Evaluating Genetic Counseling for Individuals With Schizophrenia in the Molecular Age

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Background: Recent advances in schizophrenia genetics are shedding new light on etiopathogenesis, but issues germane to translation of findings into clinical practice are relatively understudied. We assessed the need for, and efficacy of, a contemporary genetic counseling protocol for individuals with schizophrenia. Methods: After characterizing rare copy number variation in a cohort of adults with schizophrenia, we recruited subjects from the majority of individuals who had no clinically relevant structural genetic variant. We used a pre-post study design with longitudinal follow-up to assess both the profile of need and the impact of general genetic counseling on key knowledge-based and psychological factors. Results: Thirty-nine (60.0%) of 65 patients approached actively expressed an interest in the study. At baseline, participants (n = 25) tended to overestimate the risk of familial recurrence of schizophrenia, express considerable concern related to this perceived risk, endorse myths about schizophrenia etiology, and blame themselves for their illness. Postcounseling, there was a significant improvement in understanding of the empiric recurrence risk (P = .0090), accompanied by a decrease in associated concern (P = .0020). There were also significant gains in subjective (P = .0007) and objective (P = .0103) knowledge, and reductions in internalized stigma (P = .0111) and self-blame (P = .0401). Satisfaction with genetic counseling, including endorsement of the need for such counseling (86.4%), was high. Conclusions: These results provide initial evidence of need for, and efficacy of, genetic counseling for individuals with schizophrenia. The findings may help facilitate development of a contemporary genetic counseling process that could optimize outcomes in the nascent field of evidence-based psychiatric genetic counseling.

Key words: schizophrenia/genetics/genetic counseling/genetic predisposition to disease/copy number variation/stigma

Introduction

Schizophrenia is a complex neuropsychiatric disease with evidence for genetic heterogeneity and neurodevelopmental origins.¹ Genetic variants of clinical interest are currently limited to chromosome 22q11.2 microdeletions and select other individually rare copy number variants (CNVs) that underlie emerging genetic subtypes of the illness.¹² For the vast majority of patients (>90%–95%),² no major causal factor can yet be identified and genetic counseling (Box 1) would be informed primarily by nonspecific genetic epidemiology and basic empiric recurrence risk estimates.¹³⁻⁶ Nonetheless, up to 72% of individuals with schizophrenia express a hypothetical interest in such general genetic counseling.⁷⁻⁹ and a longstanding theoretical interest exists in the literature.¹¹ The obvious next questions relate to the uptake and outcomes of counseling actually provided to patients with schizophrenia.

A recent systematic review exposed the surprising paucity of empirical research,¹² including a lack of outcome studies of genetic counseling for patients with schizophrenia. This is in stark contrast to other common complex
Box 1. What is genetic counseling?

“Genetic counseling is the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. This process integrates the following:

- Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence.
- Education about inheritance, testing, management, prevention, resources, and research.
- Counseling to promote informed choices and adaptation to the risk or condition.”


diseases like cancer, albeit where there are fewer features that may interfere with provision of standard genetic counseling (table 1). Data that are available show low referral rates and access to counseling. There is evidence of self-reported deficiencies in knowledge regarding schizophrenia etiology and risk factors among clinicians, and of widespread stigma and misconceptions, even among genetic counselors (table 1). In addition, there is speculation that attribution of schizophrenia to genetic factors could actually increase stigma and even decrease confidence in the extent to which pharmacotherapy will be helpful (“therapeutic nihilism”).

In the current study, we aimed to test for the first time the effectiveness of a standardized protocol for genetic counseling for patients with schizophrenia, as delivered by a nongenetics professional in a community setting. We strove to make this genetic counseling as close as possible to that which a genetics professional would provide in the same circumstances. We were able to exclude the majority of patients with clinically relevant genetic diagnoses, for whom this basic research-based counseling would have been inappropriate. Among patients who expressed interest in counseling, we anticipated a profile of need (distorted recurrence risk perception, associated concern, and deficiencies in knowledge) similar to that observed in family members. Based on results for relatives and research for other complex diseases, we further hypothesized that this brief genetic counseling session would result in (1) an improved understanding of the empiric recurrence risk, (2) less recurrence-related concern, (3) measureable gains in knowledge of schizophrenia etiology and risk factors, (4) decreased stigma and self-blame, and (5) high satisfaction.

Methods

Participants

Potential study participants were adults (age ≥18 years) with DSM-IV diagnoses of schizophrenia or schizoaffective disorder (collectively termed “schizophrenia”). Originally recruited through a single community outpatient clinic as part of a genetic case-control study. The process of (1) ascertainment; (2) confirmation of diagnosis; (3) acquisition of detailed medical and family histories, including review of lifetime medical records and interview of family members for collateral information where possible; (4) clinical screening; and (5) molecular characterization of rare CNVs using the Affymetrix® Genome-Wide Human SNP Array 6.0 for this case-control study is described elsewhere. As recommended, patients with karyotypic abnormalities, 22q11.2 deletions, or other clinically confirmed pathogenic CNVs likely to be associated with schizophrenia were counseled on a clinical basis by a medical genetics professional. We then approached a randomly selected subset of the remaining unrelated psychiatrically stable adult outpatients about participating in this study of genetic counseling (figure S1). The study was approved by local research ethics boards. After complete description of the study, written informed consent was obtained. No patients who expressed an interest in the study were subsequently unable to provide informed consent, or deemed too ill to receive genetic counseling on the basis of their current state of functioning.

Counseling

We developed and standardized a genetic counseling protocol for adults with schizophrenia. This was based on tested protocols for other complex diseases (Espen et al. and unpublished), the existing literature for schizophrenia, and input from medical genetics and mental health care professionals, patients, and family members. A workflow algorithm for use in clinical practice is presented elsewhere. The core educational content was drawn from previously published comprehensive reviews of the existing schizophrenia literature and is described elsewhere. The first four patients to consent were involved in the pilot testing of the counseling intervention and outcomes measures—a period also used for training the counselor (figure S1). Changes were subsequently made to improve clarity and decrease response burden. The responses of these four patients are not included in this report but were noted to be consistent with the overall results.

As part of the research protocol, all tenets of genetic counseling (Box 1) were observed. In particular, as in our previous study, we provided individualized recurrence risk estimates based on family history and the best available empiric risk data and personalized each discussion surrounding medical and family history factors that may qualitatively affect recurrence risk. All counseling (mean 46.4 [SD 11.1] minutes, not including the family history assessment that had been recently performed by a nongenetics professional) was delivered on an individual basis by a graduate student (G.C.), with oversight and supervision provided by experienced...
Each patient participated in a single genetic counseling session. Sessions were audio recorded and transcribed, where possible (n = 19 [67.9%] of 28), to (1) ensure adherence to the protocol and (2) allow for a thematic analysis of the thoughts, feelings, and questions of participants and the process of counseling. Detailed field notes were kept for nonrecorded sessions. Qualitative data were supportive of the quantitative findings and will be published separately.

Measures

Each participant completed a battery of self-administered psychological and knowledge-based questionnaires at three time points, as described below. Baseline (T0) measures were completed in person, and follow-up measures at one (T1) and seven (T2) weeks postcounseling were returned using stamped, preaddressed envelopes. To the extent possible, given literacy and attention issues in this study population, the measures used were directly comparable to those employed in our recent study of schizophrenia genetic counseling for family members. Two participants received counseling but were unable to complete paper-based measures and so only qualitative data were collected (figure S1). Another participant failed to complete either set of follow-up measures, and so his baseline quantitative responses were excluded (figure S1). Thus we present quantitative data from 25 unrelated adults with schizophrenia, all of whom completed at least one set of follow-up measures.

Recurrence Risk Perception and Associated Concern. We used standard methods in genetic counseling outcome research to assess risk perception. A visual analog scale (0%–100%) and a five-point (“Very low” to “Very high”) Likert-scale item were used to assess, respectively, perceived quantitative and qualitative lifetime morbid risk for schizophrenia to a specific family member. For each participant, we defined a quantitative risk estimate ≥10% different from the best individualized risk assessment for their specified family member as inaccurate. Concern about perceived genetic risk and familial recurrence was queried using a visual analog scale (0% = “Not at all concerned” to 100% = “Extremely concerned”).

Knowledge and Etiological Attribution. Perceived (subjective) knowledge of schizophrenia etiology was assessed using a visual analog scale (0% = “Don’t understand at all” to 100% = “Understand very clearly”). Participants also completed a questionnaire developed for the study comprising 14 true or false items (table S1). Etiological
Caution was also taken to avoid biasing away from change (all necessary for a cumulative score, were replaced with baseline responses to bias away from change (all rates of missing data were <2%). Where appropriate, we compared patient responses at T0 with family member responses from our previous study using standard tests. All analyses were done using SAS version 9.2 (SAS Institute, Inc., Cary, NC), with statistical significance defined as *P* < .05.

### Analyses

We tested for within-participant differences in responses provided at T0 and T1, and to assess retention of any change at T2. Visual inspection and the Cramér-von Mises criterion were used to test the normality of each difference distribution, with subsequent use of the paired Student’s *t* test (*t* ) or the nonparametric paired Wilcoxon signed-rank test (S) as appropriate. Coefficients of determination (*R*²) were calculated from single-variable linear regression models. Missing values in follow-up measures, where necessary for a cumulative score, were replaced with baseline responses to bias away from change (all rates of missing data were <2%). Where appropriate, we compared patient responses at T0 with family member responses from our previous study using standard tests. All analyses were done using SAS version 9.2 (SAS Institute, Inc., Cary, NC), with statistical significance defined as *P* < .05.

### Results

Thirty-nine (60.0%) of 65 patients approached actively expressed an interest in the study (figure S1), with no significant differences between those who did and did not express an interest (table S3). Basic demographic and clinical characteristics of final study participants (table 2) were representative of the patient population in this region and measures of illness severity and premorbid and current functioning (table 2 and data not shown) suggest this study cohort is comparable to other general schizophrenia populations. No participant had previously received genetic counseling.

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### Table 2. Demographic and Clinical Features of Unrelated Adults With Schizophrenia Participating in a Study of Genetic Counseling

<table>
<thead>
<tr>
<th></th>
<th>Participants With Schizophrenia (n = 25a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age at time of counseling (years)</td>
<td>46.8 (12.6)</td>
</tr>
<tr>
<td>Age at onset of psychosis (years)</td>
<td>22.6 (4.7)</td>
</tr>
<tr>
<td>NART-estimated full scale premorbid IQ</td>
<td>102.8 (9.6)</td>
</tr>
<tr>
<td>Number of liveborn offspring</td>
<td>1.0 (1.4)</td>
</tr>
<tr>
<td>Female sex</td>
<td>10 (40.0)</td>
</tr>
<tr>
<td>European ancestry</td>
<td>24 (96.0)</td>
</tr>
<tr>
<td>Family history of psychosis</td>
<td>7 (28.0)</td>
</tr>
<tr>
<td>Ever married</td>
<td>11 (44.0)</td>
</tr>
<tr>
<td>Childless</td>
<td>14 (56.0)</td>
</tr>
<tr>
<td>Education</td>
<td>Did not complete high school</td>
</tr>
<tr>
<td></td>
<td>Completed high school (only)</td>
</tr>
<tr>
<td></td>
<td>Completed some postsecondary education</td>
</tr>
<tr>
<td>Primary source of concern about recurrence</td>
<td>Niece/nephew</td>
</tr>
<tr>
<td></td>
<td>Offspring</td>
</tr>
<tr>
<td></td>
<td>Grandchild</td>
</tr>
<tr>
<td></td>
<td>Sibling</td>
</tr>
<tr>
<td></td>
<td>No person of concern</td>
</tr>
</tbody>
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aNot including *n* = 4 involved in pilot testing, *n* = 2 unable to complete paper-based measures, and *n* = 1 who failed to complete either set of follow-up measures (see text and figure S1 for details).

bDefined as age at first treatment for psychosis; none with childhood onset schizophrenia.

cNational Adult Reading Test.

dDefined as having a first degree relative with a psychotic illness.

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### Recurrence Risk Perception and Associated Concern

Participants initially reported high levels of concern about familial recurrence, usually in relation to a niece/nephew (unmodified mean empiric recurrence risk estimate ~3%) or offspring (unmodified mean empiric recurrence risk estimate ~13%) (table 2). Fifteen (62.5%) of 24 participants gave inaccurate estimates of the recurrence risk (all overestimates). Concern and quantitative estimates of recurrence risk were well-correlated (*F[1,22] = 18.5, P = .0003; adjusted *R*² = 0.43) (figure 1a). We also observed a correlation between quantitative and qualitative estimates of risk (*F[1,22] = 18.1, P = .0003; adjusted *R*² = 0.43) (figure 1b). Responses regarding risk and concern, and their correlations, were strikingly similar to those of family members of individuals with schizophrenia (table S4; figure 2).
One week postcounseling (T1), the mean recurrence risk estimate had decreased by two-fifths (figure 2a), with a concomitant decrease in mean recurrence-related concern of almost half (figure 2b) and in the number of subjects with inaccurate overestimates of the risk \((n = 8)\). Risk was also qualitatively described as lower at T1 than at T0 \((S = 50, df = 21, P = .0072)\). However, at T2 the mean level of concern and the mean qualitative risk description were no longer significantly different from T0 (figure 2b; table S4).

**Knowledge and Etiological Attribution**

Although a common etiological attribution of schizophrenia was “genetics,” participants endorsed diverse factors including perceived abuse in childhood (figure 1c). Significant and lasting improvements were observed postcounseling in mean perceived knowledge (figure 2c) and in mean knowledge quiz score \((T1: t = 2.8, df = 21, P = .0103; T2: t = 3.7, df = 20, P = .0013)\) (table S4).

Responses by item are displayed in table S1. A majority of respondents \((T1: 90.9\%)\) also agreed with a statement, suggesting that their improved understanding of schizophrenia etiology might improve their compliance with pharmacotherapy.

**Psychological Functioning**

At baseline, perceived personal contribution to the schizophrenic illness and self-blame were well-correlated \((F[1,23] = 16.7, P = .0005; \text{adjusted } R^2 = 0.40)\) (figure 1d). As expected, visual analog and Likert scale measures of self-blame were also correlated \((F[1,23] = 10.9, P = .0031; \text{adjusted } R^2 = 0.29)\). Compared with relatives, levels of guilt and self-blame were significantly greater on average (table S4). Many participants reported having blamed themselves or others even more in the past than they did at the time of counseling. At T1, measures of self-blame (table S4) and the mean total ISMI score \((t = 2.8, df = 21, P = .0111; \text{table S5})\) were significantly lower. However,
differences were no longer significant at T2 relative to T0 (tables S4, S5).

Satisfaction
Satisfaction with genetic counseling was high, with most participants endorsing that they “felt better” after the counseling (86.4%), that the counseling was valuable to them (90.9%), and that genetic counseling should be offered to all adults with schizophrenia (86.4%) (table S2). Levels of satisfaction were similar to those observed in our previous study of family members. The sole individual who consistently expressed dissatisfaction stated, “I don’t think the origin of my Illness lies in Genomes. I believe every person is born with their own series of Genes and what is made of them makes them their own person [sic].” He believed his illness to have been caused by, “…poor diet as a child, [and] very little interaction with other children,” and had not wanted to consider other possibilities.

Fig. 2. Selected significant benefits of genetic counseling for individuals with schizophrenia. (a) Participants’ estimated risk of familial recurrence of schizophrenia to a specific family member (dashed line indicates mean of personalized recurrence risk assessments quoted to participants). (b) Participants’ concern related to familial recurrence. (c) Participants’ perceived knowledge about the illness. (d) Participants’ level of self-blame. In (d), the nonsignificantly greater mean at 7 weeks postcounseling was driven primarily by a single respondent whose results returned to his baseline subsequently. See Methods section for item details. *P < .05, **P < .005, and ns = nonsignificant. All summary data and P values are presented in table S4. Error bars represent upper 95% confidence intervals.
Targeted Follow-Up

Upon noting the transient nature of some immediate benefits, we added a post-hoc experiment to investigate the potential effects of repetition of counseling. Twelve of the first 17 participants approached were available for a second iteration of genetic counseling 16 weeks after their first counseling session. The study protocol was repeated with the counselor unchanged and follow-up assessments again at 1 and 7 weeks postcounseling, but with relatively less emphasis in the genetic counseling session placed on knowledge provision and more on understanding feelings of self-blame. Ten of 12 counseling sessions were audio recorded and transcribed. In general, further lasting gains in understanding of the recurrence risk and schizophrenia etiology, and a decrease in recurrence-associated concern, were observed, and satisfaction was again high (table S6).

We made an initial attempt to assess the potential impact of a simple acquiescence bias associated with the sole item about treatment compliance by, on repeat testing, reversing its wording. We observed no change in the strength of the response, with 8 of 10 respondents at T1 and T2 who completed this section now disagreeing with the negative statement. However, as before, no lasting change in either the mean level of self-blame (T0: 15.6%, T2: 14.9%; S = 4, df = 10, P = .6406) or the mean total ISMI score (T0: 2.0, T2: 1.9; t = 0.1, df = 9, P = .9011) was observed at seven weeks postcounseling.

Discussion

To our knowledge, this is the first study of genetic counseling for individuals with schizophrenia. The counseling needs of patients, with respect to distorted recurrence risk perception, associated concern, and deficiencies in knowledge, were broadly consistent with those of family members, but patients tended to have higher levels of self-blame. These preliminary data suggest that, as hypothesized, genetic counseling may improve understanding of the recurrence risk, psychological functioning, and knowledge about the illness, with outcomes similar to but not as lasting as those observed in family members. Thus the presence of a psychotic disorder (table 1), and the absence of a clinically relevant genetic variant, do not appear to be absolute contraindications to providing helpful genetic counseling.

Evidence-Based Counseling

Taking an evidence-based approach is recognized as essential for all clinical interventions including genetic counseling. This may be particularly important in the context of a disease like schizophrenia that is fraught with misconceptions and stigma. How, therefore, is it possible that this is the first study to ever investigate the efficacy of genetic counseling for individuals with schizophrenia? We speculate that the illusion of data generated by the many reviews and commentaries on this topic may inadvertently give a false impression about the existing evidence. Others may feel that studying genetic counseling necessitates molecular genetic diagnoses or more individualized recurrence risk estimates as afforded, eg, by the Gail model for breast cancer, or would be of no value to individuals with cognitive impairments who may not reproduce (table 1). The results of this initial study may help dispel such misconceptions, and also emphasize the need for further study in this area. Our findings are in line with similar studies of the efficacy of genetic counseling in other multifactorial diseases and established practice in medical genetics. There are immediate and long-term implications for clinical practice and for private and public financial support for genetics services.

Recurrence Risk Perception and Associated Concern

Optimization of risk perception accuracy is a common challenge in clinical practice, but the results for individuals with schizophrenia were comparable to those for a group of family members. Varying descriptions of risk (eg, “low” or “high”) associated with similar numerical estimates emphasize the need to frame risks for patients in different, complementary ways. The perceived recurrence risk was an incomplete predictor of concern, however, and the significant reduction in the latter was not lasting. Pharmacological and other advances that decrease the burden of illness associated with schizophrenia may also facilitate the alleviation of concerns about familial recurrence.

Recurrence risk estimates quoted to patients participating in this study were generally modest (≤13%). We note, however, that the number of offspring born to two affected parents, where the recurrence risk approaches that of an autosomal dominant condition, may be increasing. An accurate knowledge of the recurrence risk, even if higher than initially anticipated, may benefit the patient even in the absence of specific preventative measures. In the context of reassurance about the inability to predict or control the future, it may be helpful to emphasize that early diagnosis and effective management can improve outcomes.

Knowledge and Etiological Attribution

Incomplete knowledge of the genetic origins of any complex disease is the rule, and is rarely seen as an impediment to providing helpful genetic counseling. In this study, relaying details about the current state of knowledge helped to dispel myths about schizophrenia etiology and risk factors, including the myth that there exist specific independent nongenetic factors (eg, childhood trauma, including perceived abuse) of moderate or greater effect.
Providing genetic counseling also seemed to engender an improved sense of confidence in that knowledge. Our results are consistent with those of a recent study involving parents of children with autism, where respondents valued hearing about genetic discoveries even if not directly relevant to their own family. For example, a failure to distinguish between genetic and inherited was common. Conveying recent molecular genetic evidence that confirms a long-standing hypothesis about the importance of de novo mutations may have helped to decrease self-blame and reconcile the presence of a genetic disease with an absence of a family history, the most common situation for individuals with schizophrenia. It is also important to be transparent about the limits of our knowledge. We strove to temper hype surrounding psychiatric genetics by, eg, explaining the known genetic heterogeneity of schizophrenia and the probabilistic nature of all risk variants identified.

**Stigma and Self-Blame**

The results suggest that individuals with schizophrenia may on average endorse greater self-blame regarding their illness than do their mothers and other family members. In this sense, they demonstrate an even greater need for genetic counseling than do unaffected relatives. We found no evidence that attribution of schizophrenia to genetic factors increases stigma or blame. Indeed, typical genetic counseling may even affect a lasting reduction in these features in a subset of individuals. Expanding the scope of lasting benefit could therefore be a key goal of future research. However, it may be that while for some self-blame is malleable and the result of underlying misconceptions about the illness that can be remedied with accurate information, for others self-blame may reflect delusional thinking more amenable to improved treatment of the underlying schizophrenic illness (table 1). Notably, none of the participants had molecular genetic diagnoses. Initial data regarding 22q11.2 deletions in schizophrenia, and pathogenic CNVs in autism, suggest that having a clinically relevant genetic anomaly could further alleviate guilt and self-blame and decrease stigma by raising awareness.

**Opportunities for Further Gains**

Some positive effects of genetic counseling appeared short-lived, consistent with studies of psychoeducational approaches in schizophrenia, where repetition is often needed to a degree unfamiliar to most genetic counselors and standard genetic counseling approaches (table 1). For example, our results and post-hoc additional counseling sessions suggest that additional counseling sessions, different approaches, and/or extended support may help more patients achieve a lasting reduction in self-blame or stigma. Clearly, additional studies will be needed.

**Implementation**

These results indicate that, in the absence of a clinically relevant genetic variant or other complicating factors, a trained clinician may be able to deliver a standardized genetic counseling-type intervention with measurable benefit to the patient with schizophrenia. Taking a family history is standard practice in psychiatry, as in the rest of medicine. Many psychiatrists already see genetic counseling as within their potential scope of practice, and demand is likely to increase over time. Our results provide initial evidence of patient interest, feasibility, and efficacy related to such an approach. While counseling provided by a genetic counselor with expertise in psychiatric genetics would be the ideal, this may not be realistic for general genetic counseling for such a common disease. The challenge, however, remains for physicians to triage patients appropriately for genetic counseling. In addition to concerns about the genomic literacy of psychiatrists and psychiatric residents, there may be low awareness of the roles that genetic counselors can play on a clinical team. Expanding knowledge and application of genetic counseling in psychiatry will likely require both additional genetics training for psychiatrists and increased training in psychiatric disease for medical genetics professionals. The former would help to improve the genomic literacy of psychiatrists, while the latter may help to reduce the self-reported personal discomfort in discussing psychiatric illness and limited knowledge about clinical features and treatment.

**Advantages and Limitations**

Major strengths of this study include the detailed molecular and clinical characterization of the patients, use of an evidence-based manual, and assessments at multiple time points using standard measures of genetic counseling outcomes. A particular advance of the genetic counseling protocol used was to incorporate information about 21st century molecular genetic discoveries into the content, a feature not included in preexisting descriptions of general psychiatric genetic counseling. Where possible, we used measures previously employed in our study of schizophrenia genetic counseling for family members, allowing for direct between-group comparisons. The provision of counseling by a nongenetics professional using a standardized protocol was a novel approach to addressing the problems resulting from the well-recognized dearth of medical geneticists and genetic counselors. Anecdotal evidence from our clinical practice and others supports our interpretations of the primary results. Trends related to retention of benefits that did not reach statistical significance in our study may have done so with a larger group. Nonetheless, more data are needed to both replicate these findings and examine specific contextual factors that may modulate interest and
efficacy. Improved training of the counselor may result in even better outcomes although genetic counseling provided by board-certified genetic counselors, eg, is likely not scalable to large clinical trials or current clinical practice environments.

Arguably, in this study we did not conduct a “typical” genetic counseling assessment or session. As one would expect for an initial research study of this kind, our assessment and counseling protocol was more detailed, provided more information, and had a novel focus on conveying, even to individuals where these do not directly apply, general information about recent genetic findings of actual clinical relevance. Today, indications for clinical genetic testing in schizophrenia using chromosomal microarrays include only comorbid intellectual disability or autism spectrum disorder, multiple congenital anomalies, or an increased index of suspicion for 22q11.2 deletion syndrome. These existing criteria appear insufficient to identify many of the patients harboring clinically pathogenic CNVs, and thus most clinicians will currently be unable to replicate our optimal molecular characterization protocol in their clinical practice. This should however not preclude the provision of general genetic counseling as provided in this study.

All patients in this study had broadly defined schizophrenia. Counseling of individuals with psychotic mood and other disorders may present different challenges, and require a different approach. Participants were recruited from a typical community mental health clinic; we did not recruit from university health clinics or otherwise preferentially enrol higher functioning patients. Nevertheless, participants were all psychiatrically stable outpatients who had previously agreed to participate in our genetic case-control study. While these factors may have had an impact on the participants’ receptiveness to genetic counseling, these patients would also presumably be representative of those most likely to seek out this service. Lastly, nonrandomized, uncontrolled trials come with well-known caveats but often represent essential first steps toward more sophisticated study designs. Best practices in genetic counseling for schizophrenia remain to be demonstrated empirically via, eg, randomized control trials.

Conclusions

This study of genetic counseling for individuals with schizophrenia provides initial evidence for (1) needs for counseling similar to those observed in family members; (2) feasibility, with provision of such general counseling by a nongenetics professional; and, (3) immediate benefits accrued postcounseling. The results may help to optimize the process and thus outcomes in the nascent field of evidence-based psychiatric genetic counseling. While these data support efficacy in the absence of individual genetic test results, they also have implications for communicating clinically relevant genetic findings to patients—a growing consideration in genome-wide microarray and next-generation sequencing studies of schizophrenia where such results may be discovered. Further studies of providing clinical genetics services for schizophrenia may help to reduce stigma associated with the illness and to ensure that this population benefits from genomic research to the same extent as those with other common complex diseases.

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