NACC Project #2000-06  
Consortium on Alzheimer's Genetics

Principal investigator  
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Collaborating centers  
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Project description  
The Consortium on Alzheimer's Genetics (CAG) is a collaborative research project involving investigators at seven Alzheimer's Disease Research Centers. The project proposes to identify genetic polymorphisms and mutations that increase the risk of developing late-onset AD. Initial efforts to understand the role of genetics in AD focused on large multi-generational familial AD pedigrees, and led to the discovery of mutations in the APP, PS1, and PS2 genes that cause early onset familial AD. Late-onset AD is considerably more genetically complex than early-onset AD. APOE-4 is the only established genetic risk factor for late-onset AD, but there are ample data indicating that additional genes are involved. Although more than 30 genetic polymorphisms have been reported to be associated with late-onset AD during the last five years, it has been difficult to confirm these reports. Many will prove to be false positive associations due either to type I error (especially a concern given the large number of generally small studies) or bias due to population admixture. In contrast to prior approaches, the CAG focuses on discordant sibships using family-based association methods, which are not subject to bias due to population admixture. In addition, the likelihood of type I error will be decreased by using a positional candidate approach, selecting genes for testing based on their location in linkage peaks identified in ongoing linkage screens and on their plausible role in AD neuropathogenesis. This project builds upon the consortium’s preliminary work in developing methods for data collection and ongoing accomplishments in ascertaining nearly 150 sib-pairs. The additional 350 sib-pairs planned for enrollment in this project will attain the 500 discordant sib-pairs needed to detect the genes of modest effect likely to play a role in late-onset AD.

Contact information  
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Rev. 02/07/2005