Project among African-Americans to Explore Risks for Schizophrenia (PAARTNERS)

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Schizophrenia (SZ) is a severe mental illness with an approximate lifetime method risk of 1% regardless of culture or ethnic group studied. The person with SZ usually experiences positive symptoms, such as hallucinations, delusions, formal thought disorder and, sometimes, catatonic symptoms; and negative symptoms such as diminished or inappropriate affect, and deficits in cognition, volition, memory and perception. Treatment is fairly effective against positive symptoms, but most medications and other treatments are ineffective against negative symptoms or even worsen them. Most people with the illness have some degree of disability: many cannot work and do not marry or raise families. Disability in SZ correlates more highly with negative than positive symptoms. SZ is clearly a biological illness with important genetic determinates. PAARTNERS is a multi-site, NIMH-funded study that seeks to identify genetic polymorphisms that confer susceptibility to SZ among African-Americans.

**OBJECTIVES**

- To identify biologically related people who can provide usable information and establish a searchable database.
- To evaluate and compare existing and promising diagnostic measures, including genetic measures in assessing SZ.
- To collect and analyze the biopsychosocial dimensions of SZ in African-Americans.
- To increase the understanding of SZ among the African-American community.
- To prepare a publicly accessible resource of data (repository) per National Institute of Mental Health (NIMH) Human Genetics Initiative guidelines.

**BACKGROUND**

SZ is a common, disabling illness that affects all cultures and ethnic groups. There is no cure for the illness. Most current medications are effective primarily against the positive symptoms with little or no effect on the negative symptoms. Indeed, most current medications may even exacerbate negative symptoms. Disability in SZ correlates more highly with the negative symptoms than with the positive. As there is no curative treatment and, since the illness involves so much disability, it is incumbent upon neuroscientists to endeavor to understand the etiology and pathogenesis of this devastating illness (1).

Both environmental and genetic factors contribute to the liability to this illness, but currently it is thought that genetic factors account for more of the liability. However, the pattern of inheritance is complex and, although some multi-generational families with a Mendelian-like pedigree exist, they are very much the exception rather than the rule. Thus, the illness is almost certainly polygenic. At the molecular level, SZ will probably turn out to be heterogeneous.

Contribution to the genetic basis of SZ in African-Americans may come both from Africa and Europe. Therefore, studies that have looked only at subjects of European origin may tell only part of the story. This and the relative dearth of multi-generational families with a Mendelian-like pedigree exist, they are very much the exception rather than the rule. Therefore, 75 healthy African-American subjects will be recruited at each site. They will be matched to the study population and will undergo all procedures that study participants do.

**RESULTS**

- As of January 2006, 95 ASPs, 403 TRIOs and 13 MPs have been completed (1). UT’s numbers are respectively 7, 10 and 1 as of April 2006 (2).
- Overall total subjects is 1507 as of January 2006 (1).
- These numbers represent 29%, 58% and 22% of the projected goal overall (1) and 14%, 18% and 14% for UT (2).
- Currently, UT has served more ASPs and MPs in process (2).

**DISCUSSION**

- To our knowledge, this is the most comprehensive project of its kind.
- It is a study focusing on a minority population under-represented in mental health research and in medical research in general.
- The majority of our recruitment is from the southeastern United States, a region under-represented in mental health research.
- We are using a model that forges ties with community health advisors and other representatives of the community to facilitate and gain the trust of African-American communities.
- We have established dialogue and partnership with the communities before beginning recruitment.
- We are about to start assessing neurocognitive controls to help interpret behavioral-dependent measures, specifically the CNP data. We had hoped to use the extensive normative data the University of Pennsylvania has already gathered but significant site differences have appeared.

**REFERENCES**


**METHODS**

**ETHICAL CONSIDERATIONS**

Because of sensitivity to possible concerns regarding studying biological factors in particular racial/ethnic groups, possible concerns about exploitation, and the stigma of mental illness, investigators at the University of Alabama at Birmingham (UAB), the central site of the study, held a number of things prior to beginning the study. They consulted with the University’s School of Medicine (Department of Research and Evaluation)’s human subjects committees for approval and they designed a website to invite dissemination of pertinent results to the community.

**SELECTION OF PARTICIPATING SITES**

- Regions with predominately African-American populations in the southeastern United States, based on data generated from the 1990 US Census, located in the South Atlantic (NC, SC, GA), Southeast (TN, AL, MS), and one selected mid-Atlantic state (PA).

**RECRUITMENT AND DIAGNOSTIC ASSESSMENT**

- Participants are:
  - University of Alabama at Birmingham (UAB)
  - University of North Carolina at Chapel Hill (UNC)
  - Medical University of South Carolina (MUSC)
  - University of Mississippi (U of M)
  - University of Kentucky (UK)
  - University of Pittsburgh (PIT)
  - University of Tennessee (UT)
  - University of Texas (UT)

**PARTICIPANT INCLUSION CRITERIA**

- SZ and SZAD probands and their families
- Probands and index family members of African-American descent
- Parent-offspring pairs. Inclusion criteria for parent-offspring pairs are use of these family types:
  - Adopted sibling pairs (ASP)
  - Probands with SZ or SZAD will be at least one sibbing diagnosed with SZ or SZA
  - Trio families (TRIO)
  - Probands and both parents. If one or both parents are unavailable, siblings may substitute. Other family members may be included
  - Multiples families (MP)
  - Probands with at least one other first-degree family member with SZ or SZA and at least eight other first to fourth-degree family members
- Probands and other affected family members must be at least 18 years of age, unaffected family members, 16 years of age or older
- Project goal: 400 ASPs, 800 TRIOs and 60 MPs
- UT’s project goal: 50 ASPs, 180 TRIOs and 30 MPs

**RECRUITMENT AND DIAGNOSTIC ASSESSMENT**

- Recruitment is done by local sites
- Faculty practices, UT residents’ clinics, VA/other hospitals, mental health centers and case management organizations, case factors, ethnically focused brochures, newspaper articles, etc.
- Diagnosis
  - Diagnoses are, for Genetic Studies (DGSS)
  - Family Interview for Genetic Studies (FIGS)
  - Medical interview
  - Having three three things, the case is summarized into four summary, which is presented to a consensus diagnosis meeting with the entire team
  - In those meeting a Best Estimate Final Diagnosis (BEFD) is reached by the team
- Neurocognitive Assessment
  - Each subject is administered a computerized neuropsychological profile (CNP)
  - Four tests is collected from each subject, 1st which goes in the NIMH repository for establishment of cell lines for further studies and 2nd which goes in the UAB repository for DNA analysis
- Linkage Analyses and Allelic Testing Mating
  - Linkage Analysis to SZ Linkage analyses using ASPs and affected sib pairs (ASP) based on multiplex linkage methods
  - Correlation-based Analysis for SZA and SZA analyses relating magnetic neurocognitive phenotype to SZA or SZA pathways
  - Quantitative Trait Linkage: Analyses of neocognitive phenotype and the SZA phenotype
- Mating: Mating is at best in order without linkage mapping will be used – two criteria must be satisfied
  1. A subset of specific genetic variations underlying liability to schizophrenia be differentiated substantively in frequency between the two contrasting populations – "2"
  2. And that these variants account for a substantial (measurable portion of) liability – "3"

**TECHNOLOGY-ESCAPED FAMILIES TRAINING (BETT)**

- Both environmental and genetic factors contribute to the liability to this illness, but currently it is thought that genetic factors account for more of the liability. However, the pattern of inheritance is complex and, although some multi-generational families with a Mendelian-like pedigree exist, they are very much the exception rather than the rule. Thus, the illness is almost certainly polygenic. At the molecular level, SZ will probably turn out to be heterogeneous.

- Contribution to the genetic basis of SZ in African-Americans may come both from Africa and Europe. Therefore, studies that have looked only at subjects of European origin may tell only part of the story. This and the relative dearth of studies in mental health research in the African-American community are the reasons for conducting the PAARTNERS study (1).