

Genetic Research in Mental Illness

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Ethics of Genetics in Research: Perils and Promises
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Genetic research in psychiatric disorders, with few exceptions, is not different from genetic research in other complex disorders. Differences are mainly in the minds of those who study other disorders.

“The analysis suggests that strong protections for the rights and welfare of subjects and their family members can be incorporated into survey and pedigree research protocols without hindering projects with extensive consent requirements.”

- Botkin, J.R., *JAMA*, 2001

“...in contemporary society, common diagnoses such as cancer, diabetes, and arthritis are in general no longer considered highly sensitive conditions. In contrast, conditions with a behavioral or psychiatric component, such as alcoholism or schizophrenia, remain stigmatizing.”

- Botkin, J.R., *JAMA*, 2001

Response

“Botkin’s separation of psychiatric from nonpsychiatric disorders is unwarranted, as modern medicine recognizes no fundamental distinction between them.”

“Many highly visible people publicly discuss their diabetes or cancer, and others discuss their mood or anxiety disorders, schizophrenia, or substance abuse. Many patients with cancer, like some with psychiatric disorders, experience job discrimination and stigma based on their diagnosis.”

“Botkin’s proposal would stigmatize psychiatric disorders by encouraging exaggerated concerns about risk without a sound empirical basis.”

“We suggest that further consideration of this issue be informed by empirical data along with the views of scientists, ethicists, patients, and family advocacy groups.”

-Levinson et al., *JAMA*, 2001

Genetic research of psychiatric disorders,
with few exceptions, is no different than
genetic research for other disorders.
Therefore, I will present some procedures
we use.

Procedures

- Diagnostic Assessment
- Family History
- Procedures for contacting relatives
- Confidentiality
- Minors
- Competence
- National Repositories

Systematic Diagnostic Assessment

- A variety of structured diagnostic assessments are available which have been validated and are used in genetic research in psychiatric disorders

Diagnostic Interview for Genetic Studies (DIGS)

INTERVIEWER: For each positive response, ask the following standard probes:

Were you convinced?

How did you explain it?

Did you change your behavior?

How often did this happen?

How long did it last?

Record an example of each positive response in the margins.

		No	Yes	Susp- ected	Unk
1.	Has there been a time when . . .				
1.a)	you heard voices? For example, some people have had the experience of hearing people's voices whispering or talking to them, even when no one was actually present.	0	1	2	9
1.b)	you had visions or saw things that were not visible to others, or had unusual physical sensations, tastes or smells?	0	1	2	9
1.c)	you had beliefs or ideas that others did not share or later found out were not true—like people being against you, people trying to harm you, or people talking about you, or believing you were being given special messages (e.g., through the TV or the radio)?	0	1	2	9

Family History

- A variety of family history methods have been developed and validated for collecting pedigree structure and family history from relatives and informants.
- Since information can be obtained from multiple informants, the information on relatives can be compiled into a Best Estimate diagnosis for relatives who cannot be directly interviewed.

Family History Screen (FHS)

2. Has anyone on the list ever had a serious mental illness, emotional problem, or nervous breakdown? 0 1 9

If no or don't know, go to Q 3

If yes ask: A. Who was that? Anyone else? (until no more names are given)

0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9
Mother	Father	Sib. #1	Sib. #2	Sib. #3	Sib. #4	Sib. #5	Child #1	Child #2	

3. Has anyone on the list ever seen a psychiatrist, psychologist, social worker, or other health professional for a psychological or emotional problem? 0 1 9

If no or don't know, go to Q 4

If yes ask: A. Who was that? Anyone else? (until no more names are given)

0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9	0 1 9
Mother	Father	Sib. #1	Sib. #2	Sib. #3	Sib. #4	Sib. #5	Child #1	Child #2	

Family Interview for Genetic Studies (FIGS)

Relationship to proband of person being described ☐ Sib ☐ Parent ☐ Other Detail: _____

DEPRESSION

Interviewer: *If bipolar disorder is likely, complete the Mania section first, and complete this checklist if mania seems unlikely.*

1a. Looking back over his/her entire life, and not counting times just after the death of a loved one, was he/she depressed most of the day, nearly every day, for two weeks or more? (By depressed we mean sad, down in the dumps, didn't care, talking about suicide, crying a lot, things like that.)

0 = NO 1 = YES 9 = UNK

IF NO go to 1b (otherwise SKIP to 1c):

1b. Or a period of being anxious, irritable or worried most of the time? Or: "falling out," or feeling nervous, tense, unable to sleep because of nerves, or slowed down for a couple of weeks?

0 = NO 1 = YES 9 = UNK

If NO to 1a AND 1b, SKIP to Interviewer Instructions below this box.

1c. What is the longest period of time he/she was ever like that? (If unsure, record description.)

1 = Pretty/very sure it was at least 2 weeks → Informant's best estimate of number of WEEKS: _____

2 = Might have been 2 weeks, not sure.

3 = Doubt it was 2 weeks, not sure.

4 = Pretty or very sure it was less than 2 weeks → Informant's best estimate of number of DAYS: _____

1d. How many periods like that has he/she had in his/her life:

1 = 1 (explore whether there were several episodes with partial remission)

2 = 2 or more. → Informant's best estimate of number of periods: _____

9 = Unsure (Record description.)

1e. How old was he/she the first time this happened? Age: _____ If UNK, was it < age 41? YES NO UNK

1f. How old was he/she the last time he/she was depressed? Age: _____ If UNK, was it ≥ age 18? YES NO UNK

Procedures for Contacting Relatives

- Permission to contact family members is obtained by probands who usually discuss with their family members first
- Before contacting a relative, staff are aware of exactly how permission was obtained and have a clear plan as to how to refer to this information.
- If contact with the subject as arranged by a family member, only that fact can be mentioned.

Confidentiality

- A **Certificate of Confidentiality** ensures that researchers cannot be forced to release any research data in which the subject is identified, even under a court order or subpoena, without the subject's written consent.
- **Locked files** – All records are kept in locked files accessible only to the research staff and institutional personnel as part of routine audits.
- **Disguised pedigrees** – All identifying information is omitted or disguised in the publication of research results.

Confidentiality continued

- **Electronic Files** – Electronic information is stored on computer operating systems that have researcher-restricted password access.
- **Blood Samples** are labeled with coded IDs only and are stored in a locked laboratory
- All staff and faculty involved in the research undergo **training in HIPAA, Good Clinical Practices and Human Subjects.**

Minors

- Minors can "assent" not "consent" for their own involvement in research. NYSPI requires written assent from minors older than seven.
- A parent/guardian must also sign a consent form agreeing to allow their child/adolescent to assent to participate in the research.

Competence

- For projects involving individuals with diagnoses such as schizophrenia or autism spectrum an **Independent Clinical Monitor**, having no affiliation with or vested interest in the project, assesses the subject's capacity for consent before they are enrolled.
- When a non-objecting patient has been found to lack sufficient capacity to consent, he/she are so informed. Consent to his/her participation in research may be provided by a surrogate. The **assent of the patient** is also required to the extent that the patient is capable of providing assent.

National Repositories

- The subject's clinical data and DNA collected will be maintained as a national resource by the National Institute of Mental Health (NIMH) to qualified research scientists around the world who are studying patterns of medical and mental illness in families and finding the genes that make people more likely to suffer from the mental disorders under investigation in the current study. Only an ID number is attached to the DNA and clinical data at NIMH; there is no personal information attached.
- In addition, the subject may give separate consent to allow their DNA to be used for the study of problems other than those under investigation in the current study.

Consent Form

If you agree to allow the National Institute of Mental Health to share your DNA with researchers who study other problems or disorders, check this box: ☐

If you do not agree to allow the National Institute of Mental Health to share your DNA with researchers who study other problems or disorders, check this box: ☐

I agree to participate in this study.

Signature: _____ Date: _____

Printed Name: _____

Standardized procedures for conducting research in the genetics of psychiatric disorders have been developed and are successfully being used.