Subscore	4.84 (0.37)	4.83 (0.38) ***
Naming Lion	1.00 (0.00)	0.98 (0.14)
Naming Rhino	0.91 (0.28)	1.00 (0.00) *
Naming Camel	0.98 (0.14)	0.98 (0.14)
Naming Total	2.84 (0.55)	2.96 (0.19)
Forward Digit span	0.92 (0.27)	0.96 (0.19)
Backwards digit span	0.92 (0.27)	1.00 (0.00) *
Vigilance	1.00 (0.00)	1.00 (0.00)
Serial subtraction	2.90 (0.30)	3.00 (0.00)*
Attention Total	5.59 (0.85)	5.93 (0.24) **
Sentence repetition	1.83 (0.55)	1.98 (0.24)
Phonemic fluency	0.51 (0.50)	0.92 (0.27) ***
Language Total	2.25 (0.74)	2.93 (0.25) ***
Automobile-boat	0.98 (0.13)	1.00 (0.00)
Horse-tiger	0.90 (0.30)	0.98 (0.14)
Abstraction Total	1.87 (0.39)	1.98 (0.14) *
Delayed recall	3.46 (1.51)	4.35 (0.73) ***
Recall Category cue	0.29 (0.46)	0.19 (0.39)
Recall Multiple choice cue	0.94 (1.08)	0.48 (0.67) **
Orientation	5.95 (0.32)	5.98 (0.14)

Supplement 5. Table: Perfomance of patients and controls on MMSE and MoCA.
* $p < .01$, ** $p < .001$, *** $p < .0001$

		Cube	Verbal Recall	LDSF	LDSB	Semantic Fluency	Phonemic Fluency	Category Switching	Similarities	Go/No-Go
BARS	**Pearson Correlation**	-.083	-.036	.142	.115	-.281	-.085	-.181	-.097	-.174
	Sig. (2-tailed)	.587	.802	.345	.450	.065	.582	.239	.516	.242
	N	45	51	46	45	44	44	44	47	47
25 foot walk seconds (trial 2)	**Pearson Correlation**	.125	-.076	.096	.123	-.315	-.207	-.144	-.125	.111
	Sig. (2-tailed)	.369	.576	.497	.392	**.028**	.153	.325	.391	.427
	N	54	57	52	51	49	49	49	49	53
Pegboard seconds (dominant hand, trial 2)	**Pearson Correlation**	-.195	-.019	.024	-.238	-.436	-.314	-.348	-.322	-.243
	Sig. (2-tailed)	.142	.883	.857	.077	**.001**	**.021**	**.010**	**.018**	.066
	N	58	62	57	56	54	54	54	54	58

Supplement 6. Table: Test of correlations between subtests within the CCAS/Schmahmann Scale and BARS total score, 25-foot walk, and 9 Hole Peg Board (dominant hand). Performance evaluated using Pearson r (Cohen, 1988).

Domain	Test	z score difference between patients and controls	One tailed paired t-test		
			t	*df*	*p*
Executive function	Trails B (s)	7.30	-6.535	62	0.000
Language	Verb for noun (TS/17)	6.44	-8.342	49	0.000
Executive function	Go/no-go (commission mistakes) (TM)	3.26	6.55	51	0.000
Executive function	Trails A (s)	3.17	-8.133	62	0.000
Cerebellar neuropsychiatric scale	Psychosis spectrum positive (TS)	2.30	3.6	38	0.001
Cerebellar neuropsychiatric scale	Emotion regulation negative (TS)	1.88	5.327	39	0.000
Language	Phonemic fluency (TC)	1.78	-8.434	49	0.000
Language	Semantic fluency (TC)	1.72	-8.335	49	0.000
Cerebellar neuropsychiatric scale	Psychosis spectrum negative (TS)	1.55	4.328	38	0.000
Executive function	Go/no-go (TS/2)	1.44	-6.381	63	0.000
Frontal systems behavior scale	Total score (self rating) (TS/255)	1.44	9.908	54	0.000
Frontal systems behavior scale	Dysexecutive (self rating) (TS/85)	1.43	8.823	54	0.000
Frontal systems behavior scale	Apathy (self rating) (TS/85)	1.42	7.985	54	0.000
Cerebellar neuropsychiatric scale	Emotion regulation positive (TS)	1.38	3.982	39	0.000
Working memory	Reversed digit span (TS/16)	1.37	-9.408	59	0.000
Cerebellar neuropsychiatric scale	Autism spectrum negative (TS)	1.31	4.713	38	0.000
Cerebellar neuropsychiatric scale	Social skill positive (TS)	1.29	3.842	38	0.000
Frontal systems behavior scale	Apathy (family rating) (TS/85)	1.28	6.731	38	0.000
Executive function	Category switching accuracy(TC)	1.27	-7.235	49	0.000
Verbal memory	Word delayed recall (TS/15)	1.14	-3.987	68	0.000
Language	Pseudoword decoding at 60 seconds (TS/52)	1.11	-4.153	45	0.000
Abstract reasoning	Similarities (TS/36)	1.11	-7.032	58	0.000
Frontal systems behavior scale	Total score (family rating) (TS/255)	1.07	5.465	38	0.000
Working memory	Longest reversed digit span (TS/8)	1.05	-8.541	61	0.000
Language	Pseudoword decoding at 30 seconds (TS/52)	1.00	-6.015	41	0.000
Social communication disorders checklist	Total (TS/24)	0.91	4.086	39	0.000

Executive function	Letter-number sequencing Time (s)	0.88	3.702	45	0.001
Cerebellar neuropsychiatric scale	Social skill negative (TS)	0.86	3.138	38	0.002
Executive function	Trails B - trails A (s)	0.81	-2.156	76	0.017
Visual-spatial ability	Cube (TS/2)	0.81	-4.442	61	0.000
Attention and vigilance	Longest forward digit span (TS/9)	0.79	-5.7	62	0.000
Working memory	Longest forward digit span (TS/9)	0.79	-5.7	62	0.000
Frontal systems behavior scale	Dysexecutive (family rating) (TS/85)	0.78	4.18	38	0.000
Verbal memory	Verbal paired associates-I (TS/32)	0.70	-4.354	59	0.000
Verbal memory	Learning slope	0.70	-4.304	59	0.000
Verbal memory	Verbal paired associates-II (TS/8)	0.68	-4.683	58	0.000
Working memory	Months backwards time (s)	0.61	2.515	46	0.008
Frontal systems behavior scale	Disinhibition (self rating) (TS/85)	0.61	3.567	54	0.001
Attention and vigilance	Forward digit span (TS/16)	0.55	-4.698	60	0.000
Working memory	Forward digit span (TS/16)	0.55	-4.698	60	0.000
Frontal systems behavior scale	Disinhibition (family rating) (TS/85)	0.45	2.442	38	0.010
Visual-spatial ability	Judgment of line orientation (TS/15)	0.44	-3.233	58	0.001
Executive function	Total DKEFS set loss mistakes (TM)	0.40	-3.675	49	0.001
Executive function	Letter-number sequencing (TS/2)	0.29	-2.012	66	0.024
Executive function	Category switching set loss mistakes (TM)	0.28	1.692	56	0.048

Supplement 7. Table: Test measures ranked by descending order for difference in z-score means between patients and controls, without *a-priori* hypothesis of CCAS domain grouping. Abbreviations. CNRS: Cerebellar Neuropsychiatric Rating Scale (Schmahmann et al., 2007), FRSBE: Frontal System Behavior Scale, SCDC: Social and Communication Disorders Checklist, TC: total correct, TS: total score, TM: total number of mistakes, S: seconds.

Cerebellar Cognitive Affective (CCAS) / Schmahmann Syndrome Scale

Administration and Scoring Instructions

The Cerebellar Cognitive Affective Syndrome (CCAS) / Schmahmann Scale is a screening instrument to detect the cerebellar cognitive affective syndrome in patients with cerebellar injury. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visual spatial skills, abstract thinking, and neuropsychiatric features. Time to administer the Scale is approximately 10 minutes in healthy controls, and approximately 12 minutes in patients with impairments. The total possible Raw Score is 120 points; the Pass / Fail measure provides a maximum fail score of 10 (i.e., 10 failed tests). A fail score of 0 is normal. In a patient with cerebellar disease, a fail score of 1 indicates Possible CCAS, a fail score of 2 indicates Probable CCAS, and a fail score of 3 or more indicates Definite CCAS.

Document the patient's name, date of birth, and hospital medical record number. Provide the patient's years of education; 1 year per school grade (completed 12th grade = 12 years), and add further years of study for college courses or degrees earned. Note the date the test was administered.

1. Semantic (Category) Fluency

<u>Administration:</u> The examiner instructs the subject: "Please name as many animals or living creatures as you can in one minute. Are you ready? Go ahead and start."

<u>Scoring:</u> Allocate one point for each correct answer given within one minute.

<u>Example:</u> Subject answers: "owl, bird, bat, cow, <u>grass</u>, bug, horse, dog" earns a score of 7 (*grass* is a set loss error).

The following count as correct answers:
Different names / genders for similar animals, e.g., mare, stallion, rooster, hen.
Categories and exemplars of the category, e.g., dog, poodle, cavalier; bird, eagle, cardinal; fish, salmon, trout
Extinct creatures count, e.g., dinosaur, pterodactyl

The following are wrong answers and do not count:
Errors, such "flower" instead of animals or living creatures
Repetitions of the same word
Conjugations of the same word – elephant, herd of elephants; dog, dogs; red bird, blue bird, yellow bird

2. Phonemic (Letter) Fluency

<u>Administration:</u> The examiner instructs the subject: "Please name as many words as you can in one minute that start with the letter F. Do not use names of people or places or repeat the same word in different forms. Are you ready? Go ahead and start"

<u>Scoring:</u> Allocate one point for each correct answer given within one minute. Errors are not counted (e.g. subject states "phone" instead of a word with the intial letter F. The same holds true for names of people, places, or any conjugation of the same word (e.g., 'fish, fishes' is incorrect, whereas 'fish, fishing" are correct as they have different meanings). Repetitions of the same word are not counted.

<u>Example:</u> Subject answers: "feather, father, friend, forgive, <u>forgiven</u>, fault, fun, <u>Philadelphia</u>, <u>feather</u>" earns a score of 6 (*Philadelphia* is a set loss error, *feather* is a repetition, *forgiven* is the same word with a different word ending).

3. Category Switching (vegetable-profession)

<u>Administration:</u> The examiner instructs the subject: "Please name a type of vegetable and then a type of profession or job, and then another vegetable and another profession, and so on, switching between the two lists. Name as many as you can in one minute. Are you ready? Go ahead and start"

<u>Scoring:</u> Allocate one point for each correct alternation between the two categories. The switching between categories is counted, and the words in the alternating categories have to be correct (and not repetitions). Errors that are not immediately self- corrected do not score points. For example, set loss errors such as "apple" instead of a vegetable are incorrect, and would not be scored. If the first word in each category that the patient produces is incorrect (e.g., not a profession, not a vegetable), then stop, make sure the patient understands the instruction, and then start again. After the first words, if the patient makes three errors in a row you can remind them what the categories are, but continue from that point on (do not start the test gain). Score only the switches / alternations between words that are in the correct categories. Examples below:

<u>Example:</u> Subject answers:

cucumber 1
doctor
celery 2
mailman 3
leek 4
teacher 5
<u>*apple*</u>
librarian 6
spinach
<u>*mailman*</u>
broccoli
secretary 7

Apple is not scored (i.e., set-loss error).
Mailman is repeated twice (i.e., repetition).
Hence the total score is 7.

4. **Verbal registration**

<u>Administration:</u> The examiner instructs the subject: “I am going to read you a list of words which I would like you to learn. Please repeat these words. I am going to ask you to give them back in a few minutes. Are you ready? Here they are.”

(Read the 5 words at rate of 1 per second. Have the subject repeat them when you are done. Then have the subject repeat them a second time with your prompt.
You may repeat this procedure until subject recalls all 5 words, but stop after 4 attempts at securing registration. Document how many words are repeated.)

<u>Scoring:</u> This part of the memory test is <u>not</u> scored.

5. **Digit Span Forward**

<u>Administration:</u> The examiner instructs the subject: “I am going to read you some numbers. Please repeat them in exactly the same order. I am going to read each sequence of numbers only once. Are you ready? Here they are”.

(Read aloud at rate of one digit per 1 second. Start with * 4 digits. If subject fails 4, try 3, and then 2. If the subject repeats 4 digits, then read the 5-digit number, then the 6-digit number and so on. Stop when you reach 8 digits, or when the subject fails the repetition. Allow one trial per digit sequence).

<u>Scoring:</u> Allocate one point per digit for the longest string of numbers correctly repeated. Any error within one string of digits (e.g. subject states “1-6-9-***4***-5” instead of “1-6-9-**2**-5” that is not immediately self corrected is an error, and the previous longest digit length achieved is scored (here 4 points, not 5).

6. **Digit Span Backwards**

<u>Administration:</u> The examiner instructs the subject: “Now I would like you to say these numbers backwards (in reverse order. If I say 5-8, I want you to say 8-5. Do you understand? I am going to read each sequence of numbers only once. Are you ready? Here they are”.
(Start with * 2 digits, stop when you reach 6 digits, or when the subject fails the reverse sequence. Allow one trial per digit sequence).

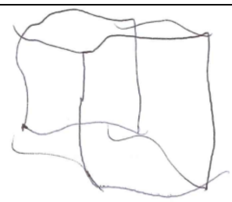
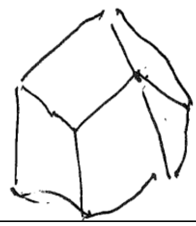
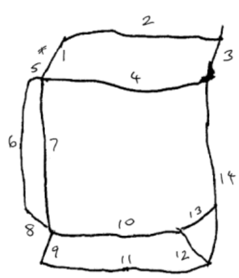
<u>Scoring:</u> Allocate one point per digit for the longest string of numbers correctly repeated. Any error within one string of digits (e.g. subject states “***8-2***-3” instead of “**2-8**-3” that is not immediately self corrected is an error, and the previous longest digit length is scored (here, 2 points not 3).

7. **Cube Draw:**

<u>Administration:</u> The examiner instructs the subject: “Please draw a cube – a six-sided box, make it transparent or see-through”. (No time limit)

<u>Scoring:</u> Allocate maximum score of 15 points if all 12 lines are present and the diagram is 3-dimensional. If there are < 12 lines or > 12 lines, and the diagram is not 3-dimensional, administer “Cube Copy” (in the latter case no points are earned for cube draw).

<u>Examples:</u>

	Correct drawing (has 12 lines and is three dimensional). Lines do not have to be perfectly drawn.
	Incorrect drawing (has 13 lines and is not a recognizable copy of the 3-D example). Move to the Cube Copy task. (If this was the Cube Copy condition, score would be 10. 12-1 for the extra line; -1 for not being 3-D).
	Incorrect drawing (has 14 lines; 2 lines more than permitted and is not 3-D). Move to the Cube Copy task. (If this was the Cube Copy condition, score would be 9. 12 – 2 for the extra lines; – 1 for not being 3-D).

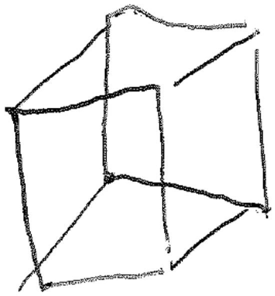
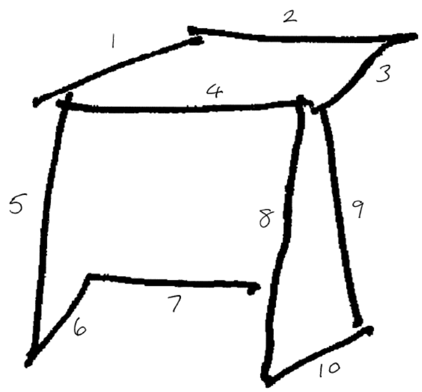
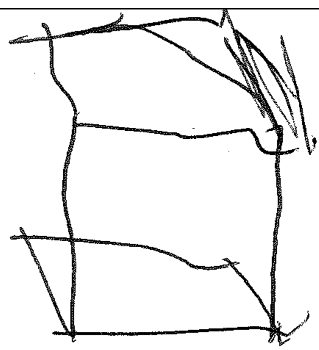
The patient should draw the cube to the best of their ability. Observe the patient do this. Inaccuracies because of untidiness or difficulty with pen control do not count as errors. The test measures visual spatial concept formation and execution, assessed by the patient’s ability to draw 12 lines and make it look 3-dimensional. It is not designed to be a measure of motor control. If the patient cannot draw the cube correctly, have them copy the cube. If the patient is too disabled from upper extremity dysmetria to hold the pen, or to hold it steady enough to draw or copy the diagram, then do not include it in the final Raw Score. In this case, the Total Raw Score will be out of 105, not 120. Also, do not count it as a Fail (in the Pass-Fail column). Make note of the fact that dysmetria was so severe as to preclude completion of this aspect of cube draw / copy.

8. **Cube Copy:**

<u>Administration:</u> The examiner instructs the subject: “Please copy the cube shown on page 2.” (No time limit)

<u>Scoring:</u> Allocate a maximum score of 12 points, that is, 1 point for each line drawn. Deduct 1 point if the image is not 3-dimensional. Deduct 1 point for each missing line. Deduct 1 point for each additional line drawn >12.

Examples:

	Correct copy. Allocate 12 points.
	Incorrect copy. Score 10 points for the 10 lines drawn. 3-dimensional concept attempted; no deduction.
	Incorrect copy. Score 10 points for the 10 lines drawn. 3-dimensional concept attempted; no deduction. No deduction for the apparent motor difficulties.

9. **Verbal recall**

Administration: The examiner instructs the subject: "What were the words that I asked you to learn earlier?"

(Subject recalls the words learned previously. Use cues and multiple choice alternatives if needed).

Scoring: Spontaneous recall of each word earns three points per word. Category cue recall earns 2 points per word and recall with multiple choice earns 1 point per word.

Example: A participant recalls the following words with the following help and receives a total score of 6+2+1 = 9 points

Spontaneous Recall	**Flower** [X]	**Robert** [ ]	**Courage** [ ]	**Speak** [ ]	**Yellow** [X]	**Subtotal** [6]
Category Cue	[ ]	[X]	[ ]	[ ]	[ ]	[2]
Multiple choice	[ ]	[ ]	[X]	[Not recalled with multiple choice]	[ ]	[1]

10. **Similarities**

Administration: The examiner instructs the subject: “How are the following words alike; what is the same about them?” (Provide one example, then test items).

Note: If subject provides answer that is partially correct (indicated with **Q**) then ask “Can you think of something more conceptual about them that they have in common or that makes them similar?” – If subject now gives a 2 point answer, score 2 points.

Scoring: Correct (best possible answer) = a conceptual answer (2 points), partially correct but not best possible = 1 point, incorrect answer or no answer = 0 points.

Scoring key and sample answers:

Nose-Ear

2 points	Senses (used for, part of) senses Sensory (receptors; parts; points) organs used to sense things Two of the five senses
1 point	Facial (parts, features); (parts of; on) your face **(Q)** Features of mammals Body parts, parts of the body **(Q)** (part of, on) your head
0 points	Provide body with smell and hearing **(Q)** Can breathe through nose and mouth Face; head **(Q)** Help you breathe and hear (or any other difference)

Sheep-Elephant

2 points	Animals; mammals; herbivores Members of the animal (kingdom, family) Quadrupeds
1 point	Both have (four legs, a tail), have four legs and a tail (names shared physical features) **(Q)** Can be tamed Both are (powerful, strong, muscular, fast)
0 points	You see them at the zoo (Circus, others) Belong to same species Are wild; live in the wild Are found in nature One has wool, the other has thick skin One is big, the other is small Or any other differences

Lake-River

2 points	Bodies of water Water
1 point	(Both are) cold, wet **Q** You can swim in them (play, exercise) **Q** Drink them **Q**
0 points	Both are blue One is large, the other is small One is long, the other is round One stands still, the other is flowing Or any other differences

Airplane - Motorcycle

2 points	(Means, Forms, Modes) of transportation; both transport people (Means, Forms, Modes) of (travel, traveling); For (travel, traveling) Vehicle; Conveyances Way of getting from one place to another Take you (places, somewhere); Carry you to a destination
1 point	Ride in both **(Q)** Both move **(Q)** Both used for pleasure or recreation Both cover a distance Have to be (steered, driven, operated), **(Q)** (Drive, steer, operate) them **(Q)** Carry (people, things) **(Q)**
0 points	Both have (motors, engines, seats, steering wheel, or other common details) **(Q)** (Run on, require) (gasoline, fuel) **(Q)** They are expensive Both mechanical **(Q)** Plane is for the air, motorcycle is for the street Plane has wings / flies, motorcycle has wheels / drives (or any other differences)

11. **Go No-Go**

Administration: The examiner instructs the subject: “I am going to tap the table. When I tap once, raise your finger then put it back down again. When I tap twice, don’t do anything. Here are two examples to make sure you understand what I mean. (Tap once, then twice). Are you ready? Here we go”.
(The intervals between the tap conditions are paced at 1 per second. The 2-tap condition has a very short inter-tap interval on the order of milliseconds that clearly distinguishes it from the 1-tap condition).”

Scoring: Notate errors of commission and omission. 0 errors = score the maximum 2 points. 1 omission or commission error = score 1 point. 2 or more errors = score 0 points.

12. **Affect**

Administration: The examiner observes the participants behavior and interaction during the test. Examiner assesses if the behaviors indicated on the scoring sheet are present. This may be supplemented by inquiring about these symptoms from the patient and / or caregiver.

Scoring: Score 6 points if none of the behaviors listed are present. Deduct one point for each behavior present.

Example: If participant presents with “difficulty with focusing attention or mental flexibility” but does not present any of the other items listed then subject earns 6-1 = 5 points.

Test categories to replace	CCAS/Schmahmann Scale Version 1A	CCAS/Schmahmann Scale Version 1B	CCAS/Schmahmann Scale Version 1C	CCAS/Schmahmann Scale Version 1D
Semantic fluency	Animals	Clothing	Sports	Furniture or appliances
	Total correct Exploratory (E) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]
	E:22.29+/-3.88	V:23.2+/-3.6	V:20.3+/-3.2	V:20.45+/-3.7
Phonemic fluency	F – Words	C – Words	L – Words	B – Words
	Total correct Exploratory (E) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]
	E:16.2+/-2.75	V18.73+/-4.5	V:18.2+/-5.75	V:19.45+/-3.7
Category switching	Vegetable/Profession	Fruits/Cities	Instruments/Body parts	Boys' names/Animals
	Total correct Exploratory (E), Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]	Total correct Validation (V) Controls [(mean)/SD]
	E: 13.82+/-1.45* V: 15.71+/-3.65	V:19.9+/-3.04	V:19.3+/-3.36	V: 21.5+/-4.18
Verbal recall	Recall target word Target word frequency Word cue Multiple choice alternatives	Recall target word Target word frequency Word cue Multiple choice alternatives	Recall target word Target word frequency Word cue Multiple choice alternatives	Recall target word Target word frequency Word cue Multiple choice alternatives
	Flower 22.76 grows in the garden tree, bush, grass **Robert** 63.18 boy's name Stephen, Michael, Joseph **Courage** 23.67 virtue or trait bravery, honesty, patience **Speak** 187.18	**Snow** 31.35 a form or precipitation rain, sleet, hail **Bus** 74.18 vehicle that transports people or things truck, train, ship **Destiny** 23.04 concept regarding the future intention, prediction, expectation **Run** 350.55	**Village** 33.57 a place where people live: city, town, suburb **Mary** 88.08 girl's name Joanne, Sally, Barbara **Happiness** 24.49 a postive emotion love, pleasure, laughter **Answer** 76.2	**Mountain** 35.39 something you can climb up hill, ladder, tree **Paris** 69.24 City London, Tokyo, Amsterdam **Violence** 23.00 a negative behavior cruelty, anger, hostility. **Sleep** 227.94

	a way of communicating shout, talk, sing **Yellow** 33.80 Color red, green, blue	something we do with our legs walk, jump, hop **Large** 41.45 describes the size of an object small, big, tiny	something you may do in a conversation respond, explain, listen **Square** 31.76 describes the shape of an object triangle, round, oval	something you may do if you are tired lie, rest, nap **Loud** 39.82 describes the quality of a sound soft, highpitched, annoying
DSF	5-9 2-1-3 4-8-7-0 1-6-9-2-5 3-0-1-2-6-4 7-3-1-9-8-4-6 2-0-5-6-9-7-3-8	9-1 5-2-7 0-4-8-6 3-5-9-7-0 2-8-3-6-1-4 8-0-7-5-9-6-3 1-4-2-3-9-0-6-8	4-0 6-1-5 2-8-3-7 2-0-3-1-9 0-2-5-4-6-3 9-8-1-7-2-4-8 1-0-8-3-7-4-6-2	9-2 7-8-5 0-4-3-1 6-3-9-7-2 1-0-8-6-4-7 2-0-1-5-6-4-9 3-5-2-1-7-9-8-4
DSB	7-1 6-1 3-8-2 4-7-0-9 6-5-2-8-1 5-9-0-3-7-4	7-1 5-0 2-9-7 4-8-3-1 6-9-0-4-8 5-3-2-1-7-0	7-1 3-2 8-1-4 0-7-6-9 3-5-2-0-6 1-5-8-7-3-9	7-1 1-6 0-8-3 5-9-7-2 8-3-1-6-4 7-2-9-5-3-0
Similarities	Nose-Ear (Fabrics / Materials) Sheep-Elephant (Animals) Lake-River (Bodies of water) Airplane-Motorcycle (Vehicles / Transportation)	Suspicious-Jealous ([Negative] Emotions) Cube-Triangle ([Geometric] Shapes) Chair-Table (Furniture) Wool-Silk (Fabrics/Materials)	Orange-Carrot (Food) Snail-Crab (Animals / shells) Shoes-Belt (Clothes, accessories) Book-Newspaper (Reading material)	Milk-Egg (Food) Hammer-Screwdriver (Tools) Sailor-Pilot (Profession / occupation) Bracelet-Earring (Jewelery / accesories)
Go/no-go	1 1 1 2 2 1 2 2 2 1 2 1 2 1	2 1 1 2 1 2 1 2 2 1 1 2 1 2	1 2 2 1 2 1 1 2 2 1 2 1 1 2	1 2 2 1 1 2 1 2 2 1 2 1 1 2

Supplement 9. Table: Re-test items for use in Versions 1B, 1C and 1D of the CCAS/Schmahmann Scale.

Test combinations were developed to avoid repetition of similar words or letters across subtests within the re-test versions of the Scale. Words with similar frequencies (Brysbaert and New, 2009) were used for the memory tests in the four versions of the Scale. Abbreviations: DSF = Digit Span Forward, DSB = Digit Span Backward.

*Category switching item in exploratory cohort comprised “fruit/furniture” of the original D-KEFS test. In the validation cohort these were changed to “vegetables/profession“ to avoid repetition of word categories within the Scale and to prevent copyright infringement. Go/no-go, DSF and DSB re-test items were derived using a research randomization tool.

Brysbaert M, New B. Moving beyond Kucera and Francis: A Critical Evaluation of Current Word Frequency Norms and the Introduction of a New and Improved Word Frequency Measure for American English. Behavior Research Methods, 2009; 41 (4): 977-990.

CEREBELLAR COGNITIVE AFFECTIVE / SCHMAHMANN SYNDROME SCALE (CCAS-Scale) VERSION 1B.

NAME:
ID#
DATE

DOB:
Education (Yrs)

Test	Instructions	RAW SCORE	PASS=0 FAIL=1
SEMANTIC FLUENCY	Score = total correct words (up to a maximum of 26 words). Fail if Score 15 or less. *(Use space bottom right for notation).* Please name as many items of clothing as you can in one minute	/26	
PHONEMIC FLUENCY	Score = total correct words (up to a maximum of 19 words). Fail if Score 9 or less. *(Use space bottom right for notation).* Please name as many words as you can in one minute that start with the letter C. Do not use names of people or places or repeat the same word in different forms.	/19	
CATEGORY SWITCHING	Score = total number of correct alternating words (up to a maximum of 15 alternations). Repetitions or set loss errors are not scored. Fail if Score 9 or less. *(Use space bottom right for notation).* Please name a fruit and then a city, and then another fruit and another city, and so on, switching between the two lists. Name as many as you can in one minute.	/15	
VERBAL REGISTRATION	This test is not scored. (The need for 4 attempts to learn 5 words raises concern for cerebral involvement). I am going to read you a list of words which I would like you to learn. Please repeat these words. I am going to ask you to give them back in a few minutes. *(Read 5 words at rate of 1 / second. Subject repeats them once, then repeats them again. Repeat trials until subject recalls all 5 words. Stop after 4 attempts.)*		

	[Snow]		[Bus]		[Destiny]		[Run]		[Large]
1st attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
2nd attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
3rd attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
4th attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]

Test	Instructions	RAW SCORE	PASS=0 FAIL=1
DIGIT SPAN FORWARD	Score = maximum string of numbers correctly repeated. Fail if Score 5 or less. I am going to read you some numbers. Please repeat them in exactly the same order *(Read aloud at a rate of 1 per second. Start with * and administer previous items if subject fails to repeat *).* 9-1 [ ] 0-4-8-6 * [ ] 2-8-3-6-1-4 [ ] 1-4-2-3-9-0-6-8 [ ] 5-2-7 [ ] 3-5-9-7-0 [ ] 8-0-7-5-9-6-3 [ ]	/8	
DIGIT SPAN BACKWARD	Score = maximum string of numbers correctly repeated. Fail if Score 3 or less. Inability to reverse 2 digits scores 0. Now please say these numbers backwards, in reverse order. *(Give example, then start with *).* (e.g., 5-8 = 8-5) *5-0 [ ] 2-9-7 [ ] 4-8-3-1 [ ] 6-9-0-4-8 [ ] 5-3-2-1-7-0 [ ]	/6	
CUBE (DRAW)	Score = 15 points if 12 lines present and diagram is 3-dimensional. If 12 lines not present or the diagram is not 3 dimensional, administer "CUBE (COPY)". Please draw a cube – a six-sided box, make it transparent or see-through. *(Use space bottom left).*		
CUBE (COPY)	Score = 12 points, 1 for each line. Deduct 1 point if not 3-D, 1 point for each line not drawn, 1 point for each additional line >12. Fail if Score 11 or less. Please copy the cube shown on PAGE 2. *(Neatness not scored).*	/15	

Draw cube here.

Notation:

Semantic Fluency	Phonemic Fluency	Category switching

VERBAL RECALL	Spontaneous = 3 points per word, category = 2 points , multiple choice = 1 point. Score = total points. Fail if Score 10 or less. Inability to recall more than 1 word from multiple choice raises concern for cerebral involvement.	RAW SCORE	PASS=0 FAIL=1

What were the words I asked you to learn earlier? *(Subject recalls the words learned previously. Use cues and multiple choice alternatives bottom left if needed).*

	[Snow]	[Bus]	[Destiny]	[Run]	[Large]
Spontaneous recall:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with category cue:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with multiple choice:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]

/15

SIMILARITIES Correct answer (conceptual) = 2 points, partial answer (concrete) = 1 point, incorrect answer / no answer = 0 points. Score = total points. Fail if Score 6 or less. Key-bottom right.

How are the following words alike; what is the same about them? (*Provide example, then test items).*

(e.g., Sheep/Elephant = Animals) 1.Suspicious/Jealous [__/2] 2.Cube/Triangle [__/2] 3. Chair/Table [__/2] 4. Wool/Silk [__/2]

/8

GO NO-GO 2 points for no errors, 1 point for one error, 0 points for two or more errors. Score = total points. Fail if Score 0.

I am going to tap the table. When I tap once, please raise your finger then put it back down again. When I tap twice, don't do anything. *(Give an example of each condition to make sure subject understands).*

2 - 1 - 1 - 2 - 1 - 2 - 1 - 2 - 2 - 1 - 1 - 2 - 1 - 2

/2

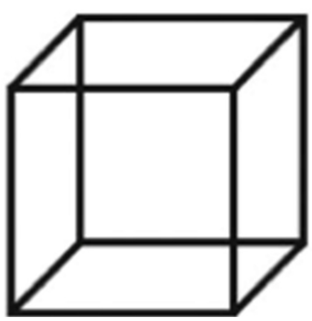
AFFECT Score 6 points if none are present. Subtract 1 for each item present. Fail if Score 4 or less. *(Rater assesses if the following are present, incorporating input from patient and/or caregiver)*

[ ] Difficulty with focusing attention or mental flexibility
[ ] Emotionally labile, incongruous emotions, appears hopeless or depressed
[ ] Shows easy sensory overload or avoidant behaviors
[ ] Expresses illogical thoughts or paranoia
[ ] Lacks empathy, is apathetic, or has blunted affect
[ ] Angry or aggressive, irritable, oppositional, difficulty with social cues and social boundaries

/6

TOTAL SCORE /120 /10

Calculate total raw score (1st column) and total number of failed tests (2nd column).
1 failed test = Possible CCAS; 2 failed tests = Probable CCAS; 3 or more failed tests = Definite CCAS



Copy the cube here.

CUES AND MULTIPLE CHOICE ITEMS FOR VERBAL RECALL TEST					
Test word	**Snow**	**Bus**	**Destiny**	**Run**	**Large**
Cue	A form of precipitation	Vehicle that transports people or things	Concept regarding the future	Something we do with our legs	Describes the size of an object
Multiple choice items	Rain	Truck	Intend	Run	Small
	Sleet	Train	Destiny	Walk	Big
	Snow	Ship	Prediction	Jump	Tiny
	Hail	Bus	Expect	Hop	Large

SIMILARITIES	**Correct conceptual answers (examples)**	**Partial correct / concrete answers (examples)**
Suspicious/jealous	Emotions, negative emotions	Make you sad/angry/upset
Cube/Triangle	Geometrical shapes	You draw them
Chair/Table	Furniture	You put things on them, have legs
Wool/Silk	Fabrics, materials, come from animals	You wear them, soft

Hoche, Güell, Vangel, Sherman, Schmahmann
Ataxia Unit, Cognitive Behavioral Neurology Unit, Schmahmann Laboratory for Neuroanatomy and Cerebellar Neurobiology, Department of Neurology, Massachusetts General Hospital.

CEREBELLAR COGNITIVE AFFECTIVE / SCHMAHMANN SYNDROME SCALE (CCAS-Scale) VERSION 1C.

NAME:
ID#
DATE
DOB:
Education (Yrs)

		RAW SCORE	PASS=0 FAIL=1
SEMANTIC FLUENCY	Score = total correct words (up to a maximum of 26 words). Fail if Score 15 or less. *(Use space bottom right for notation).*		
Please name as many sports as you can in one minute		/26	
PHONEMIC FLUENCY	Score = total correct words (up to a maximum of 19 words). Fail if Score 9 or less. *(Use space bottom right for notation).*		
Please name as many words as you can in one minute that start with the letter L. Do not use names of people or places or repeat the same word in different forms.		/19	
CATEGORY SWITCHING	Score = total number of correct alternating words (up to a maximum of 15 alternations). Repetitions or set loss errors are not scored. Fail if Score 9 or less. *(Use space bottom right for notation).*		
Please name an instrument and then a body part, and then another instrument and another body part, and so on, switching between the two lists. Name as many as you can in one minute.		/15	

VERBAL REGISTRATION — This test is not scored. (The need for 4 attempts to learn 5 words raises concern for cerebral involvement).

I am going to read you a list of words which I would like you to learn. Please repeat these words. I am going to ask you to give them back in a few minutes. *(Read 5 words at rate of 1 / second. Subject repeats them once, then repeats them again. Repeat trials until subject recalls all 5 words. Stop after 4 attempts.)*

	[Village]	[Mary]	[Happiness]	[Answer]	[Square]
1st attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
2nd attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
3rd attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
4th attempt	[ ] -	[ ] -	[ ] -	[ ] -	[ ]

DIGIT SPAN FORWARD — Score = maximum string of numbers correctly repeated. Fail if Score 5 or less.

I am going to read you some numbers. Please repeat them in exactly the same order *(Read aloud at a rate of 1 per second. Start with * and administer previous items if subject fails to repeat *).*

4-0 [ ]   2-8-3-7 * [ ]   0-2-5-4-6-3 [ ]   1-0-8-3-7-4-6-2 [ ]
6-1-5 [ ]   2-0-3-1-9 [ ]   9-8-1-7-2-4-8 [ ]

/8

DIGIT SPAN BACKWARD — Score = maximum string of numbers correctly repeated. Fail if Score 3 or less. Inability to reverse 2 digits scores 0.

Now please say these numbers backwards, in reverse order. *(Give example, then start with *).*

(e.g., 5-8 = 8-5)   *3-2 [ ]   8-1-4 [ ]   0-7-6-9 [ ]   3-5-2-0-6 [ ]   1-5-8-7-3-9 [ ]

/6

CUBE (DRAW) — Score = 15 points if 12 lines present and diagram is 3-dimensional. If 12 lines not present or the diagram is not 3 dimensional, administer "CUBE (COPY)".

Please draw a cube – a six-sided box, make it transparent or see-through. *(Use space bottom left).*

CUBE (COPY) — Score = 12 points, 1 for each line. Deduct 1 point if not 3-D, 1 point for each line not drawn, 1 point for each additional line >12. Fail if Score 11 or less.

Please copy the cube shown on PAGE 2. *(Neatness not scored).*

/15

Draw cube here.

Notation:

Semantic Fluency	Phonemic Fluency	Category switching

VERBAL RECALL	Spontaneous = 3 points per word, category = 2 points , multiple choice = 1 point. Score = total points. Fail if Score 10 or less. Inability to recall more than 1 word from multiple choice raises concern for cerebral involvement.	RAW SCORE	PASS=0 FAIL=1

What were the words I asked you to learn earlier? *(Subject recalls the words learned previously. Use cues and multiple choice alternatives bottom left if needed).*

	[Village]	[Mary]	[Happiness]	[Answer]	[Square]
Spontaneous recall:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with category cue:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]
Recall with multiple choice:	[ ] -	[ ] -	[ ] -	[ ] -	[ ]

/15

SIMILARITIES	Correct answer (conceptual) = 2 points, partial answer (concrete) = 1 point, incorrect answer / no answer = 0 points. Score = total points. Fail if Score 6 or less. Key-bottom right.

How are the following words alike; what is the same about them? (*Provide example, then test items).*

(e.g., Sheep/Elephant = Animals) 1.Orange/Carrot [__/2] 2.Snail/Crab [__/2] 3. Shoes/Belt [__/2] 4. Book/Newspaper [__/2]

/8

GO NO-GO	2 points for no errors, 1 point for one error, 0 points for two or more errors. Score = total points. Fail if Score 0.

I am going to tap the table. When I tap once, please raise your finger then put it back down again. When I tap twice, don't do anything. *(Give an example of each condition to make sure subject understands).*

1 - 2 - 2 - 1 - 2 - 1 - 1 - 2 - 2 - 1 - 2 - 1 - 1 - 2

/2

AFFECT	Score 6 points if none are present. Subtract 1 for each item present. Fail if Score 4 or less. *(Rater assesses if the following are present, incorporating input from patient and/or caregiver)*

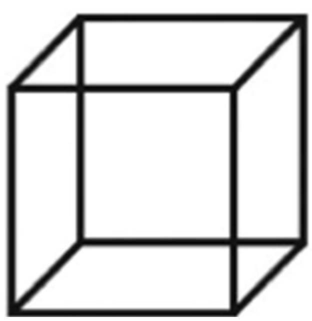
[ ] Difficulty with focusing attention or mental flexibility
[ ] Emotionally labile, incongruous emotions, appears hopeless or depressed
[ ] Shows easy sensory overload or avoidant behaviors
[ ] Expresses illogical thoughts or paranoia
[ ] Lacks empathy, is apathetic, or has blunted affect
[ ] Angry or aggressive, irritable, oppositional, difficulty with social cues and social boundaries

/6

TOTAL SCORE

/120 /10

Calculate total raw score (1st column) and total number of failed tests (2nd column).
1 failed test = Possible CCAS; 2 failed tests = Probable CCAS; 3 or more failed tests = Definite CCAS



Copy the cube here.

CUES AND MULTIPLE CHOICE ITEMS FOR VERBAL RECALL TEST					
Test word	**Village**	**Mary**	**Happiness**	**Answer**	**Square**
Cue	A place where people live	Girl's name	A positive emotion	Something you may do in a conversation	Describes the shape of an object
Multiple choice items	City	Joanne	Love	Answer	Triangle
	Town	Sally	Happiness	Respond	Round
	Village	Barbara	Pleasure	Explain	Oval
	Suburb	Mary	Laughter	Listen	Square

SIMILARITIES	**Correct conceptual answers (examples)**	**Partial correct / concrete answers (examples)**
Orange/Carrot	Food	Can make juice, eat them, color
Snail/Crab	Animals, shell	Small, live in the ocean, crawl
Shoes/Belt	Clothing accessories	Leather, color
Book/Newspaper	Reading material, information	Paper, words

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CEREBELLAR COGNITIVE AFFECTIVE / SCHMAHMANN SYNDROME SCALE (CCAS-Scale) VERSION 1D.

NAME:
ID#
DATE

DOB:
Education (Yrs)

		RAW SCORE	PASS=0 FAIL=1
SEMANTIC FLUENCY	Score = total correct words (up to a maximum of 26 words). Fail if Score 15 or less. *(Use space bottom right for notation).* Please name as many items of furniture or appliances as you can in one minute	/26	
PHONEMIC FLUENCY	Score = total correct words (up to a maximum of 19 words). Fail if Score 9 or less. *(Use space bottom right for notation).* Please name as many words as you can in one minute that start with the letter B. Do not use names of people or places or repeat the same word in different forms.	/19	
CATEGORY SWITCHING	Score = total number of correct alternating words (up to a maximum of 15 alternations). Repetitions or set loss errors are not scored. Fail if Score 9 or less. *(Use space bottom right for notation).* Please name a boy's name and then an animal, and then another boy's name and another animal, and so on, switching between the two lists. Name as many as you can in one minute.	/15	
VERBAL REGISTRATION	This test is not scored. (The need for 4 attempts to learn 5 words raises concern for cerebral involvement). I am going to read you a list of words which I would like you to learn. Please repeat these words. I am going to ask you to give them back in a few minutes. *(Read 5 words at rate of 1 / second. Subject repeats them once, then repeats them again. Repeat trials until subject recalls all 5 words. Stop after 4 attempts.)*		

	[Mountain]		[Paris]		[Violence]		[Sleep]		[Loud]
1st attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
2nd attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
3rd attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
4th attempt	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]

		RAW SCORE	PASS=0 FAIL=1
DIGIT SPAN FORWARD	Score = maximum string of numbers correctly repeated. Fail if Score 5 or less. I am going to read you some numbers. Please repeat them in exactly the same order *(Read aloud at a rate of 1 per second. Start with * and administer previous items if subject fails to repeat *).* 9-2 [ ] 0-4-3-1 * [ ] 1-0-8-6-4-7 [ ] 3-5-2-1-7-9-8-4 [ ] 7-8-5 [ ] 6-3-9-7-2 [ ] 2-0-1-5-6-4-9 [ ]	/8	
DIGIT SPAN BACKWARD	Score = maximum string of numbers correctly repeated. Fail if Score 3 or less. Inability to reverse 2 digits scores 0. Now please say these numbers backwards, in reverse order. *(Give example, then start with *).* (e.g., 5-8 = 8-5) *1-6 [ ] 0-8-3 [ ] 5-9-7-2 [ ] 8-3-1-6-4 [ ] 7-2-9-5-3-0 [ ]	/6	
CUBE (DRAW)	Score = 15 points if 12 lines present and diagram is 3-dimensional. If 12 lines not present or the diagram is not 3 dimensional, administer "CUBE (COPY)". Please draw a cube – a six-sided box, make it transparent or see-through. *(Use space bottom left).*		
CUBE (COPY)	Score = 12 points, 1 for each line. Deduct 1 point if not 3-D, 1 point for each line not drawn, 1 point for each additional line >12. Fail if Score 11 or less. Please copy the cube shown on PAGE 2. *(Neatness not scored).*	/15	

Draw cube here.

Notation:

Semantic Fluency	Phonemic Fluency	Category switching

VERBAL RECALL	Spontaneous = 3 points per word, category = 2 points , multiple choice = 1 point. Score = total points. Fail if Score 10 or less. Inability to recall more than 1 word from multiple choice raises concern for cerebral involvement.	RAW SCORE	PASS=0 FAIL=1

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	[Mountain]		[Paris]		[Violence]		[Sleep]		[Loud]
Spontaneous recall:	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
Recall with category cue:	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]
Recall with multiple choice:	[ ]	-	[ ]	-	[ ]	-	[ ]	-	[ ]

/15

SIMILARITIES	Correct answer (conceptual) = 2 points, partial answer (concrete) = 1 point, incorrect answer / no answer = 0 points. Score = total points. Fail if Score 6 or less. Key-bottom right.

How are the following words alike; what is the same about them? (*Provide example, then test items).*

(e.g., Sheep/Elephant=Animals) 1. Milk/Egg [__/2] 2.Hammer/Screwdriver [__/2] 3. Sailor/Pilot [__/2] 4.Bracelet/Earring [__/2]

/8

GO NO-GO	2 points for no errors, 1 point for one error, 0 points for two or more errors. Score = total points. Fail if Score 0.

I am going to tap the table. When I tap once, please raise your finger then put it back down again. When I tap twice, don't do anything. *(Give an example of each condition to make sure subject understands).*

1 - 2 - 2 - 1 - 1 - 2 - 1 - 2 - 2 - 1 - 2 - 1 - 1 - 2

/2

AFFECT	Score 6 points if none are present. Subtract 1 for each item present. Fail if Score 4 or less. *(Rater assesses if the following are present, incorporating input from patient and/or caregiver)*

[ ] Difficulty with focusing attention or mental flexibility
[ ] Emotionally labile, incongruous emotions, appears hopeless or depressed
[ ] Shows easy sensory overload or avoidant behaviors
[ ] Expresses illogical thoughts or paranoia
[ ] Lacks empathy, is apathetic, or has blunted affect
[ ] Angry or aggressive, irritable, oppositional, difficulty with social cues and social boundaries

/6

TOTAL SCORE

/120 /10

Calculate total raw score (1st column) and total number of failed tests (2nd column).
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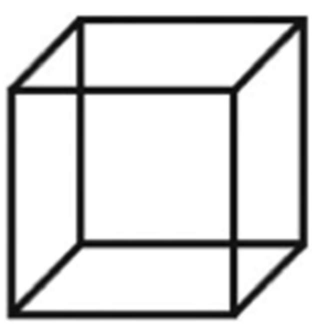

Copy the cube here.

CUES AND MULTIPLE CHOICE ITEMS FOR VERBAL RECALL TEST					
Test word	**Mountain**	**Paris**	**Violence**	**Sleep**	**Loud**
Cue	Something you can climb up	Name of a city	A negative behavior	Something you may do if you are tired	Describes the quality of a sound
Multiple choice items	Hill	London	Cruelty	Sleep	Soft
	Ladder	Paris	Anger	Lie	Loud
	Mountain	Tokyo	Hostility	Rest	Bang
	Tree	Amsterdam	Violence	Nap	Knock

SIMILARITIES	**Correct conceptual answers (examples)**	**Partial correct / concrete answers (examples)**
Milk/Egg	Food, recipe ingredient	White, refrigerate
Hammer/Screwdriver	Tools	Metal, you hold them, use in construction
Sailor/Pilot	Profession, navigate vessels	Wear uniform
Bracelet/Earring	Jewelry, accessories	You wear them, shiny, expensive

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