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ORIGINAL COMMUNICATION

Cognitive deficits in spinocerebellar ataxia type 1, 2, and 3

K. Bürk
C. Globas
S. Bösch
T. Klockgether
C. Zühlke
I. Daum
J. Dichgans

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K. Bürk, MD (✉) · C. Globas, MD ·
S. Bösch, MD · J. Dichgans, MD
Department of Neurology
University of Tübingen
Hoppe-Seyler-Str. 3
72076 Tübingen, Germany
Tel.: +49-7071/29-82141
Fax: +49-7071/29-5260
E-Mail: buerk@uni-tuebingen.de

T. Klockgether, MD
Department of Neurology
University of Bonn
Bonn, Germany

C. Zühlke, PhD
Institute of Human Genetics
University of Lübeck
Lübeck, Germany

I. Daum, PhD
Department of Clinical Neuropsychology
University of Bochum
Bochum, Germany

Abstract Cognitive impairment was studied in distinct types of spinocerebellar ataxia (SCA): eleven SCA1, 14 SCA2, and 11 SCA3 individuals and 8 age- and IQ-matched controls. All were submitted to a neuropsychological test battery that comprised tests for IQ, attention, executive function, verbal and visuospatial memory. Executive dysfunction was prominent in SCA1 as compared with controls and all other SCA types. Mild deficits of verbal memory were present in SCA1, SCA2 and SCA3. The neuropathological pattern in different SCA types suggests that these cognitive deficits are not likely to be contingent upon cerebellar degeneration but to result from disruption of a cerebrocerebellar circuitry presumably at the pontine level.

Key words spinocerebellar ataxia · cerebellum · cognition · executive dysfunction

Introduction

The spinocerebellar ataxias (SCA) are a group of dominantly inherited neurological disorders characterised by progressive ataxia that results from degeneration of the cerebellum and its afferent and efferent connections. In most families, there is clinical and neuropathological evidence for additional involvement of brainstem, basal ganglia, spinal cord and peripheral nervous system. The most frequent SCA mutations – SCA1, SCA2, and SCA3 – have been shown to be unstable CAG trinucleotide repeat expansions present within coding regions of the respective genes [21, 30, 32]. Despite genetic and neuropathological similarities, the distinct SCA mutations have some characteristic phenotypical features. The frequency of cognitive impairment, for instance, is variable between different SCA types. Mild mental deterioration, such as e. g. emotional lability, has been observed in 5 to 25 % of SCA1 patients in advanced stages of the disease. Genis et al., for example, described 'frontal-like' symptoms as euphoria and emotional instability in Spanish SCA1 individuals [18]. In clinical descriptions of SCA2, the frequency of cognitive deficits varies from 5 to 19 % [7, 9, 15, 41]. Most clinical investigations of SCA3 individuals of various ethnic origins emphasise the absence of cognitive dysfunction [8, 11, 17, 34]. In a large clinical description of Portuguese SCA3 patients, Sequeiros and Coutinho found mild loss of memory to be restricted to 2 out of 143 individuals [39].

Comparative studies of intellectual function in distinct types of SCA have not been performed to date. The present study, therefore, aimed [1] to compare the profile of cognitive impairment in patients carrying the SCA1, SCA2, and SCA3 mutation, and [2] to discuss the results with regard to the neuropathological characteristics of the distinct mutations. Several methodological shortcomings may complicate a comparative analysis of

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cognitive function in hereditary ataxia. First, neuropsychological investigations of founder populations are not representative owing to their homogeneous genetic background. To exclude an observation bias, patients were therefore selected from unrelated German SCA kindreds. Second, there is evidence for a broad decline of cognitive skills, including memory and executive function, during normal ageing [14]. In addition, we have shown that neuropsychological test performance is related to the disease duration, but not to the size of the expanded allele in SCA2 individuals [6]. Therefore, it was appropriate to exclude subjects aged above 65 years and to match test persons for subject variables such as age, disease duration and age of onset.

Patients and methods

Patients and Controls

Eleven SCA1, 14 SCA2, and 11 SCA3 patients were selected from a larger patient pool (Tübingen Ataxia Base). The criteria for selection were (1) moderate cerebellar syndrome with comprehensible speech and limited limb ataxia, (2) age below 66 years in order to avoid any cognitive phenomena related to age, and (3) a score of 24 or below on the MMS to exclude dementia. The control group consisted of 8 volunteers recruited through personal contact. None of the control subjects had a history of neurological disease and/or psychiatric symptoms or was taking medication at the time of the testing. Genetic testing for CAG repeat expansion was performed as described elsewhere [21, 30, 32]. The size of the expanded CAG repeat varied from 42 to 49 in SCA1, from 36 to 44 in SCA2, and from 63 to 75 in SCA3. Patients received clinical and neuropsychological testing at their homes. Severity of upper limb ataxia, dysarthria and ataxia of stance were rated on a scale ranging from zero (absent) to five (most severe) (Klockgether et al. 1990).

Neuropsychological testing

Each subject gave verbal consent to the neuropsychological testing prior to the study and was instructed that he or she could discontinue participation at any stage in accordance with ethical committee requirements. The neuropsychological tests, chosen specifically for their minimal or absent reliance on motor performance in order to minimise any influence on test performance by dysarthria and appendicular ataxia. They were administered following the protocols described extensively in the literature [6]. The test battery comprised the *Similarities (Verbal IQ) and Picture Completion (Performance IQ)* subtests from the short version of the German version of the *Wechsler Adult Intelligence Scale (WIP)* [12], the *Mini Mental State Test (MMS)* (general intellectual abilities) [16], the subtest *Digit Span* of the *Wechsler Memory Scale-Revised (WMS)* (with forward and backward reproduction being tested separately) (attention and working memory) [43], the immediate copy and delayed reproduction of the *Rey-Osterrieth Complex Figure* (visuospatial processing and memory) [31, 33], a modified version of the *Wisconsin Card Sorting Test (WCST)* (fronto-executive functions) [28], the reproduction of a prose passage from the *Wechsler Memory Scale* immediately and 30 min after presentation (verbal memory) [12], and the immediate and delayed recall of 16-item categorised and uncategorised *Word Lists* (verbal memory) [10]. The consecutive categories (CC) list contained words belonging to four superordinate semantic categories (e. g. animals), presented sequentially so that all words belonging to one category followed each other. In the randomised categories (RC) list, four members of four different categories were presented in randomised order; the uncategorised (RR) list contained 16 unrelated words. To assess *verbal fluency*, the subjects had to name as many items as possible from a semantic category (countries), a phonemic category (nouns starting with the letter 'B') and two switching semantic categories (male first names/vegetables) within one min each [14].

The sequence of tests was changed randomly between the individuals tested. As a consequence of limb ataxia, one SCA3 and two SCA1 patients were not able to draw the Rey-Osterrieth-Figure. The test battery had to be cut short in two other SCA2 individuals because of impaired motivation: one subject did not pass the *WCST*, the other missed the *Word Lists*. Statistical comparisons were conducted using a one-way analysis of variance (ANOVA) or repeated measures ANOVA where appropriate with the fixed factor group. Post-hoc paired-group comparisons were explored with Tukey's honestly significant difference (HSD). Differences were considered significant when p was less than 0.05. For correlation studies, we used Spearman's Rho. In order to achieve a global significance level of 5 % the p-values were corrected applying the Bonferoni-Holm-Adjustment. The chi square test was used to compare the non-parametric ataxia scores between groups.

Results

Neuropsychological Performance: There was no difference with regard to age, age of onset, disease duration and IQ estimates (for further details see Table 1). Patients did not differ in the general severity of the disease: The comparison of the ataxia scores did not differ between groups (ataxia of stance: χ^2-test: $p = 0.2779$).

The mean performance on the MMS of SCA1 patients differed significantly from controls. Analysis of the Digit Span test did not yield any significant group differences.

Visuospatial Function: Visuospatial function, as tested with the Rey-Osterrieth Complex Figure with respect to copying, delayed recall and proportional recall of the initial copy, was unimpaired in all SCA types.

Verbal Memory: SCA individuals had minor problems in reproducing the prose passage of the Wechsler Memory Scale, but these differences did not reach statistical significance. On the Word Lists, the test performance was influenced by group, list type (RR, RC, CC) and delay (immediate vs. delayed recall) but there was no significant interaction of these factors as demonstrated by repeated measures ANOVA of the Word List recall. All SCA mutations were associated with deficits of the immediate and delayed recall of the Word Lists, but after correction of the crude p-values, only the comparison of the immediate recall of the RC list was significant. Overall, the impairment was most prominent in SCA1 individuals.

Executive Functions: SCA2 individuals had problems in generating nouns from one phonemic category, while SCA1 subjects had major problems in finding words from switching semantic categories indicating fronto-executive dysfunction. The crude p-values reached significance for the generation of phonemic and alternating semantic categories while corrected p-values were

Table 1 Comparative analysis of neuropsychological test performance in SCA 1, SCA2, SCA3, and Controls. Significant crude p-values are given in italics, significant corrected p-values in bold

	SCA1 (N = 11)		SCA2 (N = 14)		SCA3 (N = 11)		Controls (N = 8)			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p-value	F-value
Age (years)	48.6	9.4	44.0	13.4	52.1	10.8	48.0	9.0	0.3569	1.1086 (3; 43)
Age of onset (years)	40.0	6.0	35.4	13.5	41.5	11.3	–	–	0.3587	1.0578 (2; 35)
Disease duration (years)	8.9	5.4	8.4	5.9	11.4	3.4	–	–	0.3397	1.1159 (2; 35)
Verbal IQ	110.1	7.3	106.5	5.4	111.9	14.8	113.3	16.6	0.5110	0.7821 (3; 43)
Performance IQ	102.0	8.3	106.4	7.3	108.6	10.3	108.9	11.6	0.3109	1.2314 (3; 43)
MMS	28.1	1.7	29.2	1.0	29.1	1.1	29.8	0.5	**0.0259**	3.4305 (3; 43)[1]
Digit Span										
Digit Span Forward	6.2	1.1	6.1	0.9	5.8	1.3	6.6	1.2	0.4691	0.8613 (3; 43)
Digit Span Backward	4.3	1.0	4.2	1.1	4.0	0.9	4.5	1.4	0.7962	0.3404 (3; 43)
Rey-Osterrieth Complex Figure										
Copy	46.1	1.4	46.6	0.6	45.7	2.0	45.7	1.4	0.3445	1.1429 (3; 40)
Recall	27.7	7.8	27.8	7.8	27.5	7.7	31.0	8.6	0.7706	0.3763 (3; 40)
Proportional Recall	59.8	16.5	59.6	16.5	59.8	15.6	67.6	18.0	0.6938	0.4865 (3; 40)
Wechsler Memory Scale										
Immediate Recall	8.4	1.8	6.6	3.6	8.3	4.3	10.3	4.3	0.1562	1.8355 (3; 43)
Delayed Recall	5.9	1.6	4.8	3.7	6.5	4.4	7.9	3.8	0.2656	1.3706 (3; 43)
Word Lists										
Immediate recall CC	5.5	2.1	6.8	2.8	6.5	1.7	9.4	3.2	*0.0154*	3.9232 (3; 42)[1]
Immediate recall RC	4.6	1.4	5.3	1.5	6.5	1.7	9.4	3.2	**< 0.0001**	10.2003 (3; 42)[1, 2, 3]
Immediate recall RR	3.5	1.4	4.7	1.8	5.5	2.9	6.1	2.1	0.0582	2.7089 (3; 42)
Delayed recall CC	2.2	1.5	3.6	2.0	3.4	1.9	5.0	2.8	*0.0433*	2.9738 (3; 42)[1]
Delayed recall RC	2.0	1.9	2.1	1.9	1.6	1.6	3.9	4.1	0.2130	1.5663 (3; 42)
Delayed recall RR	0.3	0.5	0.6	0.8	1.4	1.4	1.6	1.8	*0.0474*	2.8937 (3; 42)
Verbal Fluency										
Semantic category	17.5	6.5	18.4	4.9	19.0	6.5	24.3	12.2	0.2379	1.4674 (3; 43)
Phonemic category	7.7	2.3	7.3	3.9	8.6	3.4	11.8	3.5	**0.0297**	3.3054 (3; 43)[2]
Switching categories	10.9	2.1	11.9	3.1	13.0	2.5	14.4	2.2	*0.0322*	3.2347 (3; 43)[1]
Wisconsin Card Sorting Test										
Categories	4.9	0.8	5.2	1.4	5.2	1.6	5.5	1.4	0.8249	0.3003 (3; 42)
Random errors	8.3	2.7	5.3	3.2	3.8	2.8	3.1	2.5	**0.0019**	6.0627 (3; 39)[1, 4]
Perseverative errors	3.1	2.9	2.4	2.2	0.6	1.0	0.3	0.8	**0.0138**	4.0682 (3; 39)[1, 4]

[1] SCA1 vs. Controls; [2] SCA2 vs. Controls; [3] SCA3 vs. Controls; [4] SCA1 vs. SCA3

statistically not significant. On the WCST, SCA1 patients produced significantly more random and perseverative errors not only than controls, but even more than SCA3 subjects.

Influence of cerebellar motor symptoms on the test performance

The test performance on the Rey-Osterrieth-Figure was not related to the severity of the limb ataxia while the results of two other tests (Digit Span: forward, Verbal Fluency: generation of nouns from alternating semantic categories) showed a weak inverse correlation to the dysarthria scores (Spearman's Rho –0.3709, p = 0.026, and –0.3352, p = 0.0457). These correlations were not significant after applying the Bonferoni-Holm-Adjustment.

Discussion

This is the first study to analyse comparatively the cognitive profile of the most frequent SCA types. Significant impairment on verbal memory and fronto-executive tasks was found in all SCA types, but most prominent in SCA1. Among non-demented SCA1, SCA2 and SCA3 patients, SCA1 individuals scored lowest on the MMS.

Based on functional imaging studies showing cerebellar activation independent of motor control during attentional tasks [1], cerebellar patients would also be expected to have defective attention, but there was no evidence for such deficits in all SCA types tested. The finding of intact visuospatial processing and memory is in accordance to other neuropsychological studies in cerebellar patients [4, 13], while other authors found deficient visuospatial function [5, 38, 42].

Among non-demented SCA individuals, neuropsy-

chological deficits were most prominent in SCA1: on the WCST, deficits of executive function emerged with SCA1 patients producing significantly higher error rates for both random and perseverative errors not only as compared with controls, but even compared with SCA3 patients. The present data are in accordance with those of Kish et al., who described poor performance on the WCST in SCA1 individuals of North American, and thus distinct genetic origin [23]. In other studies, similar, but more subtle executive deficits have also been reported in SCA2 and SCA3 patients [6, 25, 40]. Imaging studies demonstrating cerebellar activation during performance of executive tasks reflect the close functional relationship of cerebellum and frontal cortex [22].

In addition, mild deficits of verbal memory were most prominent in SCA1 individuals, but also obvious in SCA2 and SCA3 patients. Since the test battery lacks a recognition paradigm, a simple learning deficit cannot be absolutely excluded as a cause of the observed memory deficits.

On the other hand, functional imaging studies demonstrated activation of prefrontal areas during the free recall of word lists [3, 20]. So, defective recall of verbal material in SCA individuals could be interpreted as a symptom of prefrontal dysfunction. There is anatomical evidence that prefrontal association areas are tightly linked to the cerebellum via pontine structures [2, 35, 36] while efferent connections arising from the dentate nucleus and projecting to the prefrontal cortex represent the feedback limb of this cerebrocerebellar circuitry [26, 27, 37]. SCA1, SCA2 and SCA3 all show the common feature of severe cerebellar degeneration, but differ in their additional extracerebellar degeneration. The different severity of cognitive impairment in SCA1, SCA2 and SCA3 is therefore likely to result from their characteristic extracerebellar damage [15, 18, 19, 29]. Since cortical structures are usually preserved in SCA1 and SCA3, the executive dysfunction is not likely to result from damage to the frontal lobe itself [18, 19]. If disruption at the pontine level was responsible for the executive deficits in SCA, the cognitive decline should be correlated to the extent of pontine involvement. Indeed, brain stem atrophy is more pronounced in SCA1 and SCA2 than in SCA3 [15, 18, 19, 29, 39]. Thus this would be consistent with a disruption of the cerebrocerebellar circuitry at the pontine level causing cognitive dysfunction in SCA. A combined volumetric and neuropsychological study will be appropriate for investigating the possible correlation of pontine atrophy and cognitive deficits in SCA1, SCA2 and SCA3.

References

1. Allen G, Buxton RW, Wong EC, Courchesne E (1997) Attentional activation of the cerebellum independent of motor involvement. Science 275:1940–1943
2. Allen GI, Tsukahara N (1974) Cerebrocerebellar communication systems. Physiol Rev 54:957–1006
3. Andreasen NC, O'Leary DS, Arndt S, Cizadlo T, Hurtig R, Rezai K, Watkins GL, Ponto L, Hichwa R (1995) Short term and long term verbal memory: A positron emission tomography study. Proc Natl Acad Sci USA 92:5111–5115
4. Appollonio IM, Grafman J, Schwartz V, Massaquoi S, Hallett M (1993) Memory in patients with cerebellar degeneration. Neurology 43:1536–1544
5. Bracke Tolkmitt R, Linden A, Canavan AG, Rockstroh B, Scholz E, Wessel K, Diener HC (1989) The cerebellum contributes to mental skills. Behav Neurosci 103:442–446
6. Bürk K, Globas C, Bösch S, Gräber S, Abele M, Brice A, Dichgans J, Daum I, Klockgether T (1999) Cognitive deficits in spinocerebellar ataxia 2 (SCA2). Brain 122:769–777
7. Bürk K, Stevanin G, Didierjean O, Cancel G, Trottier Y, Skalej M, Abele M, Brice A, Dichgans J, Klockgether T (1997) Clinical and genetic analysis of three German kindreds with autosomal dominant cerebellar ataxia type I linked to the SCA2 locus. J Neurol 244: 256–261
8. Burt T, Blumberg P, Currie B (1993) A dominant hereditary ataxia resembling Machado-Joseph disease in Arnhem Land, Australia. Neurology 43: 1750–1752
9. Cancel G, Dürr A, Didierjean O, Imbert G, Bürk K, Lezin A, Belal S, Benomar A, Abada Bendib M, Vial C, Guimaraes J, Chneiweiss H, Stevanin G, Yvert G, Abbas N, Saudou F, Lebre AS, Yahyaoui M, Hentati F, Vernant JC, Klockgether T, Mandel JL, Agid Y, Brice A (1997) Molecular and clinical correlations in spinocerebellar ataxia 2: a study of 32 families. Hum Mol Genet 6:709–715
10. Channon S, Daum I, Polkey CE (1989) The effect of categorization on verbal memory after temporal lobectomy. Neuropsychologia 27:777–785
11. Coutinho P, Andrade C (1978) Autosomal dominant system degeneration in Portuguese families of the Azores Islands. A new genetic disorder involving cerebellar, pyramidal, extrapyramidal and spinal cord motor functions. Neurology 28:703–709
12. Dahl G (1972) WIP REDUZIERTER WECHSLER-INTELLIGENZTEST Reduced Wechsler Intelligence Test. Meisenheim/Glan: Hain
13. Daum I, Ackermann H, Schugens MM, Reimold C, Dichgans J, Birbaumer N (1993) The cerebellum and cognitive functions in humans. Behav Neurosci 107:411–419
14. Daum I, Gräber S, Schugens MM, Mayes AR (1996) Memory dysfunction of the frontal type in normal ageing. Neuroreport 7:2625–2628
15. Dürr A, Smadja D, Cancel G, Lezin A, Stevanin G, Mikol J, Bellance R, Buisson GG, Chneiweiss H, Dellanave J, et al. (1995) Autosomal dominant cerebellar ataxia type I in Martinique (French West Indies). Clinical and neuropathological analysis of 53 patients from three unrelated SCA2 families. Brain 118:1573–1581

16. Folstein MF, Folstein SE, McHugh PR (1975) MMST Mini-Mental-Status-Test – Deutschsprachige Fassung: Kessler J, Folstein SE, Denzler P. Weinheim: Beltz
17. Fowler HL (1984) Machado-Joseph-Azorean disease. A ten-year study. Arch Neurol 41:921–925
18. Genis D, Matilla T, Volpini V, Rosell J, Davalos A, Ferrer I, Molins A, Estivill X (1995) Clinical, neuropathologic, and genetic studies of a large spinocerebellar ataxia type 1 (SCA1) kindred: (CAG)n expansion and early premonitory signs and symptoms. Neurology 45:24–30
19. Gilman S, Sima AA, Junck L, Kluin KJ, Koeppe RA, Lohman ME, Little R (1996) Spinocerebellar ataxia type 1 with multiple system degeneration and glial cytoplasmic inclusions. Ann Neurol 39:241–255
20. Grasby PM, Frith CD, Friston KJ, Bench CRSF, Dolan RJ (1993) Functional mapping of brain areas implicated in auditory-verbal memory function. Brain 116:1–20
21. Kawaguchi Y, Okamoto T, Taniwaki M, Aizawa M, Inoue M, Katayama S, Kawakami H, Nakamura S, Nishimura M, Akiguchi I, et al. (1994) CAG expansions in a novel gene for Machado-Joseph disease at chromosome 14q32.1. Nat Genet 8:221–228
22. Kim SG, Ugurbil K, Strick PL (1994) Activation of a cerebellar output nucleus during cognitive processing. Science 265:949–951
23. Kish SJ, el Awar M, Schut L, Leach L, Oscar Berman M, Freedman M (1988) Cognitive deficits in olivopontocerebellar atrophy: implications for the cholinergic hypothesis of Alzheimer's dementia. Ann Neurol 24:200–206
24. Klockgether T, Schroth G, Diener HC, Dichgans J (1990) Idiopathic cerebellar ataxia of late onset: natural history and MRI morphology. J Neurol Neurosurg Psychiatry 53(4):297–305
25. Maruff P, Tyler P, Burt T, Currie B, Burns C, Currie J (1996) Cognitive deficits in Machado-Joseph disease. Ann Neurol 40:421–427
26. Middleton FA, Strick PL (1994) Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. Science 266:458–461
27. Middleton FA, Strick PL (1997) Dentate output channels: motor and cognitive components. Prog Brain Res 114:553–566
28. Nelson HE (1976) A modified card sorting test sensitive to frontal lobe defects. Cortex 12:313–324
29. Orozco G, Estrada R, Perry TL, Arana J, Fernandez R, Gonzalez Quevedo A, Galarraga J, Hansen S (1989) Dominantly inherited olivopontocerebellar atrophy from eastern Cuba. Clinical, neuropathological, and biochemical findings. J Neurol Sci 93:37–50
30. Orr HT, Chung MY, Banfi S, Kwiatkowski TJJ, Servadio A, Beaudet AL, McCall AE, Duvick LA, Ranum LP, Zoghbi HY (1993) Expansion of an unstable trinucleotide CAG repeat in spinocerebellar ataxia type I. Nat Genet 4:221–226
31. Osterrieth P (1944) Le test de copie d'une figure complex. Arch Psychol 30:205–256
32. Pulst SM, Nechiporuk A, Nechiporuk T, Gispert S, Chen XN, Lopes Cendes I, Pearlman S, Starkman S, Orozco Diaz G, Lunkes A, DeJong P, Rouleau GA, Auburger G, Korenberg JR, Figueroa C, Sahba S (1996) Moderate expansion of a normally biallelic trinucleotide repeat in spinocerebellar ataxia type 2. Nat Genet 14:269–276
33. Rey A (1942) L'examen psychologique dans les cas d'encephalopathie traumatique. Arch Psychol 28:112
34. Rosenberg RN, Nyhan WL, Bay C, Shore P (1976) Autosomal dominant striatonigral degeneration. Neurology 26:703–714
35. Schmahmann JD, Pandya DN (1995) Prefrontal cortex projections to the basilar pons in rhesus monkey: implications for the cerebellar contribution to higher function. Neurosci Lett 199: 175–178
36. Schmahmann JD, Pandya DN (1997) Anatomic organization of the basilar pontine projections from prefrontal cortices in rhesus monkey. J Neurosci 17:438–458
37. Schmahmann JD, Pandya DN (1997) The cerebrocerebellar system. Int Rev Neurobiol 41:31–60
38. Schmahmann JD, Sherman JC (1998) The cerebellar cognitive affective syndrome. Brain 121:561–579
39. Sequeiros J, Coutinho P (1993) Epidemiology and clinical aspects of Machado-Joseph disease. Adv Neurol 61:139–153
40. Storey E, Forrest SM, Shaw JH, Mitchell P, Gardner RJ (1999) Spinocerebellar ataxia type 2: clinical features of a pedigree displaying prominent frontal-executive dysfunction. Arch Neurol 56:43–50
41. Wadia NH (1984) A variety of olivopontocerebellar atrophy distinguished by slow eye movements and peripheral neuropathy. Adv Neurol 41:149–177
42. Wallesch CW, Horn A (1990) Long-term effects of cerebellar pathology on cognitive functions. Brain Cogn 14: 19–25
43. Wechsler D (1987) WMS-R WECHSLER MEMORY SCALE – REVISED Wechsler Memory Scale – Revised. Manual. San Antonio: The Psychological Corporation Harcourt Brace Jovanovich, Inc