

HCU Neurocognitive Abstract

A Longitudinal Study of Cognitive Function in Classical Homocystinuria Demonstrates Distinct Deficits in Inhibitory Control

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ABSTRACT (1,952/2,000 characters, including spaces)

Background:

Classical homocystinuria (HCU) is a rare autosomal recessive disorder of methionine metabolism. Neuropsychiatric abnormalities are common in HCU; however, the presentation is variable. The objective of this study was to determine if the NIH Toolbox Cognition Battery of tests (NIHCB) can provide further insight on cognitive deficits in HCU.

Methods:

This is a prospective, observational, longitudinal, multicenter, multinational, natural history study of HCU. Cognitive function (fluid and crystallized) was assessed at baseline and every 6 months using the age-normalized NIHCB administered 1:1 via tablet.

Results:

Sixty-two patients with HCU were enrolled as of 15 JUL 2021 (52% male; age range 5-53 years; 94% white) and had a median of 5 visits over 3.3 years. Intra-class correlation (ICC) scores indicated a high level of stability in cognition scores across the study period. Overall cognition was found to be impaired in HCU patients with a Total Composite Score (TCS) mean score of 86.8 (SD=20.00). Significant differences were observed in cognitive performance between subdomains, with the greatest deficit in inhibitory control (mean=81.0, SD=16.47), while receptive vocabulary was nearly normal (mean=98.0, SD=15.49). Concomitant treatment with betaine or formula was associated with a significant improvement in performance in several subdomains, as well as the mean TCS (no betaine versus betaine, 77.3 and 89.5, respectively, p=0.012).

Discussion:

This is the first study to examine cognitive deficits in HCU patients longitudinally using the NIHCB. ICC analysis indicated that cognitive scores were stable over the period studied. Subdomain analysis of the NIHCB demonstrated the greatest deficit in inhibitory control, while betaine and formula treatment were associated with higher cognitive scores. These results suggest there are unique areas of cognition affected by HCU and may provide support for focused evaluation and treatment.

DISCLOSURES

BG, MSM: Consultant, Travere Therapeutics.

SV, FG, YC, MS, LP: Employees and stockholders, Travere Therapeutics.

HL: Investigator and consultant, Travere Therapeutics, Inc.

Questions asked during submission:

- Presentation type: oral presentation, poster presentation, or both
 - BOTH
- Submission category, subcategory, topics, etc
 - Amino acid disorders
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Proposed key words: Homocystinuria, genotypes, total homocysteine concentration, natural history

Key meeting/submission information:

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