Reviewer's report

Title: Family-based clusters of cognitive test performance in familial schizophrenia

Version: 2 Date: 15 April 2004

Reviewer: I.I. Gottesman

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Given the focus on methodological innovations using sophisticated clustering techniques and multidimensional scaling, a more appropriate journal with a more appreciative audience may be Psychometrika or Biometrika.

2. Absent a normal control group, there seems to be no way to talk about the specificity of your findings for schizophrenia. That is, your results may be true of normal families with respect to these same neuropsychological variables. A discussion of this point could show the importance of your findings for all families. Discuss the implications of NOT having a normal control group.

3. Among the suggested criteria for an endophenotype (Gottesman & Gould, 2003) are their demonstrable heritability via twin and family studies and the power to distinguish between schizophrenics and normals. Heinrichs (2001, Oxford U. Press) in his book "In Search of Madness--Schizophrenia and Neuroscience" provides important meta-analyses of relevant variables showing that most have low power (small effect sizes) to distinguish between patients and controls. Please discuss your selected variables in this light.

4. Please comment on your inclusion of the cases with a diagnosis of schizophreniform disorder. They are likely to add noise to the data, although given your cases being familial may be an exception. Is the diagnosis given after 6 months of follow without any change of diagnosis being considered?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. OPCRIT is the usual designation for what you call OCCPI.

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Discretionary Revisions (which the author can choose to ignore)

1. Your text gives the impression that the term and use of endophenotype is a recent development. It traces back to 1972 when it was introduced into psychopathology by Gottesman & Shields in their book "Schizophrenia and Genetics". Further, the term is not restricted to psychological test data, but can be used with imaging and biochemistry etc.

2. Your findings are supported by a number of other investigators should you choose to add them: e.g., Braff, Greene, Erlenmeyer-Kimling, Leonard & Freedman, etc.

3. You may wish to point out that a very large proportion of cases of schizophrenia DO NOT have a positive family history, some 81% do not have an affected parent or sibling.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the
major compulsory revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes

**Declaration of competing interests:**

NONE