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A multivariate perspective on schizotypy and familial association with schizophrenia: A review

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Abstract

Although generally accepted that schizotypal personality disorder diagnosis is more prevalent among relatives of individuals with schizophrenia and may be associated with genetic liability to schizophrenia, it seems likely that this diagnosis is itself heterogeneous and thus perhaps not as useful in identifying genes that affect schizophrenia risk (i.e. endophenotypes) as it could be. In contrast, symptoms and dimensions of schizotypal personality disorder may be more etiologically homogeneous, and thus more useful in genetic studies. The current review evaluated and consolidated evidence to date regarding specific symptoms and dimensions of schizotypal personality disorder among non-psychotic relatives of schizophrenia patients. Comparisons were made with relatives of affective disorder patients and non-psychiatric controls. Findings indicate strong support for elevation of social-interpersonal schizotypal symptoms among relatives of schizophrenia patients versus other groups along with moderate specificity. Results suggest only a small elevation of cognitive-perceptual and disorganized symptoms in relatives of schizophrenia patients and results for disorganized symptoms were inconsistent across studies. Thus, evidence to date supports further investigation of genetic associations between symptoms of schizotypal personality disorder and schizophrenia, and suggests that social-interpersonal symptoms may be particularly promising in genetic analyses of schizophrenia.

Keywords

Schizotypy; Schizophrenia; Relatives; Familiality; Social; Endophenotype

There is substantial evidence that genetic liability to schizophrenia is present among non-psychotic relatives of schizophrenia patients (Gottesman & Bertelsen, 1989), and can produce observable “schizophrenia-like” traits in these relatives even in the absence of frank psychosis (e.g., Snitz, MacDonald, & Carter, 2006; Thompson, Watson, Steinhauer, Goldstein, & Pogue-Geile, 2005; Toomey, Seidman, Lyons, Faraone, & Tsuang, 1999). Identification of such traits that genetically correlate with schizophrenia is an important strategy for enhancing detection of genes that affect schizophrenia risk [i.e. endophenotypes (Gottesman & Gould, 2003; Gottesman & Shields, 1972)] and there is evidence that

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symptoms of schizotypal personality disorder may be particularly useful in this regard (Seeber & Cadenhead, 2005).

Observations of schizophrenia-like traits in the family members of schizophrenia patients (e.g., social isolation/withdrawal, suspiciousness, irritability, eccentricity) can be found among the earliest descriptions of schizophrenia (*Dementia Praecox*) by Kraepelin (1919) and Bleuler (1911) (among others), both of whom hypothesized the existence of a “latent schizophrenia” syndrome among relatives [i.e. “schizotypy” (Gottesman, 1991; Kendler, 1985; Meehl, 1962)]. Contemporary models of genetic liability to schizophrenia can be traced back to the work of Sandor Rado and Paul Meehl, who built upon the observations of Kraepelin and Bleuler to extend the idea of “latent schizophrenia”. Rado (1953) introduced the term “schizotype” (schizophrenic genotype) to describe non-psychotic individuals who displayed schizophrenic traits such as anhedonia, reduced affect, and interpersonal impairments, and thus seemed to share a common genetic liability with schizophrenia. Meehl (1962) proposed that the sub-clinical, “schizophrenia-like” characteristics observed in relatives were manifestations of the interaction between an inherited “neural integrative defect” predisposing to schizophrenia, which he termed “schizotaxia”, and the environmental experiences of that individual. According to Meehl, the typical outcome of this interaction was a specific personality organization characterized by traits previously described by Kraepelin (1919) and Bleuler (1911): interpersonal aversiveness, anhedonia, ambivalence, and cognitive slippage. After Rado (1965), Meehl referred to this syndrome as “schizotypy” and to these individuals as “schizotypes”. He theorized that although a subset of schizotaxic individuals would develop schizophrenia, schizotypy would be the more typical manifestation of inherited liability to schizophrenia.

Kety and colleagues, in the context of the Danish Adoption Study (Kety, Rosenthal, Wender, & Schulsinger, 1968), took an important early step towards clarifying the role of genetic factors in “latent schizophrenia” by demonstrating that the schizophrenia-like traits associated with this syndrome were more prevalent among reared-apart biological relatives of adoptees with schizophrenia compared to the biological relatives of controls (Kety et al., 1968; Kety et al., 1994), thus providing strong support that this syndrome was genetically associated with schizophrenia. Kety grouped these schizophrenia-like traits into five categories (interpersonal deficits, atypical speech, cognitive/perceptual distortions, affective deficiencies, and neurotic symptoms) and proposed the diagnosis “borderline schizophrenia” to describe this syndrome. The criteria for this proposed diagnosis were subsequently modified by Spitzer et al. (1979) and first incorporated into the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; American Psychiatric Association, 1980) as Schizotypal Personality Disorder (for reviews see Kendler, 1985; Siever & Gunderson, 1983).

At present, revisions of the schizotypal personality disorder diagnosis are actively being discussed for the new DSM 5 (www.dsm5.org), including a shift towards a more multidimensional model of schizotypal and other personality disorders (Lynam & Widiger, 2001; Widiger & Trull, 2007). Even so, it remains under debate whether the latent structure of schizotypy is best represented by a taxonic or dimensional model (e.g., Beauchaine, Lenzenweger, & Waller, 2008; Rawlings, Williams, Haslam, & Claridge, 2008a, 2008b). In the current review, we take a multivariate approach in our examination of schizotypy and familial association with schizophrenia, which is consistent with both multitaxonic and multidimensional hypotheses. None of studies reviewed here expressly address the issue of taxa versus dimensions. Nevertheless, multivariate research is typically couched in terms of “dimensions” and for consistency, we also use this terminology.

The current diagnostic criteria for schizotypal personality disorder encompass a range of schizotypal characteristics, including "...social and interpersonal deficits...cognitive or perceptual distortions and eccentricities of behavior..." (DSM-IV-TR; American Psychiatric Association, 2000). Data from family, twin, and adoption studies suggest that schizotypal personality disorder is heritable (estimated at .61; Torgersen et al., 2000) and the incidence of schizotypal personality disorder among non-psychotic first-degree adult relatives of schizophrenia patients is estimated to be between 4.2% and 14.6% (Pogue-Geile, 2003; Tsuang, Stone, & Faraone, 1999) compared to 2–3% among the general population (Raine, 2006) [odds ratio estimated at 5.0 (Kendler & Gardner, 1997)]. A genetic correlation between schizotypal personality disorder diagnosis and schizophrenia is further supported by recent linkage analysis and genetic modeling studies (Fanous et al., 2007; Lien et al., 2009; Picchioni et al., 2010).

Specificity to schizophrenia liability also has been examined. These results indicate that the prevalence of schizotypal personality disorder is significantly greater in non-psychotic first-degree relatives of schizophrenia patients (6.9%) than in relatives of patients with schizoaffective disorder (2.8%), affective psychosis (2.5%), or non-psychotic affective disorders (2.3%) (K.S. Kendler et al., 1993; Pogue-Geile, 2003), although there are some contradictory findings (e.g., Erlenmeyer-Kimling et al., 1995; Kety et al., 1994). Finally, schizotypal personality disorder is more strongly familially associated with schizophrenia than other Cluster A personality disorders (e.g., paranoid, schizoid) and avoidant personality disorder, despite some overlap of symptoms (K.S. Kendler et al., 1993; Parnas, Cannon, Jacobsen, Schulsinger, & Mednick, 1993).

Given the above evidence, there is clear support for a familial (and likely genetic) association between the diagnosis of schizotypal personality disorder and schizophrenia, suggesting potential utility for identifying individual genes contributing to schizophrenia risk [i.e. "endophenotype strategy" (Gottesman & Gould, 2003; Gottesman & Shields, 1972)]. However, even if schizotypal personality disorder is itself genetically associated with schizophrenia, sensitivity of the schizotypal personality disorder diagnosis to specific schizophrenia risk genes would be compromised to the extent that this diagnosis is genetically, as well as phenotypically heterogeneous. Genetic heterogeneity is problematic from the standpoint that to be useful in genetic studies, an endophenotype must be sensitive to as few schizophrenia risk genes as possible, and have limited sensitivity to non-schizophrenia risk genes and environmental effects. Alternatively, one or more individual symptoms or symptom dimensions of schizotypal personality disorder may be phenotypically and genetically more homogeneous, and perhaps more sensitive to specific genetic liabilities to schizophrenia, than is the diagnosis itself. It is therefore important to determine if specific symptoms or dimensions of schizotypal personality disorder are elevated among relatives of schizophrenia patients compared to controls and relatives of non-schizophrenia patients. Examination of the components of schizotypy through behavioral genetic methods can inform genetic studies of schizophrenia, and advance diagnostic, etiological, and treatment research (Livesley, 2005).

Over the previous two decades, several studies have taken this important step of examining the degree to which particular symptoms, or symptom dimensions, of schizotypal personality disorder are elevated among non-psychotic relatives of schizophrenia patients. Given the methodological variability among these studies, and in light of the potential utility of schizotypy in genetic analyses of schizophrenia, the upcoming revision of the DSM, and a resurgence of interest in negative symptoms and psychotic-like experiences in the general population (e.g., A. S. Cohen, Emmerson, Mann, Forbes, & Blanchard, 2010; Kelleher & Cannon, 2011), it seems important and timely to consolidate and evaluate the evidence to date regarding individual schizotypy symptoms in non-psychotic relatives of schizophrenia

patients. With this goal in mind, we reviewed studies that examined dimensions and symptoms of schizotypal personality disorder among relatives of schizophrenia patients in contrast to non-psychiatric controls and/or relatives of other psychiatric groups.

Methodological considerations

Before reviewing this set of studies, there are several key methodological issues relevant to the task of evaluating and synthesizing these data that should be discussed. One broad issue pertains to comparison group characteristics, including psychiatric status, method of ascertainment, and population representativeness. Studies vary in terms of how thoroughly potential “healthy” controls are screened for psychiatric illness, ranging from “no diagnosis” (psychiatrically healthy individuals whose relatives also are healthy), to “unscreened” (individuals and their relatives may or may not have psychiatric diagnoses). Both extremes can be problematic, as a “supernormal” control group can inflate index/control differences (Kendler, 1990), and confound the effect of relatedness to a schizophrenia proband with relatedness to any psychiatrically ill individual. Conversely, unscreened controls may inadvertently include individuals who themselves have a schizophrenia-spectrum diagnosis. In addition to judicious screening of controls, another worthwhile albeit less common strategy is to use relatives of control probands. This is a strong technique for minimizing confounds with recruitment strategy and increasing sample representativeness. In this review, we give more weight to those studies that utilized comparison groups (control probands or their relatives) that were screened only for psychosis and demographically matched to the index relatives.

Similar issues pertain to index relative samples, which typically consist of first-degree relatives (including parents, siblings, and/or offspring) of the index schizophrenia proband. Although all are first-degree relatives, these individuals can differ in several ways, including age at recruitment and risk for schizophrenia [relative risk: parents ~ 5%, siblings and offspring ~ 10% (K. S. Kendler et al., 1993)]. In addition, although many studies do exclude relatives with a history of psychosis, this is not always the case; inclusion of “unscreened” relatives could inflate index relative/control differences.

Assessment is another area of methodological import. The type of instrument used to assess schizotypal personality disorder symptoms can affect the outcome and interpretation of results. Use of different measures may influence the factor structure of schizotypal symptoms, potentially providing more information about the structure of the instrument versus that of the latent construct (Wuthrich & Bates, 2006). There also is evidence that compared to interview-based measures, questionnaires may be less sensitive to certain schizotypal traits in relatives, particularly social deficit symptoms of schizotypy (Catts, Fox, Ward, & McConaghy, 2000; Kendler, Thacker, & Walsh, 1996) and perhaps behavioral eccentricities. However, use of interview-based measures also brings methodological challenges, such as maintaining interviewer blindness and rater reliability. Consequently, measurement differences may lead to inconsistencies regarding which schizotypal traits appear most salient in relatives. Given the concerns about questionnaire measures, in our review we tend to weight results from interview-based assessments more heavily.

Finally, there is an ongoing debate regarding the phenotypic factor structure purported to underlie schizotypal traits in relatives. Proposed factor solutions range from two (Siever & Gunderson, 1983; Widiger, Frances, Warner, & Bluhm, 1986) to seven (Kendler, McGuire, Gruenberg, & Walsh, 1995) and seem to depend a large part on study methodology, including sample characteristics, use of questionnaire versus interview measures, as well as the content of these measures (Parnas, Licht, & Bovet, 2005; Wuthrich & Bates, 2006). Bergman et al. (2000) tested five models using data from interview measures of schizotypal

personality disorder conducted with adult, first-degree relatives of schizophrenia patients and concluded that the best fit was provided by the following three-factor model: 1) social-interpersonal symptoms (i.e. “negative schizotypy”), including excessive social anxiety, lack of close friends, constricted affect, and suspiciousness; 2) cognitive-perceptual symptoms (i.e. “positive schizotypy”), such as ideas of reference, magical thinking, and unusual perceptual experiences; suspiciousness also loaded on this factor; and 3) disorganized symptoms of odd speech and odd behavior. This model closely resembles the three factor symptom structure often associated with schizophrenia consisting of positive, negative, and disorganized symptoms. For the current review, data pertaining to schizotypal symptoms in relatives are presented in accordance with the three-factor model of schizotypal personality disorder supported by Bergman et al. (2000).

Review of Schizotypal Personality Disorder Symptoms in Schizophrenia Relatives

With these methodological points in mind, we now review evidence from studies that compared adult relatives of schizophrenia patients to psychiatrically healthy controls and/or adult relatives of patients with other psychiatric diagnoses on schizotypal personality disorder symptoms. Of the studies that included relatives of other psychiatric groups, all but one utilized an affective disorder as the comparison diagnosis (c.f., substance use disorders; Yaralian et al., 2000). Given the disparity in comparison diagnosis and the small sample of schizophrenia relatives ($n = 13$), we elected to not include data from Yaralian et al. (2000) on substance use disorder. Thus, among the studies reviewed below, comparison psychiatric diagnoses are limited to affective disorders. Also note that as our focus is on the familial association between the symptoms of schizotypal personality disorder and schizophrenia, we only included studies that assessed dimensions (factors) and/or individual symptoms of schizotypal personality disorder rather than just the presence or absence of diagnosis itself. As noted above, results are presented in accordance with the three-factor model of schizotypal personality disorder symptoms supported by Bergman et al. (2000): social-interpersonal, cognitive-perceptual, and disorganized. For studies that provided alternate factor solutions, we present those results with the factor (from Bergman’s three-factor solution) that best approximates the associated symptoms. Data included in the present review are presented in Tables 1 – 6.

Effect sizes are presented to aid in the comparison of results across studies. When possible, all reported indices were converted to Glass' standardized mean difference statistic ‘d’ [index relatives’ mean – control mean / control standard deviation (Smith, Glass, & Miller, 1980)]; although in some instances, it was more feasible to calculate Cohen's ‘d’ [index relatives’ mean – control mean / pooled standard deviation] (J. Cohen, 1987; Haddock, Rindskopf, & Shadish, 1998; Hasselblad & Hedges, 1995; Johnson & Eagly, 2000; Rosenthal, 1994). To the extent that the standard deviation of the index relatives is larger than that of the comparison group (which is predicted based on genetic theory), Cohen's ‘d’ will result in a more conservative estimate of effect size than Glass' ‘d’. Mean effect sizes were weighted by the conditional variance of ‘d’ (Shadish & Haddock, 1994). Cohen (1987) suggests the following guidelines for interpretation of effect size ‘d’: 0.2 = small, 0.5 = medium, 0.8 = large.

Social-interpersonal symptoms of schizotypal personality disorder

Index relatives vs. healthy controls

Factor-level comparisons—Eight studies reported comparisons between first-degree relatives of schizophrenia patients and psychiatrically healthy controls on social-

interpersonal symptoms of schizotypy; these data are presented in Table 1 (Appels, Sitskoorn, Vollema, & Kahn, 2004; Calkins, Curtis, Grove, & Iacono, 2004; Compton, Chien, & Bollini, 2009; Grove et al., 1991; Kendler et al., 1995; Kremen, Faraone, Toomey, Seidman, & Tsuang, 1998; Squires-Wheeler et al., 1997; Yaralian et al., 2000). Taken together, the overall mean effect size (d) reported by these studies is 0.67, suggesting a medium to large familial association of social-interpersonal symptoms with schizophrenia compared to no psychiatric illness.

Methodologically, the most persuasive findings are from the Roscommon Family Study (Kendler et al., 1995), also supporting a medium to large effect of social-interpersonal symptoms in first-degree relatives compared to controls (average¹ $d = 0.64$). On balance, studies utilizing interview-based measures of schizotypy reported stronger associations between social-interpersonal symptoms and schizophrenia (mean $d = 0.74$) compared to analyses based on questionnaire assessments (mean $d = 0.46$). All non-significant effects were reported by studies that used questionnaire-based assessment. These findings are consistent with previous observations suggesting low sensitivity of questionnaire-based measures to social-interpersonal schizotypy symptoms in relatives (Catts et al., 2000; Kendler et al., 1996). Overall, the results of these studies most strongly support a medium to large familial association between social-interpersonal symptoms and schizophrenia compared to no psychiatric diagnosis.

Symptom-level comparisons—Two studies (Calkins et al., 2004; Yaralian et al., 2000) also reported comparisons between first-degree relatives of schizophrenia patients and healthy controls on specific social-interpersonal symptoms and results are inconsistent (Table 1). Although some support was obtained for elevated social anxiety, no close friends, constricted affect, and suspiciousness among relatives, these results are hardly conclusive and must await further study.

Index relatives vs. affective disorder

Factor-level comparisons—Table 2 presents comparisons between first-degree relatives of schizophrenia patients and relatives of affective disorder patients on the social-interpersonal factor of schizotypal personality disorder. Factor-level comparisons were reported by three studies (Kendler et al., 1995; Schurhoff, Laguerre, Szoke, Meary, & Leboyer, 2005; Squires-Wheeler et al., 1997), and results suggest a modest effect of social-interpersonal symptoms among schizophrenia relatives ($d = 0.37$). However, results differ considerably depending on if interview- or questionnaire-based assessments were used (interview mean $d = 0.50$, questionnaire $d = 0.00$). Schurhoff et al. (2005) differed somewhat in that their comparison group consisted exclusively of relatives of bipolar disorder patients. Given the proposed genetic similarities between schizophrenia and bipolar disorder, this may have increased similarity between the schizophrenia and bipolar relative groups. On whole, the few available studies suggest that the social-interpersonal dimension is elevated in relatives of schizophrenia patients compared to affective disorder relatives, especially using interview assessments, although this may not hold true for bipolar disorder.

Symptom-level comparisons—Two studies reported symptom-level comparisons between relatives of schizophrenia patients and relatives of affective disorder patients (Lyons, Toomey, Faraone, & Tsuang, 1994; Torgersen, Onstad, Skre, Edvardsen, & Kringlen, 1993). Results from both studies suggest a small to medium effect for

¹Average effect size calculated within the same sample and not weighted by variance.

inappropriate affect (inadequate rapport)² in index relatives compared to affective disorder relatives, although additional studies are needed to confirm this finding.

Cognitive-Perceptual Symptoms

Index relatives vs. healthy controls

Factor-level comparisons—All eight studies listed in Table 1 also reported results pertaining to the cognitive-perceptual dimension of schizotypal personality disorder. As presented in Table 3, evidence from interview- (mean $d = 0.35$) and questionnaire-based (mean $d = 0.42$) measures of schizotypy both support a modest effect of cognitive-perceptual factor symptoms in relatives of schizophrenia patients compared to controls (overall mean $d = 0.37$). With respect to the individual reports, results from Kendler et al. (1995) and Calkins et al. (2004) are the most convincing given the methodological strengths of these studies, and also support a small effect of cognitive-perceptual symptoms in relatives compared to controls ($d = 0.36$ and $d = 0.24$, respectively). Finally, the significant, negative effect reported by Appels et al. (2004) suggesting less pathology among parents of schizophrenia patients compared to controls is particularly striking. Given the methodological strengths of this study, it is at this point difficult to interpret or dismiss this negative effect. Taken together, current data best support a small familial association between the cognitive-perceptual schizotypy factor and schizophrenia.

Symptom-level comparisons—Three studies reported on cognitive-perceptual symptom-level comparisons between first-degree relatives of schizophrenia patients and healthy controls and results were inconsistent. Results from Calkins et al. (2004) and Yaralian et al. (2000) suggest a small, positive effect for unusual perceptual experiences. In contrast, Appels et al. (2004) observed a significant negative association for unusual perceptual experiences and magical thinking, suggesting that relatives of schizophrenia patients endorse fewer of these symptoms than controls. As above, the available data again support a small association between cognitive-perceptual symptoms and schizophrenia.

Index relatives vs. affective disorder

Factor-level comparisons—As can be seen in Table 4, three studies reported comparisons with relatives of affective disorder patients on the cognitive-perceptual factor of schizotypal personality disorder (Kendler et al., 1995; Schurhoff et al., 2005; Squires-Wheeler et al., 1997). Results for all three studies were non-significant (mean $d = 0.04$), indicating no differences between index relatives and affective disorder relatives on this factor.

Symptom-level comparisons—Two studies reported results for individual cognitive-perceptual symptom comparisons between index relatives and relatives of affective disorder patients (Lyons et al., 1994; Torgersen et al., 1993). As with factor-level comparisons, no group differences were observed.

Disorganized Symptoms

Index relatives vs. healthy controls

Factor-level comparisons—As presented in Table 5, comparisons between index relatives and controls on the disorganized symptom factor yielded quite variable results (range: $d = 0.17$ – 0.96 ; mean $d = 0.73$) and two studies did not report a separate disorganized factor (Grove et al., 1991; Squires-Wheeler et al., 1997). For the current review, results from

²Inadequate rapport was replaced by “inappropriate affect” when the DSM-III was revised for DSM-III-R.

interview-based assessment were available from one study (Kendler et al., 1995), and suggested a large effect of disorganized symptoms among index relatives versus controls ($d = 0.96$). In this study, the disorganized factor included “cognitive slippage” and “odd speech”, but did not include “odd behavior”, perhaps contributing to the strong effect. In contrast, results from questionnaire measures indicated a small effect of disorganized symptoms (mean $d = 0.22$), perhaps due to low sensitivity to these symptoms. Overall, the strongest methods are consistent with substantial differences between first-degree relatives and controls for interview-based measures that incorporate language disorder, whereas questionnaire measures appear less sensitive. Although promising, firm conclusions regarding familiarity require additional studies preferably using interview measures of schizotypy.

Symptom-level comparisons—Two studies (Calkins et al., 2004; Yaralian et al., 2000) presented comparisons for individual disorganized symptoms and both reported non-significant findings. Although as noted, questionnaire assessments may have low sensitivity to disorganization of speech and behavior. Thus at present, the nature and importance of particular disorganized symptoms among relatives of schizophrenia patients is unclear.

Index relatives vs. affective disorder

Factor-level comparisons—Table 6 presents the results of comparisons between first-degree relatives of schizophrenia patients and relatives of affective disorder patients on the disorganized factor of schizotypal personality disorder. Comparisons yielded non-significant results, even for studies using interview measures.³ The negative effect of disorganized symptoms in relatives of schizophrenia patients versus relatives of bipolar patients is interesting ($d = -0.16$) (Schurhoff et al., 2005). Overall, results argue against specificity to schizophrenia.

Symptom-level comparisons—Two studies reported individual symptom comparisons between index relatives and relatives of affective disorder patients. Torgersen et al. (1993) found a significant, albeit modest, elevation of odd speech among index relatives ($d = 0.30$), whereas Lyons et al. (1994) reported no group differences. These results generally suggest no specificity of disorganized symptoms to schizophrenia liability.

Discussion

The goal of this review was to examine familiarity of symptoms of schizotypal personality disorder in non-psychotic, first-degree relatives of schizophrenia patients as a step toward determining genetic associations between more homogeneous dimensions of schizotypy and schizophrenia. The results can be summarized as follows:

- Social-interpersonal schizotypal symptoms showed a medium to large effect ($d = 0.67$) among relatives of schizophrenia patients compared to no psychiatric diagnosis and a small to medium effect ($d = 0.37$) compared to affective disorder, indicating strong support for familial association with schizophrenia, along with some specificity.
- Contrary to many hypotheses, cognitive-perceptual schizotypy symptoms demonstrated only small effects among first-degree relatives of schizophrenia patients compared to healthy controls ($d = 0.37$) and relatives of affective disorder patients ($d = 0.04$), suggesting limited familial association with schizophrenia and no specificity.

³Mean effect size was not calculated because only one study provided data for factor-level comparisons.

- Disorganized schizotypy symptoms demonstrated a large effect ($d = 0.96$) for interview measures that included language disorder, but only a small effect ($d = 0.22$) for questionnaire measures in relatives compared to controls. Together, results suggest some familial association with schizophrenia ($d = 0.73$). Comparisons with affective disorders yielded a small effect suggesting no specificity.

The evidence for a moderate to strong familial correlation between social-interpersonal schizotypal symptoms and schizophrenia is congruent with a large literature indicating that social deficits may be an important piece of the genetic liability puzzle (e.g., Pogue-Geile & Yokley, 2010). Among schizophrenia patients, social deficits are well documented, tend on average to be more severe and pervasive compared to other psychiatric disorders, including affective psychoses (Mueser & Bellack, 1998; Strauss & Carpenter, 1972), and often persist even if acute psychotic symptoms have diminished. In addition, prospective and retrospective evidence consistently supports worse social functioning in childhood and adolescence (prior to psychosis onset) among schizophrenia patients compared to affective disorder patients, healthy siblings, and controls (Cannon et al., 1997; Tarbox & Pogue-Geile, 2008; Willinger, Heiden, Meszaros, Formann, & Aschauer, 2001) and level of premorbid social functioning is an important (positive) correlate of individual variation in schizophrenia illness course and outcome (Bromet, Harrow, & Kasl, 1974). Finally, recent evidence from twin and family studies supports genetic correlation between child and adolescent social adjustment and schizophrenia (e.g., Picchioni et al., 2010). Given the convergent evidence from the literature and the results of the current review, there seems to be a strong argument for moving forward with studies aimed at investigating further the genetic association between social-interpersonal symptoms of schizotypy and schizophrenia. Furthermore, the apparent heterogeneity of symptoms within the social-interpersonal dimension (e.g., excessive social anxiety, lack of close friends, constricted affect, and suspiciousness) suggests the need for additional delineation of this factor in order to maximize genetic and phenotypic homogeneity of these symptoms, and their consequent utility in genetic studies.

In contrast to expectation, the data support only a small familial association between cognitive-perceptual symptoms of schizotypal personality disorder and schizophrenia with no specificity. Given that the cognitive-perceptual factor includes “positive” schizotypal features such as unusual perceptual occurrences and magical thinking, one possible explanation for such small effect sizes is that relatives may tend to underreport experiences more overtly associated with schizophrenia pathology. In several of the reviewed studies, suspiciousness/paranoid ideation correlated with both the social-interpersonal and cognitive-perceptual schizotypy factors, consistent with defensiveness among family members when asked about “schizophrenia-like” symptoms. In addition, while only provided by one study (Appels et al., 2004), evidence of lower pathology among parents of schizophrenia patients compared to controls is also notable. Theory regarding reproductive fitness effects would tend to predict especially elevated schizotypy among index parents (Kendler, 1986), but this did not seem to be the case here. Finally, these findings of minimal familial correlations may reflect developmental effects, in which psychotic-like experiences in adolescence may in fact predict eventual schizophrenia but not be familially correlated with schizophrenia in adulthood. Of course, it may also be that cognitive-perceptual schizotypy scales are less psychometrically sensitive than social-interpersonal scales, thus reducing their familial association with schizophrenia (Chapman & Chapman, 1973).

A few studies have reported similar observations of minimal or negative associations utilizing the Chapman Perceptual Aberration Scale (Chapman, Chapman, & Raulin, 1978), which tends to correlate strongly with cognitive-perceptual symptoms of schizotypal

personality disorder in relatives (Clementz, Sweeney, Hirt, & Haas, 1991). For example, Docherty and Sponheim (2008) and Glatt, Stone, Faraone, Seidman, and Tsuang (2006) reported no differences between first-degree relatives and controls on the Perceptual Aberration Scale and the Magical Ideation Scale (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994), despite relatives scoring higher (greater pathology) than controls on the Social and Physical Anhedonia scales (Chapman, Chapman, & Raulin, 1976). Further, Clementz, Grove, Katsanis, and Iacono (1991) and Katsanis, Iacono and Beiser (1990) both reported that first-degree relatives scored lower (less pathological) than controls on the Perceptual Aberration Scale, despite reporting more social and physical anhedonia than controls.

Lastly, current evidence is quite mixed for disorganized schizotypal symptoms in schizophrenia relatives compared to controls and relatives of affective disorder patients. The interview-based study that included cognitive slippage and odd speech found large effect sizes (Kendler et al., 1995), whereas the questionnaire measures were much less sensitive. Presence of language abnormalities in relatives would not be surprising given that language deficits and thought disorder are frequently reported in non-psychotic relatives of schizophrenia patients (e.g., N. M. Docherty & Gottesman, 2000; Hirsch & Leff, 1975; Hoff et al., 2005; Kinney et al., 1997), and would be consistent with observations of greater communication deficits in schizotypal individuals who are related to a schizophrenia patient compared to those without a schizophrenia relative (Torgersen et al., 2002). These results also are interesting given evidence that language disorder in childhood may predict greater risk of schizophrenia (Cannon et al., 2002; Jones, Rodgers, Murray, & Marmot, 1994).

The considerable range of reported effects for the disorganized factor is congruent with previous observations that the disorganized schizotypy factor appears less “stable” than the social-interpersonal and cognitive-perceptual factors (Bergman et al., 2000). The small number of studies and inconsistent symptom composition of the disorganized factor across studies further limits conclusions. Given the promise and variation in these results, improving the characterization and delineation of schizotypal symptoms such as disorganized speech, thought, and behavior would seem to be a high priority.

Limitations and future directions

Although there are similarities among symptoms within a single dimension of schizotypal personality disorder, each symptom represents a relatively unique deficit or behavior. To date, most studies do not report symptom-level comparisons even when factor comparisons are significant. Moving forward, examination of individual symptoms of schizotypal personality disorder, particularly within the social-interpersonal dimension, would help clarify if specific symptoms account for group differences, or if the contribution of multiple deficits within a dimension is most important. Improving phenotypic homogeneity within and across dimensions could enhance sensitivity to latent genetic and environmental components of schizophrenia, and also may advance diagnostic and etiological conceptualization of schizotypal personality disorder itself (Livesley, 2005).

Research on familial association between schizotypy and schizophrenia could benefit from further investigation of diagnostic specificity of components of schizotypal personality disorder. Only a small number of studies included relatives from other diagnostic groups, and comparison diagnoses were primarily limited to affective disorders. Such a narrow selection of diagnostic comparison groups makes it difficult to discern the extent of any specificity to schizophrenia liability. Furthermore, the nuclear family design of these studies precludes partitioning variance due to genes and variance due to shared environment. Twin and adoption studies are the only way to differentiate genetic and shared environmental effects (e.g., Picchioni et al., 2010).

Finally, the differential results across symptom dimensions support a multivariate model of schizotypal personality disorder [versus unidimensional or single taxon models (e.g., Beauchaine et al., 2008)], and are consistent with a multidimensional conceptualization of personality disorders more broadly (Lynam & Widiger, 2001; Widiger & Trull, 2007). However, these data pertain to schizotypal symptoms in relatives of schizophrenia patients, and do not necessarily reflect the latent structure of schizotypy in the general population (Beauchaine et al., 2008; Rawlings et al., 2008b). Such a distinction would be consistent with observed differences in schizotypal symptom presentation between relatives of schizophrenia patients and general population cases (for reviews, see Kendler, 1985; Tsuang, Stone, Tarbox, & Faraone, 2002), and evidence that the etiology of this diagnosis in non-relatives is likely to be heterogeneous and perhaps not necessarily associated with liability to schizophrenia (MacDonald, Pogue-Geile, Debski, & Manuck, 2001).

Conclusion

This review evaluated evidence regarding the familial association of symptoms of schizotypal personality disorder and schizophrenia compared with affective disorders and no psychiatric illness. The literature to date supports a significant familial association between social-interpersonal schizotypal symptoms and schizophrenia compared to other groups. Counter to prediction, evidence supports only a small familial association of cognitive-perceptual symptoms with schizophrenia; although possible under-reporting of cognitive-perceptual symptoms may play a role. The results for disorganization symptoms are mixed, with interview measures that incorporate language disorder appearing very promising in contrast to questionnaire measures. Taken together, the results of this review support the importance of multivariate partitioning of schizotypy and moving forward with further investigations of genetic associations between symptoms of schizotypal personality disorder and schizophrenia. They further suggest that social-interpersonal symptoms may be particularly promising as one means toward improving our understanding of the genetic puzzle of schizophrenia.

Highlights

- Reviewed symptoms of schizotypal personality in relatives of schizophrenia patients.
- Comparisons were made with relatives of affective disorder patients and controls.
- Interpersonal symptoms were sensitive and specific to schizophrenia familial liability.
- Cognitive-perceptual and disorganized symptoms had limited sensitivity and specificity.
- Social-interpersonal symptoms may be useful in genetic analyses of schizophrenia.

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Table 1
Social-Interpersonal Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Non-Psychiatric Controls

Study	Relatives of Schizophrenia Probands				Schizotypy Assessment		Comparison with Psychiatrically Healthy Controls ^b		
	Relationship to Proband (n)	Sex % male	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	screening criteria (n)	match to schiz rels	effect size
Grove et. al, 1991	parents, sibs, half-sibs (61)	46.0%	35	unscreened	SSP	Social-Interpersonal Factor	no diagnosis (18)	n/a	$d^1 = 1.65^{***}$
Kendler et al, 1995 (Roscommon Family Study)	1st degree rels (314)	n/a	n/a	no schiz or schizoaif	SIS	Average Effect Size Negative Schizotypy Factor Poor Rapport Alloofness/Coldness Guardedness Odd Behavior Avoidant Symptoms Factor Social Isolation Social Anxiety Hypersensitivity Apparent Anxiety Social Dysfunction Factor Low Motivation Low Occupational Function Suspicious Behavior Factor Hypervigilance Irritability	1st degree rels of unscreened control probands; no schiz or schizoaif (575)	n/a	$d^6 = 0.64^{\ddagger}$ $d^3 = 0.62^{***}$
Squires-Wheeler et. al, 1997 (New York High Risk Study)	offspring (48)	n/a	24.3	unscreened	PDE	Negative Schizotypy Factor No Close Friends Inappropriate Affect Poverty of Speech Poverty of Emotion Indifference Odd Behavior/Appearance	unscreened offspring of no diagnosis parents (84)	age, race	$d^2 = 1.10^{***}$
Kremen et. al, 1998	1st degree rels (40)	22.5%	m: 40.8 f: 42.9	no psychosis or substance abuse	SPQ	Social-Interpersonal Factor	< 70 on the MMPI-168 (44)	age, sex, race	$d^5 = 0.41^{7d}$ m: n.s. f: n.s.
Yaralian et. al, 2000	relatives (13)	92.3%	29.9	unscreened	SPQ	Social-Interpersonal Factor Social Anxiety No Close Friends Constricted Affect Paranoid Ideation ^c	no family history schiz-spectrum or alcohol/drug abuse (51)	age, sex, race	$d^2 = 0.08$ n.s. n.s. n.s. $d^4 = 0.75^*$
Appels et. al, 2004	parents (36 couples)	50.0%	median: 54.9	no psychosis or substance abuse	SPQ	Negative Schizotypy Factor Social Anxiety No Close Friends Constricted Affect Suspiciousness ^c	no psychotic, affective, substance, or personality d/o (26 couples)	age, sex, handedness, education, IQ	n.s.

Study	Relatives of Schizophrenia Probands			Schizotypy Assessment			Comparison with Psychiatrically Healthy Controls ^b		
	Relationship to Proband (n)	Sex % male	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	screening criteria (n)	match to schiz rels	effect size
Calkins et. al, 2004	parents, sibs, offspring (124)	49.2%	46.5	no psychosis	SPQ	Social-Interpersonal Factor Social Anxiety No Close Friends Constricted Affect Suspiciousness ^c	no diagnosis (109)	sex	$d^I = 0.55^{***}$ $d^I = 0.53^{***}$ $d^I = 0.52^{***}$ $d^I = 0.36^{**}$; n.s.
Compton et. al, 2009	parents, sibs, offspring (28)	17.9%	n/a	No psychosis or mood d/o	SPQ	Social-Interpersonal Factor	No mood or psychotic d/o, self or 1 st or 2 nd degree rels (32)	n/a	n.s.
Overall Mean Effect Size for Factor-Level Comparisons ⁷									d = 0.67

Note: SSP - Schedule for Schizotypal Personalities (Interview), SIS - Structured Interview for Schizotypy, PDE - Personality Disorder Examination (Interview), SPQ - Schizotypal Personality Questionnaire (self-report), MMPI - Minnesota Multiphasic Personality Inventory, unscreened - psychiatric diagnoses not excluded, no diagnosis - all psychiatric diagnoses excluded, schiz - schizophrenia, schizoff - schizoaffective disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons.

^aTorgersen et al, 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

^bUnless otherwise noted, healthy control groups are comprised of individual control probands

^cOn the SPQ, suspiciousness/paranoid ideation loads on both the social-interpersonal and cognitive-perceptual factors

^dTrend of significant group-by-sex interaction ($p < 0.06$) (Kremen et. al, 1998)

^IGlass' d (relative M - control M / control SD)

²Glass' d calculated by current author

³Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)

⁴Cohen's d transformed from t: $d = t(n1+n2)/\sqrt{df}(\sqrt{n1n2})$; [pooled, equal variances assumed] (Rosenthal, 1994)

⁵Cohen's d transformed from chi square: $r\phi = \sqrt{X^2/n}$; $d = 2r/\sqrt{1-r^2}$ (Johnson and Eagly, 2000)

⁶Average effect size for the four factors; not weighted by variance (Kendler, et al., 1996).

⁷Mean effect sizes were calculated for factor comparisons using the overall effect size for each study (indicated in bold) by weighting each 'd' by the inverse of the conditional variance of 'd' (Shadish & Haddock, 1994); average effect size for Kendler, et al. was used in mean effect size calculation.

p < .001

**
p < .01

*
 $p < .05$
 $p < .10$
 p value not reported

Table 2

Social-Interpersonal Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Relatives of Patients with Affective Disorders

Study	Relatives of Schizophrenia Probands				Schizotypy Assessment				Comparison with Relatives of Affective Disorder Probands			
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	proband diagnosis	screening criteria (n)	match to schiz rels	effect size		
Torgersen et. al. 1993	non-twin, 1st degree rels (134) ^a	41.8%	53.6	no schiz	SCID-II	(factor n/a) Social Anxiety Social Isolation Inappropriate Affect Suspiciousness	major depression	non-twin, 1st degree rels; no schiz (65)	age, sex	n/a $d^5 = 0.32^*$ n.s. $d^5 = 0.30^*$ n.s.		
Lyons et. al. 1994	parents, sibs, offspring (34)	50.0%	49.2	≥ 3 SPD symptoms	SIDP, SANS, SAPS	(factor n/a) Social Anxiety Social Isolation Inadequate Rapport ^c Suspiciousness	affective d/o	parents, sibs, offspring; ≥ 3 symptoms SPD (14)	age, sex, education	n/a n.s. n.s. n/a [*] n.s.		
Kendler et al. 1995 (Roscommon Family Study)	1st degree rels (314)	n/a	n/a	no schiz or schizoaff	SIS	Average Effect Size Negative Schizotypy Factor Poor Rapport Aloofness/Coldness Guardedness Odd Behavior	affective d/o	1st degree rels; no schiz or schizoaff (183)	n/a	$d^6 = 0.52^{\dagger}$ $d^3 = 0.34^*$		
						Avoidant Symptoms Factor Social Isolation Social Anxiety Hypersensitivity Apparent Anxiety				$d^3 = 0.35^{***}$		
						Social Dysfunction Factor Low Motivation Low Occupational Function				n.s.		
						Suspicious Behavior Factor Hypervigilance Irritability				$d^3 = 0.87^*$		
Squires-Wheeler et. al. 1997 (New York High Risk Study)	offspring (48)	n/a	24.3	unscreened	PDE	Negative Schizotypy Factor No Close Friends Inappropriate Affect Poverty of Speech Poverty of Emotion Indifference Odd Behavior/Appearance	affective d/o	unscreened offspring (40)	age, race	$d^2 = 0.41$		
Schurhoff et. al. 2005	parents, sibs, offspring (85)	44.7%	53.9	no schiz or bipolar	SPQ	Negative Schizotypy Factor	bipolar d/o	parents, sibs, offspring; no schiz or bipolar (95)	age, sex	$d^2 = 0.00$		

Study	Relatives of Schizophrenia Probands				Schizotypy Assessment		Comparison with Relatives of Affective Disorder Probands			
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	proband diagnosis	screening criteria (n)	match to schiz rels	effect size

Overall Mean Effect Size for Factor-Level Comparisons⁷

d = 0.37

Notes: SCID-II - Structured Clinical Interview for DSM-III-R Personality Disorders, SIDP - Structured Interview for DSM-III Personality Disorders, SANS -Scale for the Assessment of Negative Symptoms (clinician rated), SAPS - Scale for the Assessment of Positive Symptoms (clinician rated), SIS - Structured Interview for Schizotypy, PDE - Personality Disorder Examination (Interview), SPQ - Schizotypal Personality Questionnaire (self-report), unscreened - psychiatric diagnoses not excluded, schiz - schizophrenia, schizoaff - schizoaffective disorder, SPD - Schizotypal personality disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons.

^aTorgersen et al., 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

^bOn the SPQ, suspiciousness/paranoid ideation loads on both the social-interpersonal and cognitive-perceptual factors

^cInadequate rapport was replaced by "inappropriate affect" when the DSM-III was revised for DSM-III-R

¹Glass' d (relative M - control M / control SD)

²Glass' d calculated by current author

³Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)

⁴Cohen's d transformed from t: $d = t(n1+n2)/\sqrt{df}(\sqrt{n1} \ln 2)$; [pooled, equal variances assumed] (Rosenthal, 1994)

⁵Cohen's d transformed from chi square: $r_0 = \sqrt{\chi^2/n}$; $d = 2r/\sqrt{1-r^2}$ (Johnson and Eagly, 2000)

⁶Average effect size for the four factors; not weighted by variance (Kendler, et al., 1996).

⁷Mean effect sizes were calculated for factor comparisons using the overall effect size for each study (indicated in bold) by weighting each 'd' by the inverse of the conditional variance of 'd' (Shadish & Haddock, 1994); average effect size for Kendler, et al. was used in mean effect size calculation.

*** p < .001

** p < .01

* p < .05

[†] p < .10

[‡] p value not reported

Table 3
Cognitive-Perceptual Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Non-Psychiatric Controls

Study	Relatives of Schizophrenia Probands			Schizotypy Assessment			Comparison with Psychiatrically Healthy Controls ^b		
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	screening criteria (n)	match to schiz rels	effect size
Grove et. al, 1991	parents, sibs, half-sibs (61)	46.0%	35	unscreened	SSP	Cognitive-Perceptual Factor	no diagnosis (18)	n/a	$d^1 = 0.51^{\dagger}$
Kendler et. al, 1995 (Roscommon Family Study)	1st degree rels (314)	n/a	n/a	no schiz or schizoaif	SIS	Positive Schizotypy Factor Illusions Ideas of reference Suspiciousness Depersonalization Recurrent Suicidal Threats	1st degree rels of unscreened control probands; no schiz or schizoaif (575)	n/a	$d^3 = 0.36^{**}$
Squires-Wheeler et al, 1997 (New York High Risk Study)	offspring (48)	n/a	24.3	unscreened	PDE	Positive Schizotypy Factor Unusual Percep Experiences Odd Beliefs/ Magical Thinking Ideas of Reference Suspiciousness Circumstantial/ Tangential Speech	unscreened offspring of no diagnosis	age, race	$d^2 = 0.25^*$
Kremen et. al, 1998	1st degree rels (40)	22.5%	m: 40.8 f: 42.9	no psychosis or substance abuse	SPQ	Cognitive-Perceptual Factor	≤ 70 on the MMPI-168 (44)	age, sex, race	$d^5 = 0.65^{***d}$ m: n/a f: n.s.
Yaralian et. al, 2000	relatives (13)	92.3%	29.9	unscreened	SPQ	Cognitive-Perceptual Factor Unusual Percep Experiences Ideas of Reference Magical Thinking Paranoid Ideation ^c	no family history schiz-spectrum or alcohol/drug abuse (51)	age, sex, race	$d^2 = 1.02^{**}$ $d^4 = 0.87^{***}$ $d^4 = 0.87^{***}$ n.s. $d^4 = 0.75^*$
Appels et. al, 2004	parents (36 couples)	50.0%	median: 54.9	no psychosis or substance abuse	SPQ	Positive Schizotypy Factor Unusual Percep Experiences Ideas of Reference Magical Thinking Suspiciousness ^c	no psychotic, affective, substance, or personality d/o (26 couples)	age, sex, handedness, education, IQ	n/a (-) [*] n/a (-) [†] n.s. n/a (-) [*] n.s.
Calkins et. al, 2004	parents, sibs, offspring (124)	49.2%	46.5	no psychosis	SPQ	Cognitive-Perceptual Factor Unusual Percep Exper Ideas of Reference Magical Thinking Suspiciousness ^c	no diagnosis (109)	sex	$d^1 = 0.24^{\dagger}$ $d^1 = 0.38^*$ n.s. n.s. n.s.
Compton et. al, 2009	parents, sibs, offspring (28)	17.9%	n/a	No psychosis or mood d/o	SPQ	Cognitive-Perceptual Factor	No mood or psychotic d/o, self or 1 st or 2 nd	n/a	n.s.

Study	Relatives of Schizophrenia Probands				Schizotypal Assessment		Comparison with Psychiatrically Healthy Controls ^b		
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	screening criteria (n)	match to schiz rels	effect size
degree rels (32)									
Mean Effect Size f for Factor-Level C omparison ^d									
d = 0.37									

Note: SSP - Schedule for Schizotypal Personalities (Interview), SIS - Structured Interview for Schizotypy, PDE - Personality Disorder Examination (Interview), SPQ - Schizotypal Personality Questionnaire (self-report), MMPI - Minnesota Multiphasic Personality Inventory, unscreened - psychiatric diagnoses not excluded, no diagnosis - all psychiatric diagnoses excluded, schiz - schizophrenia, schizoaif - schizoaffective disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons.

^aTorgersen et al, 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

^bUnless otherwise noted, healthy control groups are comprised of individual control probands

^cOn the SPQ, suspiciousness/paranoid ideation loads on both the social-interpersonal and cognitive-perceptual factors

^dSignificant group-by-sex interaction (males > females, $p < 0.007$) (Kremen et al, 1998)

¹Glass' d (relative M - control M / control SD)

²Glass' d calculated by current author

³Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(o/\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)

⁴Cohen's d transformed from t: $d = (n1+n2)/\sqrt{df}(\sqrt{n1n2})$; [pooled, equal variances assumed] (Rosenthal, 1994)

⁵Cohen's d transformed from chi square: $r\phi = \sqrt{X^2/n}$; $d = 2r/\sqrt{1-r^2}$ (Johnson and Eagly, 2000)

⁶Mean effect sizes were calculated for factor comparisons using the overall effect size for each study (indicated in bold) by weighting each 'd' by the inverse of the conditional variance of 'd' (Shadish & Haddock, 1994)

*** $p < .001$

** $p < .01$

* $p < .05$

[†] $p < .10$

Table 4
Cognitive-Perceptual Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Relatives of Patients with Affective Disorders

Study	Relatives of Schizophrenia Probands			Schizotypy Assessment			Comparison with Relatives of Affective Disorder Probands			
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	proband diagnosis	screening criteria (n)	match to schiz rels	effect size
Torgersen et. al, 1993	non-twin, 1st degree rels (134) ^a	41.8%	53.6	no psychosis	SCID-II	(factor n/a) Illusions Ideas of Reference Magical Thinking	major depression	non-twin, 1st degree rels; no schiz (65)	age, sex	n/a n.s. n.s.
Lyons et. al, 1994	parents, sibs, offspring (34)	50.0%	49.2	≥ 3 SPD symptoms	SIDP, SANS, SAPS	(factor n/a) Illusions Ideas of Reference Magical ideation	affective d/o	parents, sibs, offspring; ≥ 3 symptoms SPD (14)	age, sex, education	n/a n.s n.s n.s
Kendler et. al, 1995 (Roscommon Family Study)	1st degree rels (314)	n/a	n/a	no schiz or schizoaffect	SIS	Positive Schizotypy Factor Illusions Ideas of reference Suspiciousness Depersonalization Recurrent Suicidal Threats	affective d/o	1st degree rels; no schiz or schizoaffect (183)	n/a	n.s.
Squires-Wheeler et al, 1997 (New York High Risk Study)	offspring (48)	n/a	24.3	unscreened	PDE	Positive Schizotypy Factor Unusual Percept Exper Odd Beliefs/ Magical Thinking Ideas of Reference Suspiciousness Circumstantial/Tangential Speech	affective d/o	unscreened offspring (40)	age, race	d² = -0.08
Schurhoff et. al, 2005	parents, sibs, offspring (85)	44.7%	53.9	no schiz or bipolar	SPQ	Positive Schizotypy Factor	bipolar d/o	parents, sibs, offspring; no schiz or bipolar (95)	age, sex	d² = 0.10
Mean Effect Size for Factor-Level Comparisons ^b										d = 0.04

Note: SCID-II - Structured Clinical Interview for DSM-III-R Personality Disorders, SIDP - Structured Interview for DSM-III Personality Disorders, SANS - Scale for the Assessment of Negative Symptoms (clinician rated), SAPS - Scale for the Assessment of Positive Symptoms (clinician rated), SIS - Structured Interview for Schizotypy, PDE - Personality Disorder Examination (Interview), SPQ - Schizotypal Personality Questionnaire (self-report), unscreened - psychiatric diagnoses not excluded, no diagnosis - all psychiatric diagnoses excluded, schiz - schizophrenia, schizoaffect - schizoaffective disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons.

^aTorgersen et al, 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

^bOn the SPQ, suspiciousness/paranoid ideation loads on both the social-interpersonal and cognitive-perceptual factors

^cGlass' d (relative M - control M / control SD)

- ² Glass' d calculated by current author
 - ³ Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)
 - ⁴ Cohen's d transformed from t: $d = t(n1+n2)/\sqrt{df}(\sqrt{n1}n2)$; [pooled, equal variances assumed] (Rosenthal, 1994)
 - ⁵ Cohen's d transformed from chi square: $r\phi = \sqrt{X^2/n}$; $d = 2r/\sqrt{1-r^2}$ (Johnson and Eagly, 2000)
 - ⁶ Mean effect sizes were calculated for factor comparisons using the overall effect size for each study (indicated in bold) by weighting each 'd' by the inverse of the conditional variance of 'd' (Shadish & Haddock, 1994)
- *** $p < .001$
- ** $p < .01$
- * $p < .05$
- [†] $p < .10$

Table 5
Disorganized Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Non-Psychiatric Controls

Study	Relatives of Schizophrenia Probands			Schizotypy Assessment		Comparison with Psychiatrically Healthy Controls ^b			
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	screening criteria (n)	match to schiz rels	effect size
Kendler et. al, 1995 (Roscommon Family Study)	1st degree relatives (314)	n/a	n/a	no schiz or schizoaffect	SIS	Odd Speech Factor Cognitive slippage Odd speech	1st degree rels of unscreened control probands; no schiz or schizoaffect (575)	n/a	d³ = 0.96^{**}
Kremen et. al, 1998	1st degree relatives (40)	22.5%	m: 40.8 f: 42.9	no psychosis or substance abuse	SPQ	Disorganized Factor	≤ 70 on the MMPI-168 (44)	age, sex, race	d⁵ = 0.22
Yaralian et. al, 2000	relatives (13)	92.3%	29.9	unscreened	SPQ	Disorganized Factor Odd behaviors Odd speech	no family history of schiz-spectrum or alcohol/drug abuse (51)	age, sex, race	d² = 0.49 n.s. n.s.
Appels et. al, 2004	parents (36 couples)	50.0%	median: 54.9	no psychosis or substance abuse	SPQ	Disorganized Factor Odd Behaviors Odd Speech	no psychotic, affective, substance, or personality d/o (26 couples)	age, sex, handedness, education, IQ	n.s.
Calkins et. al, 2004	parents, sibs, offspring (124)	49.2%	46.5	no psychosis	SPQ	Disorganized Factor Odd Behaviors Odd Speech	no diagnosis (109)	sex	d¹ = 0.17 d ¹ = 0.11 d ¹ = 0.17
Compton et. al, 2009	parents, sibs, offspring (28)	17.9%	n/a	No psychosis or mood d/o	SPQ	Cognitive-Perceptual Factor	No mood or psychotic d/o, self or 1 st or 2 nd degree rels (32)	n/a	n.s.
Mean Effect Size f or Factor-Level Comparison ns ^δ									d = 0.73

Note: SIS - Structured Interview for Schizotypy, SPQ - Schizotypal Personality Questionnaire (self-report), MMPI - Minnesota Multiphasic Personality Inventory, unscreened - psychiatric diagnoses not excluded, no diagnosis - all psychiatric diagnoses excluded, schiz - schizophrenia, schizoaffect - schizoaffective disorder, SPD - Schizotypal personality disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons.

^aTorgersen et al, 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

^bUnless otherwise noted, healthy control groups are comprised of individual control probands

¹Glass' d (relative M - control M / control SD)

²Glass' d calculated by current author

³Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)

Mean effect sizes were calculated for factor comparisons using the overall effect size for each study (indicated in bold) by weighting each 'd' by the inverse of the conditional variance of 'd' (Shadish & Haddock, 1994)

*** p < .001
 ** p < .01
 * p < .05
 † p < .10

Table 6

Disorganized Schizotypal Symptoms in Relatives of Schizophrenia Probands versus Relatives of Patients with Affective Disorders

Study	Relatives of Schizophrenia Probands			Schizotypy Assessment		Comparison with Relatives of Affective Disorder Probands				
	Relationship to Proband (n)	Sex % m	Age mean yrs	Psychiatric Status	Measure	Factor Symptom	proband diagnosis	screening criteria (n)	match to schiz rels	effect size
Torgersen et. al, 1993	non-twin, 1st degree rels (134) ^d	41.8%	53.6	no psychosis	SCID-II	Factor n/a Odd speech	major depression	non-twin, 1st degree rels; no schiz (65)	age, sex	n/a $d^5 = 0.30^*$
Lyons et. al, 1994	parents, sibs, offspring (34)	50.0%	49.2	≥ 3 symptoms of SPD	SIDP, SANS, SAPS	Factor n/a Odd speech	affective d/o	parents, sibs, offspring; ≥ 3 symptoms SPD (14)	age, sex, education	n/a n.s.
Kendler et al, 1995 (Roscommon Family Study)	1st degree rels (314)	n/a	n/a	no schiz or schizoaffect	SIS	Odd Speech Factor Cognitive slippage Odd speech	affective d/o	1st degree rels; no schiz or schizoaffect (183)	n/a	n.s.
Schurhoff et. al, 2005	parents, sibs, offspring (85)	44.7%	53.9	no schiz or bipolar	SPQ	Disorganized Factor	bipolar d/o	parents, sibs, offspring; no schiz or bipolar (95)	age, sex	$d^2 = -0.16$

Note: SCID-II - Structured Clinical Interview for DSM-III-R Personality Disorders, SIDP - Structured Interview for DSM-III Personality Disorders, SANS - Scale for the Assessment of Negative Symptoms (clinician rated), SAPS - Scale for the Assessment of Positive Symptoms (clinician rated), SIS - Structured Interview for Schizotypy, SPQ - Schizotypal Personality Questionnaire (self-report), unscreened - psychiatric diagnoses not excluded, schiz - schizophrenia, schizoaffect - schizoaffective disorder, SPD - schizotypal personality disorder, m - male, f - female, rels - relatives, n/a - not reported/not able to calculate, empty cell: not reported by original study, bold font denotes effect size for factor-level comparisons, mean effect size for factors not calculated due to insufficient data.

^aTorgersen et al, 1993 also reported results for MZ and DZ twins - all comparisons were not significant.

¹Glass' d (relative M - control M / control SD)

²Glass' d calculated by current author

³Cohen's d (relative M - control M / pooled SD) transformed from odds ratio: $d = \ln(\sqrt{3}/\pi)$ (Hasselblad & Hedges, 1995)

⁴Cohen's d transformed from t: $d = (t(n_1+n_2)/\sqrt{df})(\sqrt{n_1n_2})$; [pooled, equal variances assumed] (Rosenthal, 1994)

⁵Cohen's d transformed from chi square: $r\phi = \sqrt{X^2/n}$; $d = 2r/\sqrt{1-r^2}$ (Johnson and Eagly, 2000)

p < .001

**
p < .01

*
p < .05

[†]
p < .10