Self-reported childhood trauma correlates with schizotypal measures in schizophrenia but not bipolar pedigrees.

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Abstract

Background

Strong evidence supports the association between childhood trauma and psychotic disorders. In two different high-risk populations, we looked for a correlation between the magnitude of schizotypal dimensions and the importance of self-reported childhood trauma.

Methods

A sample of 138 unaffected first-degree relatives was recruited (67 relatives of schizophrenic probands and 71 relatives of bipolar probands). The relationship between schizotypal dimensions and childhood trauma scores was analyzed by partial correlations.

Results

A positive correlation was found between childhood trauma scores and total schizotypal scores in first-degree relatives of schizophrenic subjects but not in first-degree relatives of bipolar probands. This correlation was primarily due to a strong association with the positive dimension of schizotypy.

Conclusions

The significant correlation between childhood trauma and schizotypal dimensions in subjects at high genetic risk for schizophrenia suggests that susceptibility genes for schizophrenia may interact with childhood trauma to induce the emergence of schizotypal dimensions, mainly positive psychotic features.

Introduction

Among the several explanations invoked to explain failures to find susceptibility genes, gene-environment interaction (GxE) suggests that " ignoring nurture may have handicapped the field's ability to understand nature" (Moffitt et al., 2005). GxE can be defined as the genetic control of sensitivity to environmental factors, or as the environmental control of gene expression (Kendler & Eaves, 1986). Several recent studies demonstrated that the GxE approach can be of practical benefit as a tool in the search for genes connected with mental disorders (Kahn et al., 2003; Caspi et al., 2003, 2005; Kendler et al., 2005).

Childhood trauma has been repeatedly associated with psychotic features not only in schizophrenia (for review, see Read et al., 2005) but also in bipolar disorders (Hammersley et al., 2003; Neria et al., 2005) and schizotypy (Yen et al., 2002; Berenbaum et al., 2003). Therefore, childhood trauma may be a good candidate environmental risk factor for psychotic disorders. Schizotypy is a multidimensional construct that represents a mild imitation of the symptoms of schizophrenia (Vollema & Postma, 2002). Although schizotypy is the core feature of schizotypal personality disorder, it is thought to be a continuous or dimensional, rather a categorical construct (Irwin, 2001). Schizotypal dimensions have been described as a potential intermediate phenotype for both schizophrenia and bipolar disorders and could be the consequence of a gene-environment interaction. This association is difficult to examine prior to the identification of disease genes. The study of a population at "high genetic risk" which carries several unknown genes related to the disorder, may improve the possibility of identifying environmental risk factors. This approach may be more appropriate than studying the interaction between an environmental factor and a specific candidate gene. Studying the impact of childhood trauma on schizotypal dimensions among unaffected relatives has several advantages. Firstly, dimensional models of psychosis (positive, negative and disorganized symptoms) are becoming established as conceptually and clinically useful (Van Os et al., 2002). Secondly, first-degree relatives are free from the multiple artifacts that potentially confound research

in schizophrenia, including the effects of long-term and usually ongoing medication treatment, multiple hospitalizations or institutionalization, and prolonged functional impairment secondary to chronic disease and social deterioration.

We investigated whether childhood trauma is correlated with the phenotypic expression of schizotypyal dimensions (positive, negative and disorganized) in two different populations of unaffected first-degree relatives. We hypothesized that the correlation between childhood trauma and schizotypal dimensions could be different among these two high-risk populations.

Materials and methods

Subjects

Consecutively admitted probands meeting DSM-IV criteria for bipolar disorder or schizophrenia were recruited from a university-affiliated hospital (Psychiatry department, Paris XII University). Their unaffected first-degree relatives were contacted and asked to participate in the study. Relatives were interviewed with the French version of the Diagnostic interview of Genetic Studies (DIGS) (Nurnberger et al., 1994; Preisig et al., 1999) to confirm the absence of diagnosis of schizophrenia or bipolar disorders. We used the validated French translation (Dumas et al., 2000) of the self-rating Schizotypal Personality Questionnnaire (SPQ) (Raine, 1991), to measure schizotypal dimensions in the two different groups of first-degree relatives. This questionnaire contains 74 items with yes/no answers and identifies the three classical dimensions of psychosis (positive, negative and disorganized). The SPQ can be used in the general population to identify individual differences in schizotypal dimensions.

Subjects also completed the French translation (Paquette et al., 2004) of the Childhood Trauma Questionnaire (CTQ) (Bernstein & Fink, 1998), a 28-item self-report questionnaire, which gives scores for physical, emotional and sexual abuse, physical and emotional neglect, and a total weighted score.

The Research Ethics Board reviewed and approved the study. After completely describing the study, written informed consent was obtained from all participants.

Data analysis

Differences between groups were tested using a two-tailed t-test for continuous variables and a chi-squared test for discrete variables.

The relationships between schizotypal dimensions and CTQ scores were analyzed by partial correlation to control for the potential confounding influences of sex and age. Sex was used as covariable because of its influence on both CTQ and SPQ scores (Paquette et al., 2004; Dumas et al., 2000). Age at interview was also used as a covariable because some studies have observed a negative correlation between age of the subjects and scores for the SPQ scale and sub-scales (Venables & Bailes, 1994; Mata et al., 2005). To limit the risk of type I error due to multiple statistical tests, we examined only the total score of the CTQ, and we used Bonferroni procedure to establish the significance threshold ($p < 0.05$ divided by 12 statistical analyses; we retained $p < 0.004$). We also analyzed the variables dichotomously and calculated odds ratios and 95% confidence intervals (CI) for schizotypy given childhood trauma in the two populations of relatives. To do that, we determined the presence or absence of childhood trauma according to the cut-off of the French validation of the CTQ. The cut-off for the schizotypal dimensions was determined as the mean score of the SPQ full-score for the whole sample.

Results

The study group was composed of 67 first-degree relatives of schizophrenic probands (31men and 36 women, mean age (SD) = 54.2 (15.4) years) and 71 first-degree relatives of bipolar probands (37 men and 34 women, mean age (SD) = 53.1 (15) years). The sex ratio ($\chi 2 = 0.47$, $p = 0.49$) and the age at interview ($t = 0.43$, $p = 0.67$) did not differ between groups. The samples of first-degree relatives are composed of different types of relatives. In the two samples of relatives, the majority of the relatives are parents of the proband with an over-representation of parents in the sample of first-degree relatives of schizophrenic subjects (80.5% vs 59.2%). The highest completed school grade (education level) was recorded, according to usual conventions (Pichot et al., 1993) as a trichotomous variable (1 = elementary school; 3 = at least high school completed; 2 = intermediate between 1 and 3). However, we finally decided to pool the first two levels together because level 1 was infrequent in all groups. The two samples did not differ in terms of educational level ($p = 0.40$). In the sample of schizophrenic relatives: the mean SPQ scores (full-scale and for the positive, negative and disorganized dimensions) were 10.2 + 7.9; 3.9 + 3.8; 4.7 + 4.4 and 1.6 + 1.7 respectively; the mean CTQ score was 38.6 + 8.5. In the sample of bipolar relatives: the mean SPQ scores (full-scale and for the positive, negative and disorganized dimensions) were 9.6 + 7.5; 3.3 + 3.4; 4.3 + 4.7 and 1.9 + 2 respectively; the mean CTQ score was 39.3 + 9.8. The SPQ full-score and the CTQ score did not differ between the two groups (SPQ full-score: $p = 0.73$ and CTQ full-score: $p = 0.95$). The mean CTQ and SPQ scores were similar between males and females ($p = 0.58$ and $p = 0.77$, respectively). In the whole sample of relatives, we found a significant

positive correlation between the CTQ score and the SPQ full-score ($r = 0.27$; $p = 0.001$). This correlation was fully explained by a correlation in the sample of first-degree relatives of schizophrenic subjects ($r = 0.43$; $p < 0.0001$), whereas no significant correlation was found in the first-degree relatives of bipolar probands ($r = 0.13$; $p =$ NS). This positive correlation was found with the positive and negative dimensions of schizotypy (positive schizotypy: $r = 0.41$ and negative schizotypy: $r = 0.36$) but not with the disorganized dimension (Table 1). We have also investigated partial correlation coefficients between each schizotypal dimension and childhood trauma adjusted for the two other schizotypal dimensions. Only the correlation between positive dimension and childhood trauma remains significant.

Based on a dichotomous approach, the calculation of the odds ratios leads to similar results. The odds of having high schizotypal traits in presence of childhood trauma were higher in the population of schizophrenic relatives (OR = 3.6, 95% CI [1.09 – 11.8]) than in the population of the bipolar relatives (OR = 1.64, 95% CI [0.57 – 4.72]), which were not significant.

Discussion

We found a significant positive correlation between history of childhood trauma and schizotypal dimensions in unaffected first-degree relatives of schizophrenic subjects but not in relatives of bipolar probands. This correlation was mainly due to a strong association with the positive dimension of psychosis. To our knowledge, this is the first study exploring the influence of an environmental risk factor in two populations with different genetic backgrounds. Even though schizotypy was shown to be elevated in relatives of bipolar subjects (Kety et al., 1994; Schürhoff et al., 2005) suggesting some shared genetic vulnerability factors, the only difference between our two populations is that one is at genetic risk for schizophrenia and the other for bipolar disorders. We observed that the impact of childhood trauma on the expression of schizotypal dimensions was strongest among subjects who were at high genetic risk for schizophrenia suggesting that susceptibility genes specific to schizophrenia may interact with childhood trauma to induce the emergence of schizotypal dimensions, mainly positive psychotic features. This is in accordance with several previous reports from the literature (for review, see Read et al., 2005) showing a high influence of childhood trauma on positive dimension in schizophrenia and schizotypy. In line with our results, using a follow-up design, Spauwen et al. (2006) found an association between self-reported trauma and psychosis proneness. The strength of the association increased with a narrower psychosis definition. These authors have speculated that extended exposure to trauma may increase the risk for positive symptoms through direct effects on dopamine function. Along similar lines, Read et al. (2005) have suggested that early, prolonged, and severe traumas increase the risk for later positive symptoms through lasting on the hypothalamic-pituitary-adrenal axis. Even if associations between negative dimension and childhood trauma have been previously reported (Resnick et al., 2003; Lysaker et al., 2001), this association is more difficult to interpret. A plausible explanation is that traumatic avoidance, emotional numbing and reduced responsiveness may resemble negative dimension and may be interpreted as a reaction to the trauma. Conversely, in rodents and nonhuman primates, trauma (for example, forced swim test) has been used as a model of the negative symptoms of schizophrenia such as flattening of affect and avolition (Corbett et al., 1999). Concerning the disorganized dimension, as in previous studies, we did not show any correlation with childhood trauma (Read & Argyle, 1999; Hammersley et al., 2003). However, this could be also explained by the small variation of this dimension. Our study could be considered as an example of how an environmental factor interacting with specific susceptibility genes can influence susceptibility to a disorder or to a particular dimension of a disorder. Our results can suggest that the same dimensions have different genetic background in bipolar disorders and schizophrenia. However, there is also a more plausible explanation. The same genes cause susceptibility for a common phenotype in bipolar disorders and schizophrenia, in particular the positive dimension (Berretini, 2003; Schürhoff et al., 2003). In order to become manifest, this susceptibility needs to interact with some environmental factors. However, other factors, disorder-specific, can exert a protective or permissive role on the action of these environmental factors. For example, traits that have been associated with genetic susceptibility to bipolar disorders (i.e cyclothymic, hyperthymic or depressive temperaments) might have a protective effect on the emergence of positive schizotypal traits in the presence of childhood trauma.

The possibility that susceptibility genes for schizophrenia may increase exposure to childhood trauma can be excluded as rates of childhood trauma were similar among the two groups of relatives. However, because of the design of our study, two alternative hypotheses could be proposed. Indeed, our results could also be explained by shared family environmental factors amongst the schizophrenia relatives rather than genetic factors – this could only be ruled out by employing an adoption study design. In other words, the childhood trauma could be a proxy for other environmental risks such as social disadvantage or family discord/chaos specific to schizophrenic families. Moreover, due to the retrospective assessment of the childhood trauma, we cannot exclude that subjects reported high level of childhood trauma because they have a high level of schizotypal features. Nevertheless, the fact that no association is found in the relatives of bipolar probands suggests that a bias cannot entirely explain the association found in relatives of schizophrenic subjects between trauma and schizotypal dimensions. It is also interesting to note that despite the fact that relatives tend to be defensive in their response, the use of the SPQ discriminates the two samples of relatives. Overall, our results support the assumption that the clinical expression of the vulnerability induced by environmental risk factors depends on gene-environment interactions. Speculation about the implications of this finding should be guarded until these results are replicated as we cannot formally exclude the possibility that childhood trauma interacted with other specific environmental risk factors.

In conclusion, our findings suggest that susceptibility genes specific to schizophrenia may influence response to pathogenic environments. It is clear that if a gene's connection to disorder is conditional to the environment, this will have the natural consequence of diminishing researchers' capacity to detect the association between the gene and disorder. Research to uncover specific environmental risk factors for diseases may be more effective if we recruit samples on the basis of their high genetic loading and if we investigate which genes discriminate between exposed individuals who did, versus did not, become ill.

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Footnotes:

Declaration of interest

None

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Table 1

Correlation matrix for childhood trauma and schizotypal dimensions

	SPQ full-score	Positive	Negative	Disorganized
Mean score CTQ				
Total sample (n = 138)	0.27*	0.30*	0.13	0.20
First-degree relatives of schizophrenic subjects (n = 67)	0.42*	0.41*	0.35*	0.14
First-degree relatives of bipolar subjects (n = 71)	0.13	0.21	− 0.03	0.22

Statistical significance after Bonferroni correction

* $p<0.004$