Rachel D. Hendrix
NBDS Seminar
Seminar Title:  *Dysregulation of blood glucose levels by the hypothalamic-pituitary-adrenal axis in a model of Alzheimer's disease*.

Date and Time: Tuesday, May 30th at 12:00 PM (noon)
Site:  BioMed-II Building, Rayford Auditorium, Rm. 106

**Seminar Abstract**

***Dysregulation of blood glucose levels by the hypothalamic-pituitary-adrenal axis***

***in a model of Alzheimer's disease***

Rachel D. Hendrix

Department of Neurobiology & Developmental Sciences

University of Arkansas for Medical Sciences, Little Rock, AR 72205

Evidence for peripheral metabolic perturbations in Alzheimer’s disease (AD) has accrued in recent years, including an epidemiological comorbidity of AD and Type-2 diabetes mellitus (T2DM) and/or impaired glucose tolerance. Because cognitive deficits are prevalent in T2DM, the latter has been proposed to contribute to development of AD, but diabetics fail to accumulate amyloid β-peptide (Aβ) in the brain at any higher rate than controls. Previously our lab determined that male mice of the “BRI-Aβ42” transgenic line show significant impairment in glucose tolerance. Male BRI-Aβ42 mice overexpress Aβ1-42 (the most pathogenic form of Aβ) within the CNS without overexpressing the entire amyloid precursor protein. This model provides a unique way to study hypotheses based on accumulation of Aβ1-42, independent of APP processing; it thus circumvents possible artifacts due to bioactivity of APP or its other cleavage products. Because the hypothalamic-pituitary-adrenal (HPA) axis can effectively regulate glucose homeostasis and is under CNS control, we sought to determine its contribution to Aβ effects on glucoregulation. We used adrenalectomy as a paradigm of primary adrenal insufficiency in male BRI-Aβ42 mice and wild-type littermates. Impaired glucose regulation was partially ameliorated both in basal glucose level and glycemic rise. Changes in insulin sensitivities were also observed due to adrenalectomy but not due to Aβ1-42 expression. These results indicate that chronic activation of the HPA axis is a contributing factor in the development of impaired glucose tolerance and suggest that other mechanisms of glucoregulation also contribute.