1. Title: Family History of Stroke and MRI Abnormalities

2. Authors: Rich (lead), Burke, Evans, Howard, Toole, Others

3. Background:

Familial clustering of stroke has long been recognized, but surprisingly little is known about the clustering in diverse populations, the occurrence of familial clustering with respect to clustering of other (known) risk factors, the frequency of clustering in the general population, or the biological significance of the observed clustering. A major risk factor for stroke is having a family history of cerebrovascular disease, suggesting that a genetic factor (or factors) could be important as either a direct risk factor on stroke susceptibility or as an indirect risk factor (mediated through other factors, such as obesity, that is itself controlled by genes). Several studies have demonstrated that familial (genetic) factors may play an important role in stroke pathogenesis. There is no (known) data relating history of stroke in family members to stroke (as defined by imaging), white matter abnormalities or atrophy in any population.

4. Hypothesis:

The cross-sectional prevalence of infarctions, white matter abnormalities, and atrophy will be larger in subjects with a family history of stroke.

5. Analytic plan:

Three primary outcome variables from the MRI data set will be used: (1) infarctions by MRI, (2) white matter abnormality score, and (3) an atrophy score. For infarctions by MRI and presence of atrophy, the dichotomous outcome will be used in the logistic regression analysis. For infarctions by MRI, dichotomies will be (a) large (greater than 3 mm) versus not large and (b) large or small versus non. For white matter abnormality and atrophy scores, the individual scores will be used in the regression analysis. Family history will be categorized into (a) parental history--father with stroke, mother with stroke, and father or mother with stroke, (b) sibling history (sibling with stroke), and (c) family history (a or b). The primary analysis will focus on the increasing prevalence of infarctions, atrophy, and increasing mean rank score for white matter disease with increasing family history of stroke. The differences in family history will be estimated after adjusting for:

- Demographic model: age, race, sex
- Risk Factor model: age, race, sex, hypertension, diabetes
- Lifestyle model: age, race, sex, hypertension, diabetes, BMI, leisure time activity, educational level, alcohol use

6. Timeline:

Immediate