**Title:**

Cystic Fibrosis-related neurodegenerative disease associated with tauopathy and cognitive decline in aged CF mice

**Lay Title:**

Cystic fibrosis mice show progressive learning and memory issues associated with aging

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**What was your research question?**

Highly effective modulator therapies have significantly improved health for people with CF and the effect of aging in the context of CF needs to be explored. Our previous studies have shown that CF mouse models accurately reflect neurological symptoms of CF, so we examined the effect of aging on CF neurological health.

**Why is this important?**

Little is known about the function of CFTR in the brain and it is unclear if elexacaftor-tezacaftor-ivacaftor (ETI) or related modulators reach the brain to correct CFTR function there. With the expected increases in life-span for people with CF, it is important to know how neurological health is affected by CF with aging. This study is the first to define memory and learning issues along with associated brain pathology with aging in a CF mouse model. Understanding these memory issues will help in the development of effective therapies in the future.

**What did you do?**

We conducted a study that examined non-CF and CF mice at different ages for cognitive function using two different behavior tests that measure learning and memory. We also examined the brains for the presence of a common cause of learning and memory issues in other forms of dementia called phosphorylated-Tau (pTau). Electrical studies that examine the function of a region of the brain responsible for learning and memory were also conducted. Finally, epithelial cells from the nasal passages of people with and without CF were examined for pTau levels to see if similar processes are occurring in human samples.

**What did you find?**

Findings demonstrate that CF mice begin to show loss of memory and learning abilities by 6 to 7 months-of-age and have more severe deficits by 12 to 15 months-of-age, whereas non-CF mice did not show such a decline. We also found that CF mice have significant levels of pTau by 7 months-of-age, a finding consistent with mouse models of other neurological diseases. Electrical studies show functional deficits in CF brain regions associated with memory. Human nasal epithelial cells also show increased pTau levels in CF samples compared to non-CF samples suggesting that these processes might be relevant to humans.

**What does this mean and reasons for caution?**

Our findings show that in CF mice, there is a pathological process that develops with age resulting in reduced learning and memory abilities. Non-neurological tissue from people with CF also show signs of pTau increases meaning that similar processes leading to memory and learning issues in mice might be present in humans. CF mouse models have reflected human neurological symptoms well, but how these findings relate to human disease needs to be further studied.

**What’s next?**

Future studies need to determine how these memory impairments are occurring in CF mouse models and whether these findings relate to aging issues in people with CF. The effectiveness of ETI in preventing memory issues needs to be investigated. These studies show the importance of studying aging processes in CF.

**Original manuscript citation in PubMed**

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