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**Purpose:** To characterize white matter integrity in patients with partial ornithine transcarbamylase (OTC) deficiency (n=19; 16 female, 3 male; aged 19-59 years) compared with healthy controls (n=18; aged 19-59 years) using diffusion tensor imaging (DTI), and correlate these imaging results to neurocognitive test scores. Data were also compared between patients with late-onset, symptomatic disease (n=14; based on presentation of clinical symptoms) and those who had not yet presented symptoms (asymptomatic; n=5).

## Key takeaways:

- Fractional anisotropy (FA)[a] was significantly reduced in the frontal white matter of both late-onset and asymptomatic patients relative to controls, indicative of changes in white matter microstructure.
- The difference in IQ[b] between patients (average IQ=110; 109 for late-onset and 112 for asymptomatic patients) and controls (average IQ=123) was not statistically significant.
- Relative to controls, patients showed increased reaction times on the Stroop test[c] and poorer performance on the Comprehensive Trail Making Test (CTMT)[d], particularly on tests 4 and 5, which are the most challenging and require a higher level of attention.
- Unlike controls, in patients there was a positive correlation between reduced FA in the frontal white matter and both longer reaction times on the Stroop test and lower scores on the CTMT.

## Conclusions:

- As frontal white matter tracts underlie executive function and working memory, the finding of reduced FA within this region suggests an anatomic correlate to the deficits in executive function seen in patients with partial OTC deficiency, even those who are asymptomatic. This finding is consistent with previous findings in the literature.[1]
- DTI may elucidate subtle damages in patients with partial OTC that are not as apparent with standard neuroimaging.

[a]FA is a numerical value that describes the degree of the diffusion process.

[b]IQ was measured by the Wechsler Abbreviated Scales of Intelligence (WASI).

[c]The Stroop test assesses simple attention, gross reading speed, and divided attention, and is a measure of executive functioning.[2]

[d]The CTMT is a standardized set of 5 visual search and sequencing tasks that focus on attention, concentration, resistance to distraction, and cognitive flexibility.[3]

**Additional references:** **1.** Gyato K, et al. *Ann Neurol*. 2004;55:80-86. **2.** Gropman A. *Mol Genet Metab*. 2010;100(suppl 1):S20-S30. **3.** Comprehensive Trail-Making Test. Multi-Health Systems Inc website. http://www.mhs.com/product.aspx?gr=cli&prod=ctmt&id=overview. Accessed April 18, 2016.

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