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Purpose: To better understand hyperammonemic-induced cognitive and behavior alterations in 19 women (aged 21 to 53 years) heterozygous for ornithine transcarbamylase (OTC) deficiency.

Key takeaways:
- Although patients in this study had normal IQs, they showed a specific neuropsychological phenotype. Relative to normative values, these patients showed a significant decline in fine motor function and nonsignificant weaknesses in nonverbal memory and learning, math, and attention/executive function. In contrast, performance was significantly above normal for verbal memory, verbal learning, reading, and verbal intelligence.
- Both symptomatic (n=8) and “asymptomatic” (n=11) patients showed a similar neuropsychological phenotype, although the “asymptomatic” patients had greater preservation of strengths and less marked deficits. Neuropsychological outcome was not associated with neonatal vs late-onset mutation, and there were limited associations with urea synthesis capacity.
- The allopurinol challenge test, which measures orotic acid excretion and can provide a measure of impairment of urea synthesis activity, was not sensitive enough to yield statistically significant results that could distinguish symptomatic from “asymptomatic” patients identified by clinical symptoms.

Discussion:
- The neurobehavioral phenotype exhibited by the patients with heterozygous OTC deficiency in this study is similar to that seen in patients with a nonverbal learning disability, which is often characterized by deficits associated with disturbances in white matter, including attention/executive weaknesses along with motor, tactile, and visual-spatial deficiencies.
- At the time of publication, alterations of white matter in patients with late-onset OTC deficiency had been shown by neuroimaging and neuropathological studies. In combination with the neurocognitive data presented in the current study, these findings add to the evidence of a white matter damage model for this disorder.