Articles

Cognitive impairments in patients with congenital nonprogressive cerebellar ataxia

Maja Steinlin, MD, Marianne Styger, LicPhil and Eugen Boltshauser, MD

[+] Author Affiliations

Address correspondence and reprint requests to Dr. Maja Steinlin, Division of Neurology, University Children's Hospital, Inselspital, 3010 Bern, Switzerland; e-mail: maja.steinlin@insel.ch

Abstract

Objective: To report neuropsychologic functions and developmental problems of patients with congenital nonprogressive cerebellar ataxia.

Background: Growing interest in cerebellar function has prompted closer attention to cognitive impairments in patients with cerebellar damage.

Methods: The authors studied 11 patients with nonprogressive congenital ataxia (NPCA) with Wechsler's intelligence testing, with additional tests of attention, memory, language, visual perception, and frontal functions.

Results: Seven of the 11 patients had an IQ of 60 to 92, with marked nonverbal deficits and subnormal to normal verbal performance (group A). Four patients had an IQ of 30 to 49 without pronounced profile asymmetry (group B). Four of the 7 group A patients had decreased alertness and sustained attention, but all had normal selective attention. Tests of frontal functions and memory yielded higher verbal scores than nonverbal scores. There was no deficit on the Aachener Naming Test (similar to the Boston Naming Test), because there were marked difficulties in the majority with visuoconstructive tasks and visual perception. Group B was significantly abnormal in almost all subtests, having a less prominent but similar profile.

Conclusion: Patients with NPCA have significant cognitive deficits with an asymmetric profile and better verbal than nonverbal performance. Effects on nonverbal performance of longstanding deficits in visuospatial input during learning, the influence of impaired procedural learning, and asymmetric plasticity of the cerebral hemispheres may contribute to this uneven neuropsychological profile.

A growing interest in cerebellar function has directed closer attention to cognitive and affective changes in patients with cerebellar dysfunction.1 Advances in functional imaging techniques provide the opportunity to analyze cerebellar activity during cognitive tasks.2–4 Many studies have shown that the cerebellum seems to be important for visuospatial planning, organization and construction, speech, memory, motor and nonmotor skill acquisition, and in shifting attention between sensory modalities and in affecting regulation.2–8 Acquired cerebellar lesions or generalized degenerative cerebellar changes in adulthood result in relatively mild neuropsychological deficits.9–11 Children with acquired cerebellar lesions such as tumors have limited cognitive impairment.12,13 However, children with congenital cerebellar dysfunction like cerebellar hypoplasia or Joubert's syndrome exhibit marked cognitive developmental delay with significant cognitive impairments in adult life.14–16 There is only one report of more detailed neuropsychological assessment in children with nonprogressive ataxia and cerebellar hypoplasia.15 We analyzed neuropsychological functions in 11 patients with clinically nonprogressive congenital ataxia(NPCA), with or without cerebellar hypoplasia, addressing which deficits might result in significant developmental problems.

Methods.

Patients.

Previously we reported long-term observations in a group of 34 patients with pure NPCA with or without cerebellar hypoplasia.16 From this group, individuals older than 7 years and having an estimated developmental quotient of more than 0.5 were considered eligible for additional detailed neuropsychological assessment. Age and developmental quotient limits were chosen to make it possible to administer and to analyze more demanding neuropsychological tests. Of 14 patients, 2 patients did not agree to neuropsychological testing, and 1 patient had moved out of Switzerland

(their ages were 23, 14, and 9 years; their estimated cognitive level was close to normal in the oldest patient and mildly to moderately limited in the two others). One girl, 12 years old, was first seen by us after completion of the parent study,16 and she was later included in the testing. In total, 12 patients underwent testing (as described later). One 11-year-old patient had an IQ of 40. Due to the young age and the patient's poor performance, he was excluded because many test items were not fulfilled.

Therefore, 11 patients, 5 men/boys and 6 women/girls, were eligible for the study. They were between the ages of 8 and 28 years with a average age of 11.9 years. The social class of the patients was defined in the study by de Spiegelare et al.17: Group 1 parents were members of upper management and professional groups; group 2, white collar workers; group 3, self-employed individuals and technicians; group 4, manual workers; and group 5, unemployed. Of the 11 patients, 2 belonged to social class group 1, 3 to social class group 2, 4 to social class group 3, and 2 to social class group 4. Neuroimaging was available in eight patients. Five of the eight patients showed cerebellar hypoplasia of varying degrees; three of the eight were normal. There were normal supratentorial findings in all eight patients. For more detailed clinical and neuroimaging data, we refer to our previous paper.16 A short summary, together with the results of the neuromotor assessment is given in table 1. Each proband underwent a standardized neuromotor assessment, as suggested by Hug18 and Muggli19 to quantify the motor handicap of the limbs. Tests such as finger and foot tapping, and pronation/supination movements of the hands yielded overall difficulty with motor skills—most values were 3 SDs below the mean value.

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Table 1.

Clinical and neuroimaging findings

Neuropsychological assessment.

Neuropsychological assessment was performed in all patients by the same neuropsychologist (M. Styger) during a half day at the hospital. Testing time was 3.5 hours with a break of 30 minutes after the first 2 hours. The assessment was recorded on video. The different tests were always performed in the same order.

Due to the diversity of age and gender in our group, evaluation of results was correlated with published reference values20-35 for age (table 2) and transferred to *t* values between 20 and 80 (mean, 50; SD, ± 10) for comparison. Subtests of intelligence quotient are given in points (mean, 10; SD, ± 3).

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Table 2.

Tests performed, their normal values, and literature references

Neuropsychological tests.

All tests administered are summarized in table 2, together with normal values and references.

Due to the variable cognitive level of our patients, we obtained an intelligence quotient for all patients. For children, we chose IQ values by the adjusted short version for Swiss children of the HAWIK-R20 (Hamburg-Wechsler Intelligence Scale for Children-Revised [German version]), including the similarities, vocabulary, arithmetic, picture arrangement, and block design subtests. This short version of the HAWIK-R is known to give a good estimate of full-scale IQ.20 In addition, we used the digit span subtest to assess the verbal span. In adult patients, the complete German version of the Hamburg-Wechsler Adult Intelligence Scale-Revised (HAWIE-R) was given.21 For comparison, only subtest results common to both tests are provided.

Attention was assessed by three tests of a computer-supported test series for attention by Zimmermann and Fimm22: 1) alertness by the reaction to visual stimuli with and without acoustic warning, 2) selective attention by selective reaction to predetermined stimuli mixed in a series of irrelevant stimuli, and 3) sustained visual attention (10 minutes), which was tested at the end of the half day by marking irregular optic stimuli in a series of regular optic stimuli. Reference values for children were available from Kuhnert et al.23 The number of missing answers for

sustained visual attention is provided in percentages in table 2 because there are insufficient published normal values. For the Corsi Block Board Test, reaching five or more blocks is considered to be normal for children and adults[24] because no references for *t* values are available.

Reference values for the photo series from the Kaufman Assessment Battery for Children[25] are not available for children older than 12 years, so we expected full performance in children older than 12.

In the subtest of "Merkmalsgruppen" in Kramer's[26] intelligence test, eight pictures have to be sorted according to their different group similarities, and there are six possibilities for group similarities (sorting by color, form, etc.). Kramer[26] gives normal results; three groups in 2 minutes, or four groups were sorted correctly in 3 minutes with no sign of perseveration. There are no references for the calculation of *t* values. The Tower of Hanoi Test was administered to most patients, but we did not analyze this test because many of the patients did not understand the test instructions.

Results.

Intelligence.

IQ points for all subtests are summarized in table 3. The mean intelligence quotient of our 11 patients was 62, with a broad range from 30 to 90. IQ was not related to social class. There is no correlation of neuromotor performance to IQ (figure). In patients with IQs > 50, analysis of the subtest scores reveals an asymmetric performance profile with better verbal than nonverbal performance (see the figure). The fact that this profile is not evident in patients with lower IQ values is most likely due to the limited value of subtest analyses in this range of IQ. Therefore, for an additional discussion of test results, we included only the seven patients with IQs from 69 to 92 (mean value, 74) in group A.

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Table 3.

IQs (HAWIK-R and HAWIE-R testing*)

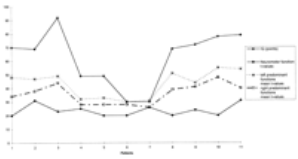

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Figure. Comparison of IQ, right/left predominant functions, and motor disability.

Attention.

In the test for alertness, patients showed delayed reaction times (RTs) with mean *t* values of 35 (table 4). Warning by an acoustic signal before the stimulus decreased the RT appropriately, but absolute RT was still delayed compared with reference values for age.

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Table 4.

Results of attention tests

The go/no-go test yielded selective attention and suppression of reaction scores within normal values for group A (mean *t* values, 80 for selective attention and 66 for selective suppression), but delayed RT.

Comparison of sustained attention by testing during 0 to 5 minutes and 6 to 10 minutes showed an increase of RT and number of wrong and missing answers, pointing to precocious fatigability and reduced endurance. The fact that Patient 8, who is the only patient with normal attention, had a low IQ of 60, indicates that overall IQ was not dependent on attention.

Memory.

Testing for verbal memory in group A yielded a normal mean *t* value for all subtests (range, 43 to 45; table 5). Patient 3 had marked problems for recognition after 1 hour due to mixing up the main word list and the interfering word list. Patient 1 had inadequate immediate recall and recall after interference, but normal memory after 1 hour. Only Patient 2 had clearly inadequate learning, recall, and memory. Comparison with results of visual design learning showed a mildly decreased normal mean *t* value (range, 40 to 44) for the subtests. Three patients had markedly insufficient values for recall as well as memory, and two of them also had deficits for verbal recall, learning, and memory. All patients showed a marked increase in wrong designs, frequently rotating pictures, or reproducing shapes inaccurately. Consequently, in all but one patient, reproduction of the Rey–Osterrieth complex figure after 1 hour was inadequate (mean *t* value, 34), but even copying the figure was difficult for most patients (as described later).

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Table 5.

Results of memory tests

Digit span scores were normal in only three patients (group A), with a mean *t* value of 40. Analyzing the two subtests separately, it indicated that all patients achieved lower scores for backward rather than forward recall. The Corsi Block Board Test results revealed a reduced ability to memorize spatial information.

Language.

Six patients in group A had average scores for naming in the four subtests (mean *t* value, 49; table 6). Naming results with a *t* value of 35 in Patient 9 correlate with his low performance in the IQ subtest of vocabulary and similarities. The highest scores were for naming of colors; the lowest were for naming of composita and situations.

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Table 6.

Results of language and visual perception tests

Visual perception.

In group A, visual perception tested by copying the Rey–Osterrieth complex figure was poor, compared with better results in Hooper's Visual Organization Test (table 6). Testing for photo series was abnormal for all patients.

Frontal functions.

Testing results for fluency in group A gave a mean *t* value of 43 for verbal fluency and only 36 for design fluency (table 7). Kramer's Merkmalsgruppen subtest was normal in five of the seven patients. Only one patient had a slight tendency toward perseveration.

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Table 7.

Results of frontal function tests

The Stroop Interference Test required increased time with a significant number of wrong answers, with mean *t* values between 36 and 38, but the increase in time caused by interference was within normal limits for all seven patients.

Discussion.

Our results support the fact that cognitive impairment is the rule in patients with con-genital nonprogressive cerebellar ataxia,14,15 and also growing evidence that the cerebellum is involved in cognitive function.1–13,36 The degree of cognitive impairment was not related to the degree of ataxia and motor deficit (figure), and neither was delay in RT in different tests related to the severity of the dysmetria. Nystagmus, only present in two children, cannot explain the children's visuomotor problems. Therefore, impaired performance in neuropsychological tests is not attributable to motor demand of the tasks. There was also no relationship between the degree of cerebellar hypoplasia in neuroimaging and cognitive performance. Nor was degree of ataxia or degree of cognitive problems related to age.

Intelligence testing divided our patients in two groups. The group with IQs greater than 50 showed a dissociative pattern, with some tests being subnormal to normal and other tests showing more marked abnormalities (figure). The pattern was similar in all these patients, with better verbal than nonverbal performance and major problems in visuospatial tasks (such as block design, Rey-Osterrieth complex figure). This was evident by comparing verbal tasks (similarities, vocabulary, and digit span) with nonverbal tasks (arithmetic, picture arrangement, and block design) in the HAWIK-R and HAWIE-R. Additional comparison was made for learning and memory in the verbalen Lern-und Merkfähigkeitstest (verbal) and Visual Design Learning Test (nonverbal), for fluency in the S-Fluency test (verbal) and 5-point test (nonverbal), and for attention span in the digit span forward (verbal) and the Corsi Block Test (nonverbal). The group with IQs less than 50 had a more generalized impairment. However, even in this second group there was a tendency toward dissociation of the neuropsychological pattern. Therefore, we conclude that congenital cerebellar dysfunction is associated with a typical neuropsychological pattern, which is more clearly expressed in patients with better overall cognitive functioning.

Our study confirms the results of Guzetta et al.15 that children with NPCA have better verbal than nonverbal performance. This pattern of neuropsychological performance has also been reported in children with congenital hydrocephalus, and it is explained by longstanding disturbance of visuospatial inputs (lesions parieto-occipitally).37 Children with congenital ataxia have similar longstanding visuospatial deficits. However, if marked visuospatial disturbance was the main factor leading to right hemispheric impairment, one would expect a correlation between motor and cognitive handicap. A correlation does not exist. The dissociative pattern depicted in the figure indicates that not only visuospatial performance but almost all right-hemisphere functions are more disturbed than left-hemisphere or bilateral functions. Considering the symmetric bilateral cerebellar pathology, these results are notable. Better left-hemispheric recovery with decreased right-hemispheric functioning is reported in children with left-side congenital infarction38 or trauma in infancy and childhood39 compared with children with right-side lesions. This is attributed to greater left-side plasticity and shifting of left-side functions to the right hemisphere39—the so-called resilience of language. In children with congenital ataxia, better left-side function might be explained by a similar mechanism.

All our patients had impaired performance in tasks attributed to frontal function. These results are not surprising considering the well-documented cerebellar-frontal connections.40 Their marked spatial-constructive difficulties suggest important cerebellar-parietal connections.

A recent study by Molinari et al.5 suggests that the cerebellum is involved in procedural learning and that mastered skills are usually preserved after cerebellar lesions. Therefore, the earlier in development that cerebellar dysfunction occurs, the more cognitive functioning is limited. This could explain why adults with cerebellar lesions show relatively mild neuropsychological problems compared with children with congenital ataxia. This theory is also supported the study of Krägeloh-Mann et al.,41 which showed that all premature babies with cerebellar atrophy have significant cognitive problems (IQ < 50), which are more pronounced than those of children with supratentorial abnormalities.

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