

## **Testing a Model of Cognitive Function with APOE and BDNF Genes and Heart Failure (Junior Investigator Award)**

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### **Abstract:**

The overall purpose of this study is to test a model of cognitive function with genetic factors (APOE and BDNF) and heart failure (HF) among adults with normal cognition, mild cognitive impairment (MCI), and Alzheimer disease (AD). HF is a risk factor for poor cognitive function possibly because of lowered cerebral blood flow and microemboli, and mainly affected cognitive domains are memory, executive function, and attention. Although etiologies of poor cognitive function among AD and MCI patients are different from among HF patients, these 3 conditions frequently co-occur. Possible shared mechanisms of poor cognitive function among both HF and cognitive impaired patients can be apolipoprotein E (APOE) and brain-derived neurotrophic factor (BDNF). APOE  $\epsilon$ 4 is known to increase the risk of developing cognitive impairment and cardiovascular disease such as HF. APOE  $\epsilon$ 2 is believed to protect against late-onset AD while increasing the risk of developing cardiovascular disease. BDNF Val66Met has been investigated as a possible biomarker of cognitive impairment along with APOE. Although the role of the two genetic factors (APOE and BDNF) has been characterized in AD, much less is known about the role of APOE and BDNF in HF in the context of cognitive function. In our pursuit to design targeted interventions to improve cognitive function among HF patients, we will use the data sets from the National Alzheimer's Coordinating Center and the Alzheimer Disease Genetic Consortium to investigate the following in this observational retrospective study: (1) To determine frequencies of APOE  $\epsilon$ 2 and  $\epsilon$ 4 and BDNF Val66Met alleles among groups of HF patients who have normal cognition (n=87), MCI (n=30), and AD (n=73), and among reference groups of people without HF who have normal cognition (n=5,589), MCI (n=1,418), and AD (n=3,328); (2) To evaluate the relationships between HF and cognitive function (i.e., memory, executive function, and attention) after controlling for age, education, APOE, and BDNF genotypes among all participants (N=10,525); and (3) To examine the relationships between APOE and BDNF genotypes and cognitive function among HF patients (n=190).