Supplementary data

**On spinocerebellar ataxia 21 as a mimicker of cerebral palsy**

**Biochemical analyses and array comparative genomic hybridization (aCGH)**

Analyses for quantitative plasma amino acids, urinary organic acids, lipid levels, phytanic acid, and VLCFA were normal. Pediatric patients with developmental delay, and/or presenting with symptoms and signs suggesting a syndrome, are evaluated for abnormal copy number variations (CNV) with aCGH. In both patients aCGH was normal.

**Genetics**

**Genome sequencing**

Libraries for sequencing on Illumina Nova-Seq 6000 (Illumina) were prepared from genomic DNA derived from blood samples of the affected individuals. Sample library preparation, sequencing, and initial bioinformatics up to base calling and demultiplexing was performed at the Science for Life Laboratory, Stockholm. An inhouse pipeline, described in detail by Stranneheim et al (e-5), was used to process reads and arrive at candidate genes.

**Sanger sequencing**

Confirmation and segregation of the detected variants was done by performing polymerase chain reaction (PCR) amplification, followed by Sanger sequencing of both strands on ABI 3730 Genetic Analyzer (Applied Biosystems Inc) using standard protocols. Primers are available upon request.

**Clinical findings**

**Patient 1**

An investigation was performed using the Griffiths Mental Developmental Scales (GMDS) when the patient was 6-year-old. His auditory and speech development was delayed, with impaired articulation. The auditory and speech development corresponded to age 4.5-year level. The performance scale, for assessment of visuo-constructive skills, and the practical reasoning scale, for assessment of logical, mathematical and memory function, yielded an overall outcome corresponding to age 4-year level. The investigators also noted that the patient had an impaired ability to communicate and interact socially. The general conclusion was that the patient did not fulfil the criteria for intellectual disability but for atypical autism, later the patient was also diagnosed with dyslexia.

The patient was evaluated again at age 13 years with the WISC-III (Weschsler Intelligence Scale for Children) yielded an average scale score of 5.3 (Full scale IQ=77). Nine out of twelve subtests in WISC-III yielded a performance below the scale score 6 (SD=-1.3). There was not significant difference between the performance in verbal respectively performance subtests. The Freedom from distractibility index (FDI) and the Processing speed index (PSI) were extremely low. Also, the subtest Vocabulary showed an extremely low result. The subtests Similarities (abstract verbal conceptualization) and Information (general knowledge) yielded results corresponding to age 9-year level. In the subtest Digit Span (short term memory/working memory) the result was below the 6-year level and the performance in the subtest Arithmetic (quantitative reasoning/solving orally administered arithmetic problems) corresponded to the age 8-year level. The patient performed relatively better in the performance tests than in the verbal tasks. Attendance to a special school was recommended.

A third evaluation was performed when the patient was 23 years old using WAIS-III-NI (Wechsler adult intelligence scale III, neuropsychological investigation) revealed extremely low results in tests measuring working memory as Digit Span Backwards. However, the patient performed essentially better when testing the visual working memory by the Block span and the patient’s concentration/attention was satisfactory when the nonverbal information was presented. The Claeson-Dahl’s test for verbal learning and retention revealed considerable episodic memory dysfunction. A vocabulary test measuring the understanding of words and verbal concepts revealed a low result. In contrast the patient showed a good verbal/oral expressiveness in the testing situation. Furthermore, a strength within the verbal domain appeared to be a good understanding of societal rules and well-developed judgment. The patient performed best in tests measuring different aspects of visual perception and visuo-motor skills. Thus, he achieved good results in e.g., Picture Completion (ability to quickly perceive visual details) and Picture Arrangement (logical/sequential reasoning, social insight). Also, in visuo-constructive tasks he performed on a high normal level. Overall, he performed well in visuo-spatial tests. Despite having a consciousness of time, the patient had a limited understanding of time-related concepts such as weeks and months. He appeared to have difficulties with keeping appointments, demonstrating pervasive considerably difficulties with theory-of-mind, impaired ability to interpret other people’s intentions and when coping with social relations. Furthermore, the patient was dependent of assistance from his parents with the handling of money.

**Patient 2**

The patient was provided with keyboarding device and wrist weights to facilitate writing. Teachers also noticed that the patient had difficulty concentrating at school, at age 10 years this patient was diagnosed with dyslexia. He has attended a regular school ever since; at age 11 years the patient went through an evaluation of his intellectual ability using the WISC-IV. The WISC-IV is an assessment of intellectual functioning in Verbal Comprehension (VC), Perceptual Reasoning (PR), Working Memory (WM) and Processing Speed (PS)intellectual functioning in Verbal Comprehension (VC), Perceptual Reasoning (PR), Working Memory (WM) and Processing Speed (PS). Block Design, a subtest for PR, was affected due to impaired dexterity but the outcome improved when the patient was tested with visual puzzles. The overall measure of general cognitive ability was within the normal range despite the fact that work memory and PS were under average for his age group. During the last visit at our center the patient declined further neuropsychological evaluation.

**References**

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