

Could Branched-chain Amino Acids Link Metabolic Dysregulation And Early Cognitive Decline?

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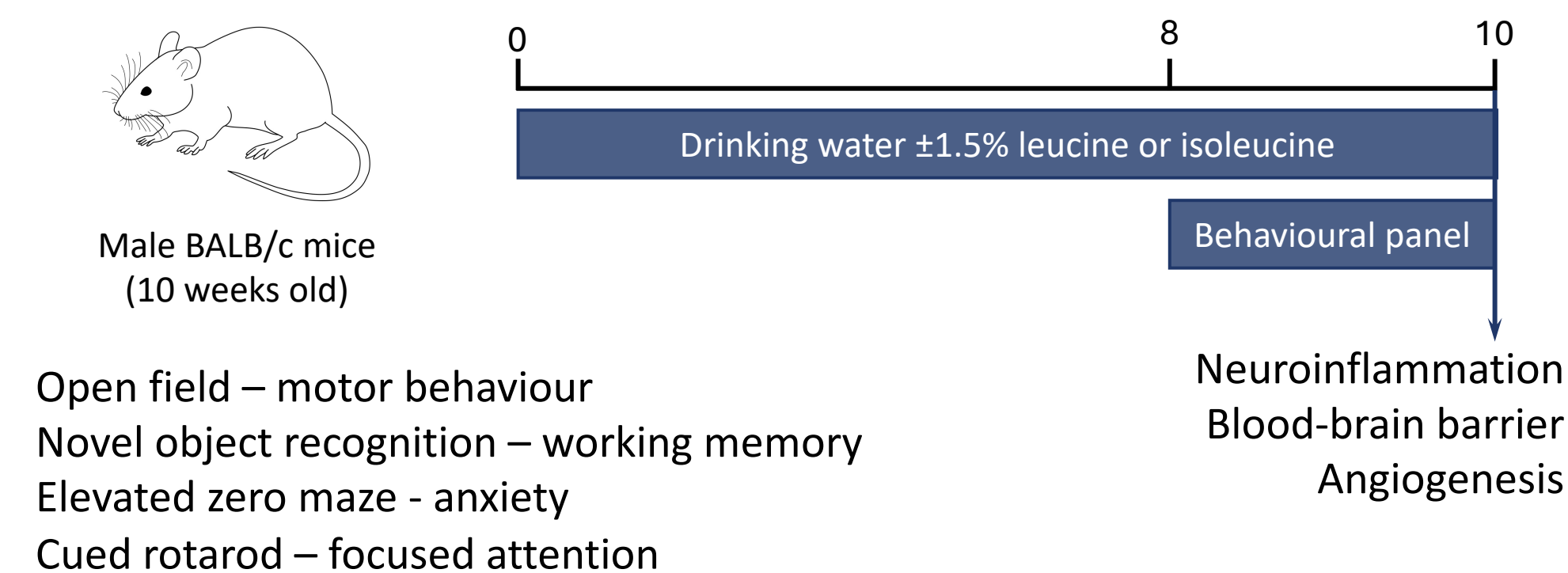
Background

Metabolic disorders such as obesity, insulin resistance and type II diabetes are major risk factors for Alzheimer's disease (AD), but it is unclear why.

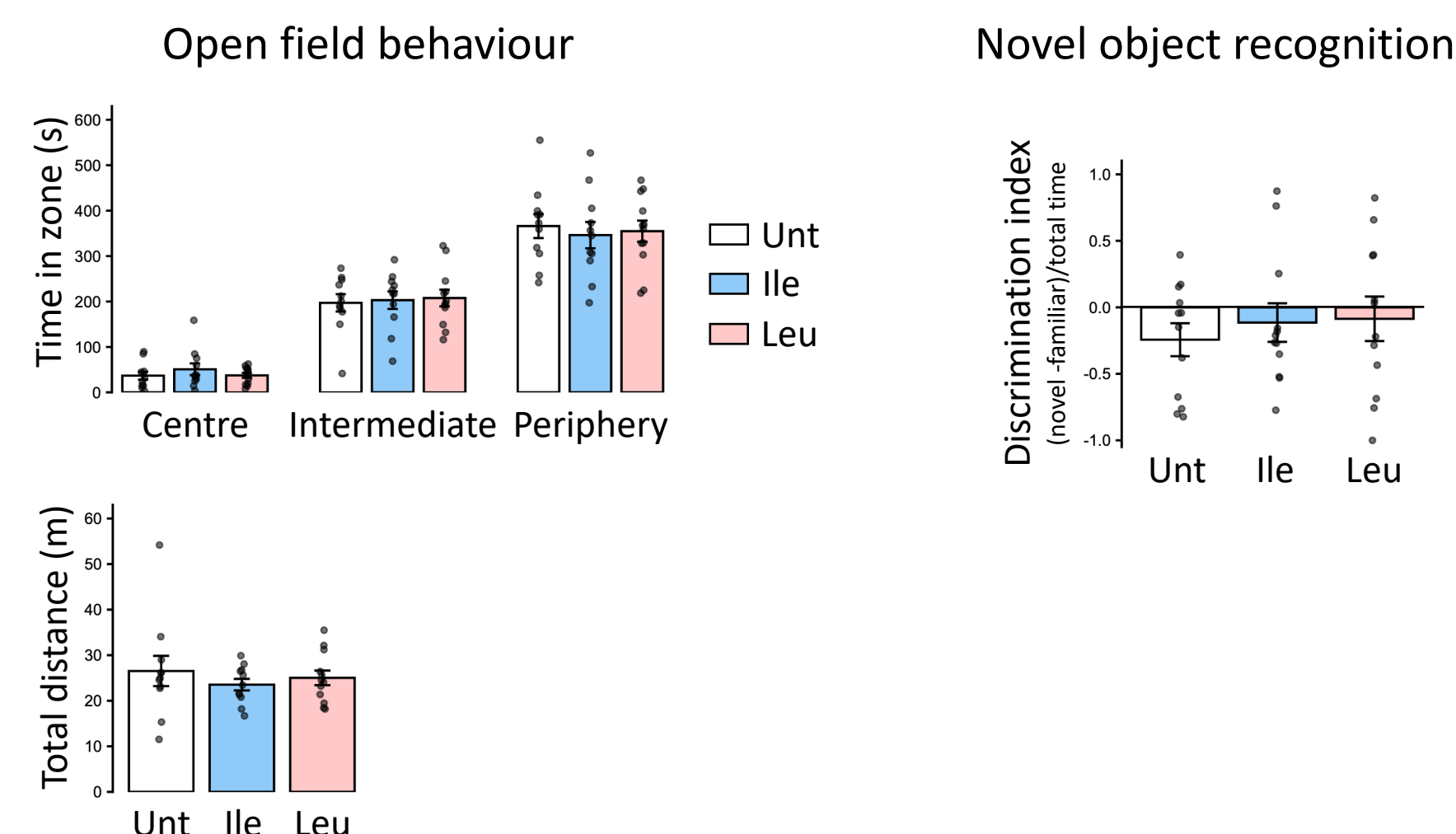
Raised circulating levels of the branched chain amino acids isoleucine and leucine is a common feature of all these disorders.

Hypothesis: BCAAs are a significant component of the link between metabolic disease and cognitive decline.

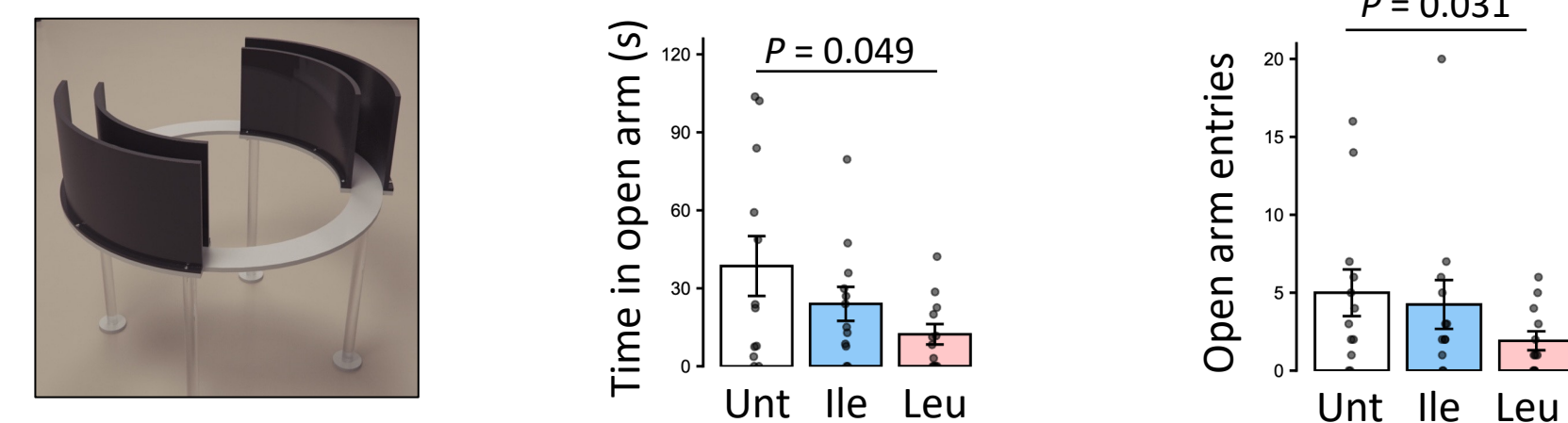
Methods



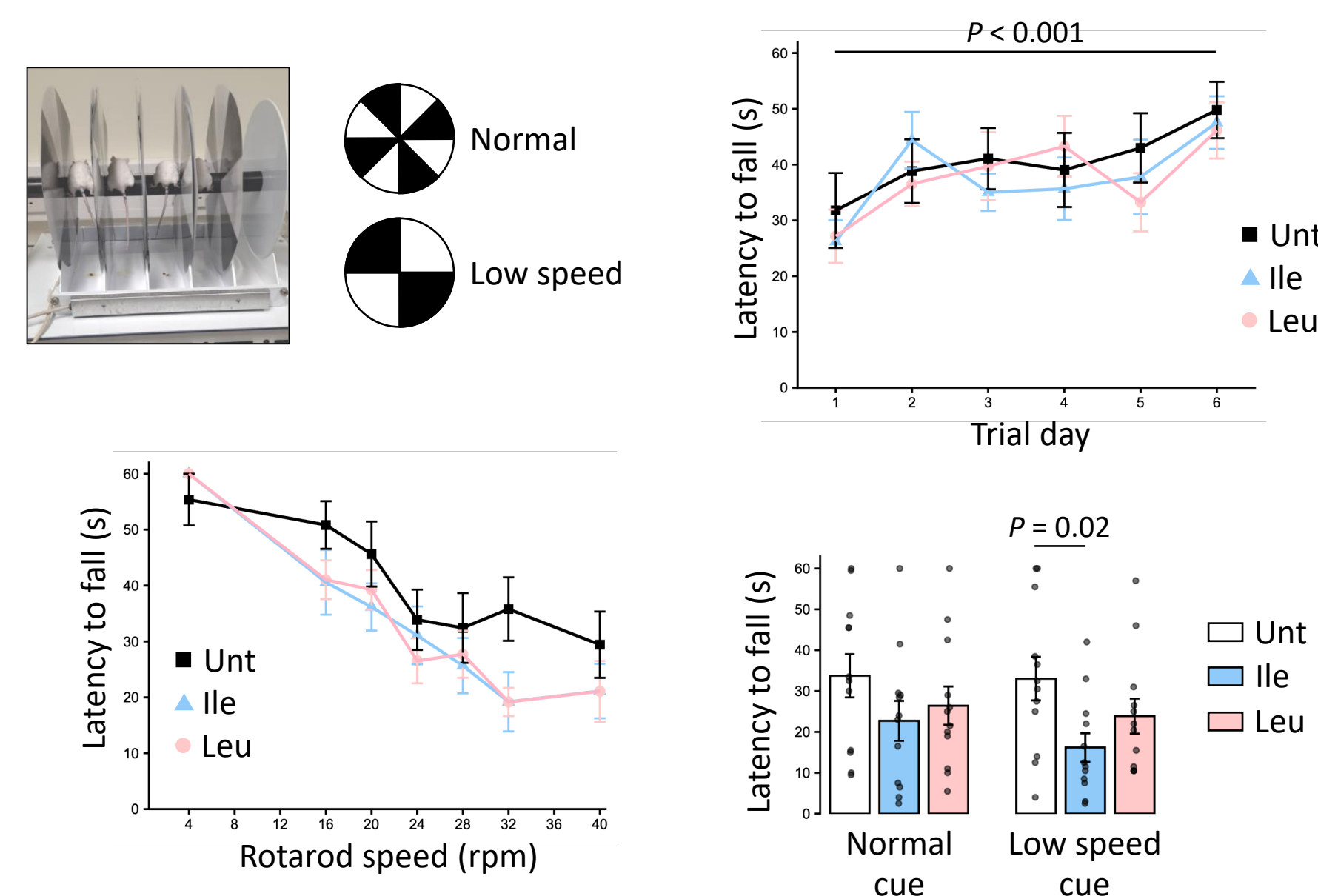
Gross motor function & memory are unimpaired



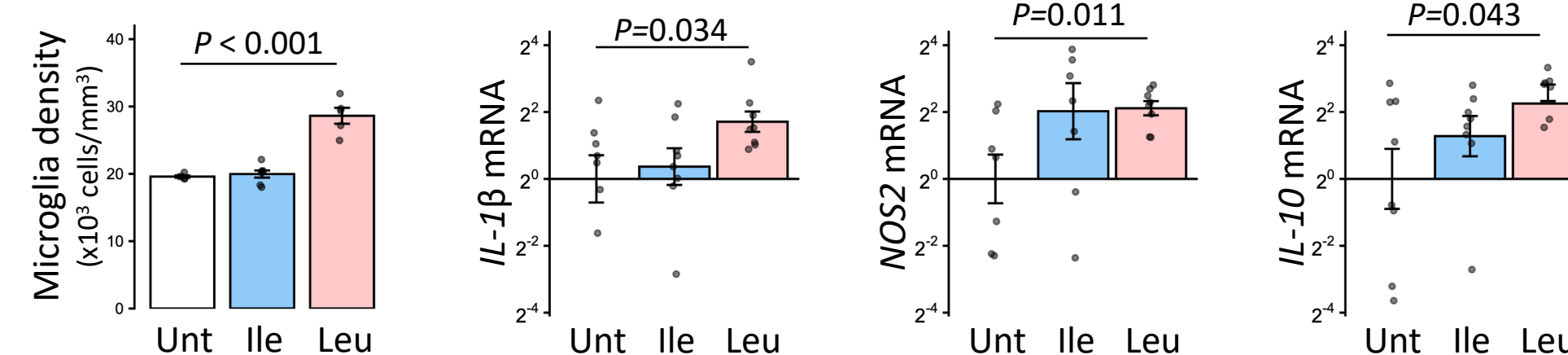
Leucine-exposed mice show signs of anxiety



Isoleucine-exposed mice struggle with split attention

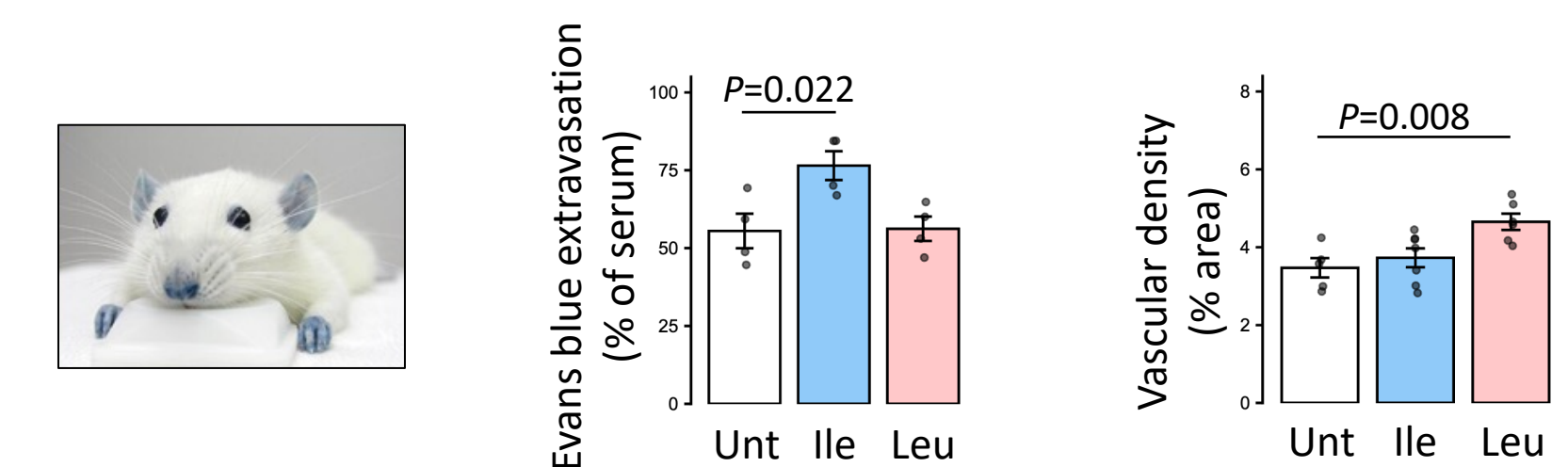


Leucine-treated mice show signs of neuroinflammation

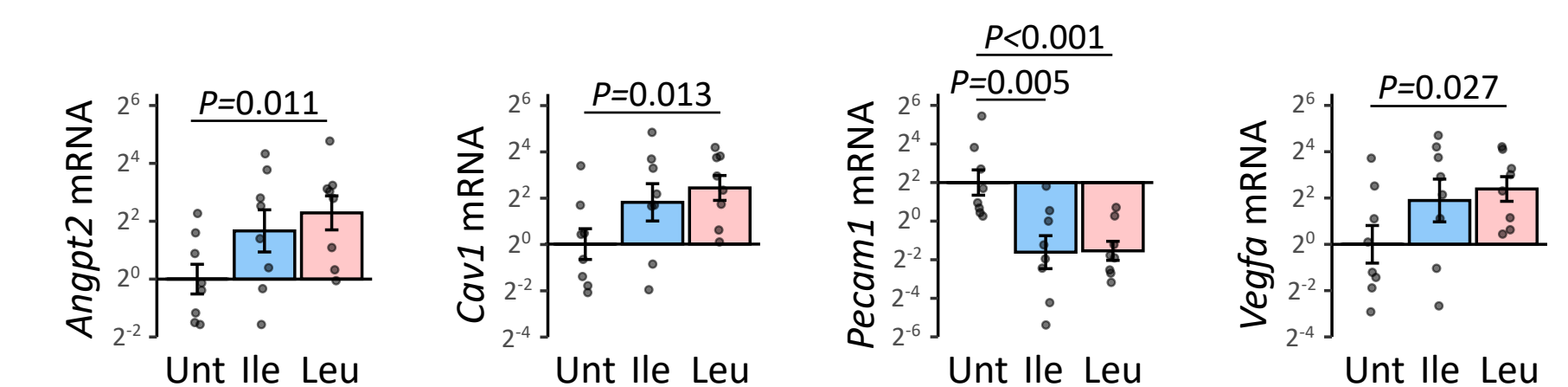


BCAA-exposed mice show cerebrovascular disruption

Isoleucine-exposed mice show blood-brain barrier leakage; leucine-exposed animals show increased cerebral vascularity



Both BCAAs induce alterations in cerebral expression of pro-angiogenic factors



Summary

Long-term exposure of mice to branched chain amino acids at levels mimicking those seen in obesity, insulin resistance and type II diabetes induce subtle cognitive changes affecting anxiety and attention.

Notably, these are reminiscent of cognitive changes seen in early-stage AD.

BCAA exposure also induces changes in neuroinflammatory and cerebrovascular parameters, again similar to those seen in human AD.

BCAA levels can be modified by diet or the gut microbiota – novel opportunities for intervention?

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