Alzheimer’s disease is the most common cause of dementia in the elderly and remains a devastating disease with currently no cure or effective therapies. The exact pathogenesis of Alzheimer’s disease is still unclear, but a leading hypothesis is that the abnormal accumulation of amyloid-beta peptides leads to the neurodegeneration underlying the dementia. While deficits in cognition and memory are the major clinical manifestations of Alzheimer’s disease, accelerated early body weight loss often occurs prior to the mental decline. Furthermore, weight loss is correlated with worsening disease progression and increased risk of death in Alzheimer’s disease. Therefore, brain circuits regulating body weight and systemic metabolism may be altered early in Alzheimer’s disease and could be intrinsic to the disease process. Our laboratory is interested in identifying the central and peripheral pathways regulating body weight and systemic metabolism that are altered early in Alzheimer’s disease. We approach this topic by: 1) investigating how amyloid-beta disrupts brain circuits in the hypothalamus, a brain region that critically regulates body weight, and how this differs from normal aging-related weight loss; 2) examining how disruption of specific hypothalamic neurons by amyloid-beta and other associated factors lead to systemic metabolic deficits; 3) identifying alterations in key metabolic factors and hypothalamic signaling pathways in human studies of Alzheimer’s disease.

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