

Cognitive functioning in patients entering a study of homocystinuria due to cystathionine beta-synthase deficiency (HCU)

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BACKGROUND: HCU is an inherited disorder of methionine metabolism, leading to abnormal accumulation of homocysteine and its metabolites. Developmental delay and intellectual disability are common among poorly controlled individuals, but early detection and consistent biochemical correction may result in improved intellectual functioning. Study CBS-HCY-NHS-01 is a prospective observational study of the natural history of patients with HCU on current therapy.

METHODS: Baseline neuropsychological testing was performed on 22 participants with a mean age of 19.7 ± 11.7 y using the NIH Toolbox Cognition Battery (NIHCB), which consists of 7 tasks measuring receptive vocabulary, word reading, processing speed, executive function, episodic memory, and working memory.

RESULTS: Diagnosis of HCU was made as newborns for 12/18 (67%) patients and later for 6 (33%); 13/21 (62%), 6/20 (30%) and 0 have experienced ocular, skeletal and vascular complications, respectively. Feasibility of the NIHCB was excellent with 21 of 22 patients able to complete all 7 tasks. Participants displayed a broad range of individual scores with some of the mean scores in the average range and some impaired. Higher plasma total homocysteine (tHcy) levels at the time of the testing were negatively associated with cognitive functioning across all domains. Moderate correlations were found between tHcy and two tasks of executive functioning: The Flanker task which measures inhibition and visual attention ($r = -.31, p = .17$) and the Dimensional Change Card Sort task which measures cognitive flexibility ($r = -.34, p = .13$).

DISCUSSION: Concurrent levels of plasma tHcy may be related to neuropsychological functioning, especially executive functioning. The NIHCB has potential for assessing the functioning of persons with HCU and may be useful for tracking response to intervention. Ongoing data collection will allow for investigation of biochemical markers and neuropsychological functioning over time.