Methods

Participants

Twenty-one children aged from 6 to 16 years and suffering from WD according to clinical guidelines for its diagnosis (8) were included retrospectively in the present study. The children had no other neurological, liver or psychiatric diseases, but all had displayed biological signs of hepatic dysfunction at diagnosis. At the time of testing, all were ranked as Child-Pugh class A and one of them was presenting with chronic liver failure. They had been treated with chelating agents for less than 18 months and according to their medical records appeared to be complying with the therapy. The patients were divided into two groups, depending on the presence of both cerebral magnetic resonance imaging (MRI) abnormalities and motor symptoms (NEUR group: 2 males, 2 females, with a median ± interquartile range of 14 ± 1 years old versus LIVER group: 10 males, 7 females; 12 ± 2). The principal demographic and clinical characteristics of the children, including disease grade, developmental history, and liver, motor and behavioural symptoms, are presented in Table 1. This study was approved by the local Ethics Committee (decision issued by the “CPP Sud Est II” dated 24 February 2016; IRB number: 00009118).

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Insert Table 1

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Assessment of cognitive abilities

All the children completed the ten main sub-tests of the French version of WISC-IV (9). This widely used battery, designed for use in children, enables the measurement of four indexes: 1) the verbal comprehension index (VCI) to assess the ability to draw upon learned information, reason through an answer and verbally express thoughts; 2) the perceptual reasoning index (PRI) that assesses the ability to draw upon visual-motor and visual-spatial skills and organize thoughts: 3) the working memory index (WMI) that assesses the ability to hold verbal information in the short-term memory, to concentrate and to manipulate it in order to produce results or reasoning processes, and 4) the processing speed index (PSI) that assesses the ability to rapidly scan and discriminate between visual information. It is also sensitive to visual-motor coordination.

Statistical analyses

First of all, the raw scores were converted to age-scaled index scores using the French standardization sample of the WISC-IV (standard index scores in healthy controls: mean = 100, standard deviation = 15).

Secondly, analyses were performed at an individual level. The index scores of each patient were assigned to one of the seven following qualitative categories: extremely low (<69), borderline (70-79), low average (80-89), average (90-109), high average (110-119), superior (120-129), very superior (>130).We also compared the discrepancy between the index scores of each patient with the frequency of occurrence observed in the standardization sample, in order to determine any abnormally high discrepancy (threshold: 10%).

Thirdly, between- and within-group analyses were performed on the aged-scaled index scores. A randomization test with 1000 randomly sampled data divisions was carried out to compare the LIVER and NEUR groups. Non-parametric Friedman’s ANOVA and Wilcoxon post-hoc tests with Bonferroni’s adjustment (critical p-value = 0.008) were used to compare the four index scores in the LIVER group. Because of its small sample size, group analyses were not performed on the NEUR group.