Insulin Resistance in late-middle age is associated with microstructural brain changes.
Erika Starks 1,2,3, Alex Birdsell 2,3,4, Sterling Johnson 2,3,4, Mark Sager 2,3,4,5, Barbara Bendlin 2,3,4

1 Neuroscience Training Program; 2 Department of Medicine; 3 Wisconsin Alzheimer’s Disease Research Center; 4 Madison VA Geriatric Research, Education & Clinical Center (GRECC); 5 Wisconsin Alzheimer’s Institute

BACKGROUND
- The incidence of diabetes mellitus type II (DMII) rises with age.
- Studies have shown that having DMII in midlife is associated with a higher risk of the development of dementia in later life.
- Insulin resistance (IR) is a hallmark for DMII and can occur independently of clinically diagnosed DMII.
- Molecular brain changes associated with IR suggest that IR can lead to increases in toxic material deposition, decreased glucose uptake and changes in small blood vessels in the brain parenchyma.
- Work in animal models suggests myelinated axons, which form the bulk of brain white matter, are susceptible to persistent hyperglycemia and low levels of central insulin.
- Diffusion Tensor Imaging (DTI) is a magnetic resonance imaging technique that is particularly sensitive tissue microstructure.
- Mean Diffusivity (MD), an index of isotropic water diffusion. In healthy brain tissue, MD tends to be low.

OBJECTIVES
In this study, we utilized DTI to assess the effect of IR on white matter health in a late-middle aged cohort. We hypothesized that higher IR would be associated with evidence of microstructural brain alteration, indexed as higher MD.

RESULTS
- Independent of age, higher HOMA-IR was associated with higher MD in cerebellum (p<.001).
- IR is associated with microstructural brain alterations, suggestive of early neurodegeneration.
- Interestingly, the majority of our sample did not meet criteria for frank diabetes, nevertheless, there was an association between altered neural microstructure and insulin resistance within the preclinical range of IR.
- Further investigation is needed to assess the extent to which these brain changes affects cognition.
- These findings are important as they suggest a thorough assessment of metabolic changes that may be associated with the development of dementia later in life. In addition to providing support for the development of neuroprotective agents that target mechanisms involved in diabetes.

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