Project Summary:

The overall goal of this project is to understand the cause of the significant individual variations in symptoms in Alzheimer’s disease (AD). Approximately 20% of patients with AD have disproportionate language or visuospatial impairments that correspond to significant hemispheric metabolic asymmetry visualized on positron emission tomography with 18-F-fluorodeoxyglucose (FDG-PET). The cause of this asymmetry is unknown and largely has been uninvestigated. Thus far, language predominant AD and visuospatial predominant AD, although recognized for the past 20 years, have not been associated with familial AD or any particular genetic factors. The lack of progress in understanding this problem is due to the tendency to group, rather than individualize, analyses. There also is a lack of image analysis methods that highlight or can recognize when statistically significant asymmetry is present in an individual. This project will develop methods to identify and analyze hemispheric asymmetry of metabolism and test the hypothesis that genetic factors account for these prominent individual differences.

We will identify patients who receive FDG-PET scans for clinical indications and have significant hemispheric metabolic asymmetry compared to historical normal control subjects. We will supplement this with FDG-PET scans in 30 patients with probable AD who have clinical evidence of selective cognitive deficits, but who do not qualify for reimbursement of these studies by insurance. We will develop and test an automated image analysis program to assess pixel-by-pixel asymmetry as compared to an atlas constructed from normal elderly subjects who already have been studied. Individuals with probable AD who demonstrate significant hemispheric metabolic asymmetry in their FDG-PET scan will undergo a second PET scan with the tracer 11C-PiB to assess asymmetry of amyloid deposition. We will collect blood samples from all individuals undergoing PET to obtain and store DNA for later genetic linkage analysis.

Potential Benefits:

When validated, this study will make possible a whole new way of evaluating individual variability of disease expression that can be the basis of further investigations into the mechanisms of developing symptoms of AD and related disorders. Insight into the causes of this variation would provide new insights about the cause of AD that could be used to develop new treatments.