UNIVERSITY of WASHINGTON
PSYCHIATRY & BEHAVIORAL SCIENCES
School of Medicine

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[Faculty Profile]

Summary of Research Program:

My research investigates the genetics of schizophrenia and neurodegenerative disorders (e.g., Alzheimer's disease [AD] and Lewy body diseases [LBDs]), primarily under the hypothesis that complex diseases like schizophrenia and late-onset AD (LOAD) are common diseases caused by a combination of rare and common variants. In schizophrenia, we perform standardized neurocognitive, neurophysiological, and clinical test batteries for the measurement of endophenotypes; we then perform genetic linkage and association analyses between these endophenotypes, such as antisaccade performance, and candidate genes or genetic variants. We found that these studies will yield different genetic variants than using the diagnosis of schizophrenia alone.

As part of my VA Merit Review project, we have use both targeted arrays to identify copy number variations (CNVs) and whole exome sequencing technology to identify genetic variants associated with schizophrenia. In these studies, we make use of family-based samples and multiplex pedigrees, using statistical methods to augment subject populations with cryptically related individuals from other studies and performing next-generation sequencing and resequencing of the whole exomes and cis-regulatory regions of these multiplex pedigrees. Once variants are identified we attempt to validate and quantify the clinical impact of these newly identified genetic risk factors, including estimates of the genotype relative risks. Our goal in this work is to discover novel therapeutic targets.

In neurodegenerative disorders, we also perform neuropathological analyses so that we can better differentiate the genetics of individuals with AD as well as those along the Lewy body spectrum. While there are a number of families with LOAD available, there is a limited number of families with multiple affected individuals with Lewy body dementia (LBD). Therefore, the genetics of LBD have been mainly case-control genetic association studies, where we have demonstrated a positive association with genes such as glucocerebrosidase and apolipoprotein E.