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Personality in Relation to Genetic Liability for Schizophrenia and Bipolar Disorder: Differential Associations with the COMT Val$^{108/158}$Met Polymorphism

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Abstract

Schizophrenia and bipolar disorder may share aspects of genetic etiology. Evidence supports the Val$^{108/158}$Met polymorphism of the Catechol-o-Methyltransferase (COMT) gene as potentially contributing to the etiology of both disorders. To determine whether the COMT gene is associated with personality traits related to genetic risk for either schizophrenia or bipolar disorder, we examined dimensions of personality psychopathology in biological relatives of individuals with the disorders. Specifically, we contrasted personality characteristics of first-degree relatives of people with schizophrenia, first-degree relatives of people with bipolar-I disorder, and nonpsychiatric control participants using scores from the Dimensional Assessment of Personality Pathology – Brief Questionnaire (DAPP-BQ). We also characterized the COMT Val$^{108/158}$Met polymorphism of subjects. Compared to controls, relatives of schizophrenia patients scored lower on stimulus seeking and higher on restrictive expression and social avoidance. Compared to relatives of bipolar patients, relatives of schizophrenia patients had lower scores on narcissism, rejectionality (i.e., rejection of ideas of others), stimulus seeking, passive-aggressive oppositionality, and self-harm. The subset of relatives of schizophrenia patients who were COMT val homozygotes exhibited lower scores on narcissism, rejectionality, and stimulus seeking than met homozygote relatives of schizophrenia patients and control participants. Although relatives of bipolar patients showed scale elevations consistent with emotional dysregulation, the scores failed to be associated with the Val$^{108/158}$Met polymorphism. Abnormally low narcissism and rejectionality in val homozygote relatives of schizophrenia patients suggests that the val allele of the COMT polymorphism may be associated with an underdeveloped self-concept phenomenologically similar to made volition and passivity experiences comprising first-rank symptoms of schizophrenia.

1. Introduction

Genes strongly influence the occurrence of schizophrenia and bipolar disorder (see Shih et al. 2004 for a review). The two disorders can manifest similar clinical features such as cognitive impairment, mood disturbance and psychosis. Both have approximately a 1% prevalence rate.

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Both are transmitted to first-degree relatives at a rate of about 10%. Evidence of familial co-transmission of schizophrenia and bipolar disorder also suggests that the disorders may share aspects of genetic etiology (Laursen et al. 2005; Cardno et al. 2002). There is some evidence that schizophrenia occurs at increased frequency in relatives of probands with bipolar disorder (Valles et al. 2000), and that bipolar disorder occurs at increased rates in relatives of probands with schizophrenia (Tsuang et al. 1980). Also, schizoaffective disorder has been shown to occur at increased rates in families of probands with schizophrenia (Kendler et al. 1998) and bipolar disorder (Rice et al. 1997). Thus, there may be phenomenological and genetic continuua spanning schizophrenia and bipolar disorder. The $Val^{108/158}$Met polymorphism of the Catechol-o-Methyltransferase (COMT) gene has been associated with schizophrenia and bipolar disorder (Chen et al., 2004; Li et al. 1997) and investigations have related the COMT region to both disorders (Badner and Gershon, 2002). Additionally, Funke et al. (2005) found evidence of the COMT gene conferring a weak general risk both for psychosis and affective illness.

Nevertheless, the mechanism by which the COMT gene exerts effect on schizophrenia and bipolar disorder may not be shared across diagnostic boundaries. While both disorders show a statistical association with the COMT gene, interaction with disorder-specific factors may alter its phenotypic expression. Indeed, the methionine (met) allele of the COMT gene has been associated with episode cycling in bipolar disorder (Kirov et al. 1998; Papolos et al. 1998), but the valine (val) polymorphism has been proposed as associated with psychosis in affective illness (Craddock et al. 2006). Similarly, although initial reports implicated the met allele in schizophrenia (e.g., Ohmori et al. 1998), a more recent meta-analysis points to the val allele predisposing aspects of schizophrenia (Glatt et al. 2003). It has also been suggested that the $Val^{108/158}$ Met polymorphism of COMT only impacts the risk of schizophrenia in populations of European ancestry (Glatt et al. 2003) or not at all (Munafo et al. 2005). To fully understand potentially different roles of the COMT gene in schizophrenia and bipolar disorder it is necessary to determine which elements of liability for each disorder are associated with COMT genotypes.

Investigators have used personality questionnaires to determine separable aspects of liability for schizophrenia and bipolar disorder. First-degree relatives of both schizophrenic and psychotic bipolar individuals show increased schizotypy and conceptual disorganization as measured by the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991), in contrast to scores of first-degree relatives of non-psychotic bipolar individuals (Schurhoff et al. 2005). Male first-degree relatives of schizophrenic individuals have been found to show elevated psychoticism on the Eysenck Personality Questionnaire (EPQ) (Eysenck and Eysenck, 1975) as compared with male relatives of psychotic bipolar or schizoaffective disorder individuals (Laurent et al. 2002). In the present study we broadly examined personality phenotypes and determined whether the COMT gene was related to traits associated with genetic liability for schizophrenia and bipolar disorder. Using a family-study design, we investigated whether personality in first-degree relatives of schizophrenia patients and bipolar disorder patients was associated with the COMT $Val^{108/158}$Met polymorphism.

When attempting to differentiate personality phenotypes associated with genetic liability for schizophrenia and bipolar disorder, researchers have generally not employed instruments that characterize a full range of personality pathology. An aim of the present study was to directly compare first-degree relatives of schizophrenia patients and bipolar disorder patients on personality traits using an index sensitive to a full-range of characteristics in order to more completely distinguish aspects of liability for the two disorders. Thus, we employed the Dimensional Assessment for Personality Pathology – Basic Questionnaire (DAPP-BQ) (Livesley and Jackson, in press) to more completely describe the differential phenotypic expression of genetic liability for schizophrenia and bipolar disorder. The DAPP-BQ has been

shown to capture the dimensions of normal personality as measured by the NEO (Larstone et al 2002), to provide consistent characterizations across clinical and non-clinical samples (Livesley et al 1998, Bagge and Trull 2003), and to be heritable (Livesley et al 1998, Jang and Livesley 1999).

Because schizotypy likely shares genetic factors with schizophrenia (Jang et al. 2005), we expected that relatives of schizophrenia patients would exhibit scores on the DAPP indicative of schizotypy (elevated cognitive dysregulation, identity problems, social avoidance, suspiciousness, callousness, and restricted expression) (Bagge and Trull, 2003). Since hyperthymic temperament (e.g., Akiskal and Mallya, 1987) has been shown to be elevated in first-degree relatives of bipolar patients (Kesebir et al. 2005), we predicted that relatives of bipolar patients would show scores on the DAPP suggestive of hyperthymic temperament (i.e., emotional dysregulation: affective lability, anxiousness, cognitive dysregulation, identity problems, insecure attachment, narcissism, passive-aggressive oppositionality, self-harm, social avoidance, and submissiveness) (Pukrop et al. 2001). These were the primary phenotypes of interest with respect to variation in the COMT gene.

2. Experimental Materials and Methods

2.1 Participants

We studied 67 first-degree biological relatives of schizophrenia probands and 28 first-degree biological relatives of schizoaffective probands (SCZ-rels), 46 first-degree relatives of bipolar disorder probands (two were relatives of probands affected by bipolar disorder with psychosis), and 87 nonpsychiatric control subjects. Because schizoaffective disorder requires sustained psychotic symptoms in the absence of mood episodes and is therefore suggestive of first-degree biological relatives of individuals with the disorder carrying genetic liability for psychosis that is independent of affective episodes, we included relatives of schizoaffective probands with relatives of schizophrenia probands in a single group. Characteristics of the subjects are presented in Table 1. All participants completed an informed consent process. The Minneapolis VA Medical Center and University of Minnesota Institutional Review Boards approved the study protocol. See supplemental material and Sponheim et al. (2006) for complete description of recruitment and clinical assessment procedures.

2.2 Instruments

Participants completed the DAPP-BQ. The DAPP-BQ is a 290-item questionnaire that is made up of 18 scales. The DAPP scales (including an example item) were Affective Lability (I often feel as if I am on an emotional roller-coaster), Anxiousness (I can feel extremely guilty even about something unimportant), Callousness (I do not feel guilty even when I hurt someone's feelings), Cognitive Dysregulation (I often feel as if I am not really there), Compulsivity (I usually do the job systematically step by step), Conduct Problems (When rules are inconvenient I break them), Identity Problems (I never really enjoy myself), Insecure Attachment (I hate being separated from someone I love for even a few days), Intimacy Problems (I feel that I cannot love anyone), Narcissism (I am only really satisfied when people acknowledge how good I am), Passive-Aggressive Oppositionality (I plan to do so many things in a day that I often don't get anything done), Rejectionality (I tend to think that my views are the only right ones), Restricted Expression (I have difficulty expressing affection for others), Self-harm (Ending my life seems to be the only way out), Social Avoidance (I don't feel very sure of myself when I am with other people), Stimulus Seeking (When I take risks, I never worry about getting hurt), Submissiveness (If I am pressured, I will usually give in), and Suspiciousness (I think that other people are always trying to cheat me). Principal components analysis has yielded 4 factors from the 18 subscales: Emotional Dysregulation, Dissocial, Inhibition, and Compulsivity (Livesley & Jang 1998).

The 18 DAPP scales have been shown to map onto Diagnostic and Statistical Manual –Fourth Edition (DSM-IV) Axis II symptom counts (Bagge and Trull, 2003), although there are no cut-off scores that are considered to be clinically significant. Each scale contains 16 items, with the exception of Suspiciousness (14 items) and Self-Harm Behaviors (12 items). Participants respond on a 5-point Likhert scale with 5 indicating the strongest agreement with the statement. If questions were left blank, the other items on the scale were averaged to compute scale scores when at least 14 out of 16 (87.5%), 12 out of 14 (85.7%), or 11 out of 12 (91.67%) of the items had responses. In the personality questionnaire assessment we included the Chapman Infrequency Scale (Chapman and Chapman, 1983), and the L and K scales from the Minnesota Multiphasic Personality Inventory – Second Edition (MMPI-2) (Pope et al. 2000) to measure response biases. Although raw scores were subject to analyses, to examine the representativeness of the study sample we computed T-scores and compared the control group with T-scores of general population samples (Livesley et al in press). Controls in the present study sample were similar to that of general population samples. The mean T-score across the 18 DAPP-BQ scales for control sample women was 46.1 (SD=3.2) and control sample men it was 45.2 (SD=3.7). Slightly lower scores probably reflected that controls were likely to have less psychopathology than a general population sample because they were screened for an absence of personal and family histories of affective and psychotic disorders in addition to needing to be absent histories of illicit drug dependence and head injury. The control subjects appear to be an appropriate sample for determining deviance of the two groups of relatives.

2.3 Genotyping

Genotyping was completed for nearly all relatives and a subset of controls. Specimens were not initially gathered from control subjects. See supplemental material for description of the genotyping procedure. The subset of genotyped controls did not significantly differ from all controls on age (t=1.63, df=77, p=.11) or gender (χ^2=.10, df=1, p=.7) composition. All groups were found to be in Hardy-Weinberg equilibrium (HWE) (SCZ-rels N=91: val/val N=24, val/met N=46, met/met=21, HWE=χ^2=.01, df=2, p=.9; BPD-rels N=46: val/val N=9, val/met N=23, met/met N=14, HWE=χ^2=.006, df=2, p=1.0; Controls N=30: val/val=9, val/met=13, met/met=8, HWE=χ^2=.5, df=2, p=.8). N size may vary across scales by up to three individuals due to instances of missing DAPP-BQ data.

3. Results

To ensure group differences were not influenced by response bias we examined validity scales using repeat-measures ANOVA with gender and group (SCZ-rel, BP-rel, Ctrl) as between subjects factors and scale (Chapman Infrequency, L, K) as a within subjects factor. The analysis yielded an interaction of group and scale (Greenhouse-Geisser, F=4.63, df=2.7, *p*=.005, η^2 =.04) but no other effects involving group or gender. Paired comparisons revealed that both relatives of schizophrenia patients (*p*=.01) and relatives of bipolar patients (*p*=.03) had lower scores on the K-scale than control subjects. This was consistent with relatives having slightly greater psychopathology than controls and indicated that the relatives did not adopt a defensive response set.

3.1 Personality characteristics of biological relatives

To determine if the groups differed in personality characteristics we used a repeated-measures ANOVA with group and gender specified as between subjects factors and scale as a within subjects factor for raw scores on all DAPP-BQ scales. The analysis revealed a main effect of group (F=3.01, df=2, 216, p=.05, η^2 =.03) and gender (F=5.11, df=1, 216, p=.02, η^2 =.02), as well as interactions of group and scale (Greenhouse-Geisser, F=4.10, df=17,1900, p<.0005, η^2 =.04) and gender and scale (Greenhouse-Geisser, F=5.64, df=8,1900 p<.0005, η^2 =.02). ANOVA's for each DAPP-BQ scale with group and gender specified as between subjects

factors revealed group effects for anxiousness, cognitive dysregulation, identity problems, passive-aggressive oppositionality, restricted expression, self-harm, social avoidance, and stimulus seeking.[i] Only effects for stimulus seeking, social avoidance, and self-harm were significant at a threshold of p=.003 that took into account the number of ANOVA's conducted. Table 2 reports means and standard deviations for the relative groups and controls on DAPP-BQ scales as well as the results of ANOVA's. Gender main effects were evident for several scales. Men had higher scores on stimulus seeking (F=6.97, df=1,221, p=.009, η^2 =.03), restricted expression (F=17.05, df=1,222, p<.0005, η^2 =.07), callousness (F=23.43, df=1,221, p<.0005, η^2 =.10), rejectionality (F=10.18, df=1,220, p=.002, η^2 =.04), conduct problems (F=31.00, df=1,221, p<.0005, η^2 =.12), and suspiciousness (F=19.18, df=1,220, p<.0005, η^2 =.08). No scale demonstrated a group by gender interaction. To evaluate dependencies resulting from studying individuals from the same family we carried out a mixed-model analysis for each DAPP-BQ scale and specified diagnosis as a fixed factor and family as a random factor. Intraclass correlations reflecting family-level variance adjusted for probands diagnosis were low with the exception of compulsivity and intimacy problems scales (see Table 2). Thus, the scales yielding group differences were minimally influenced by family-level factors.

Pair-wise comparisons revealed relatives of schizophrenia patients to have elevated scores on anxiousness (p=.04, η^2 =.02), restricted expression (p=.04, η^2 =.02), social avoidance (p=.003, η^2 =.05) and submissiveness (p=.03, η^2 =.02) scales and lower scores on the stimulus seeking scale (p<.0005, η^2 =.14) compared to controls. After Bonferroni correction group differences remained for social avoidance and stimulus seeking. It is noteworthy that Bagge and Trull (2003) found that each of the five deviant traits in relatives of schizophrenia patients show the highest correlation with avoidant personality disorder among DSM-defined personality disorders. As compared to controls, relatives of bipolar patients had elevated scores on affective lability (p=.02, η^2 =.04), anxiousness (p=.04, η^2 =.05), cognitive dysregulation (p=.02, η^2 =.05), identity problems (p=.004, η^2 =.06), insecure attachment (p=.02, η^2 =.05), passive-aggressive oppositionality (p=.005, η^2 =.08), self-harm (p<.0005, η^2 =.07), social avoidance (p=.02, η^2 =.04) and submissiveness (p=.05, η^2 =.04). Group differences remained for affective lability, anxiousness, cognitive dysregulation, identity problems, passive-aggressive oppositionality, self-harm, and social avoidance after Bonferroni correction. These traits, along with narcissism, compose the Emotional Dysregulation factor of the DAPP-BQ (Pukrop et al. 2001). Compared to relatives of bipolar patients, relatives of schizophrenia patients had significantly lower scores on narcissism (p=.02, η^2 =.04), passive-aggressive oppositionality (p=.01, η^2 =.04), rejectionality (p=.02, η^2 =.04), self-harm (p=.01, η^2 =.03), and stimulus seeking (p=.003, η^2 =.07). Upon correction for multiple comparisons all group differences remained with the exception of rejectionality.

3.2 Relation of personality deviation to COMT genotype of biological relatives

For personality characteristics on which relative groups differed from controls or from each other, we tested whether the deviations were related to COMT genotype. ANOVAs were carried out for each scale with COMT $Val^{108/158}$ Met polymorphism status (val/val, val/met, met/met) as a between subjects factor. We specified gender as an additional between subjects factor for those scales that showed gender effects in previous analyses. Main effects of COMT genotype were exclusively evident in relatives of schizophrenia patients and there were no effects involving gender. Table 3 presents means and standard deviations for the COMT genotype groups, and results of paired comparisons in the biological relatives of schizophrenia patients. Mixed-model analyses revealed minimal family-level variance as indicated by intraclass correlations of .13 or lower (see Table 3). COMT main effects for narcissism (F=5.46, df=2,76, p=.006) and rejectionality (F=4.17, df=2,76, p=.02) resulted from val/val relatives of schizophrenia patients having reduced narcissism (t=−4.21, df=38, p<.0005, η^2 =.31), and diminished rejectionality (t=−3.31, df=38, p=.002, η^2 =.22) in comparison to met homozygotes.

Importantly, val/val relatives of schizophrenia patients were also deviant from the control sample exhibiting abnormally low narcissism (t=−4.68, df=49, p<.0005, η^2 =.31) and rejectionality (t=−2.72, df=105, p=.008, η^2 =.06). Relatives of schizophrenia patients with the val/met genotype had normative levels of narcissism (t=-.71, df=127, p=.5, η^2 =.00), and rejectionality (t=−1.31, df=125, p=.2, η^2 =.01), as was the case for met/met relatives of schizophrenia patients for narcissism (t=.81, df=103, p=.4, η^2 =.01) and rejectionality (t=1.47, df=101, p=.1, η^2 =.02). The association of COMT genotype with narcissism survived correction for multiple comparisons (threshold *p*=.006) and differences between val/val and met/met relatives of schizophrenia patients for narcissism and rejectionality remained significant after Bonferroni adjustment.

Analyses revealed a trend toward a main effect of COMT genotype for stimulus seeking in the relatives of schizophrenia patients (F=2.84, df=2,76, p=.06). Although all three genotype groups in the relatives of schizophrenia patients had lower stimulus seeking scores than controls (val/val: t=−4.78, df=107, p<.0005, η^2 =.18; val/met: t=−3.17, df=127, p=.002, η^2 =.07; met/met: t=−2.47, df=103, p=.02, η^2 =.06), the relatives with a val/val genotype showed reductions in stimulus seeking in comparison with the other genotype groups [val/met (t=−2.73, df=62, p=.008, η^2 =.11) and met/met (t=−1.88, df=38, p=.07, η^2 =.08) genotypes]; however the within group genotype contrasts were no longer significant after correction of multiple comparisons. There were no main effects of COMT genotype in relatives of bipolar patients, but trends were evident for submissiveness (F=2.68, df=2,36, p=.08, η^2 =.02) and stimulus seeking (F=2.95, df=2,35, p=.06, η^2 =.02).[ii] There were no main effects of COMT genotype in the subset of genotyped control subjects.

4. Discussion

Results indicate that biological relatives of schizophrenia patients, biological relatives of bipolar disorder patients, and nonpsychiatric control subjects can be differentiated on dimensions of personality. Low levels of narcissism and stimulus seeking and a tendency toward diminished rejection of the ideas of others (i.e., rejectionality) differentiated relatives of schizophrenia patients from relatives of bipolar patients. Diminished levels of these traits were most evident in COMT val homozygote relatives of schizophrenia patients. Additionally, val homozygote relatives of schizophrenia patients scored lower on narcissism, rejectionality, and stimulus seeking than their met homozygote counterparts. Relatives of schizophrenia patients also deviated from relatives of bipolar patients by not having elevated self-harm and passive-aggressive oppositionality, and from controls in having high levels of restricted expression and social avoidance. None of these characteristics were however associated with COMT genotype. Biological relatives of bipolar and schizophrenia patients shared elevations in anxiousness, social avoidance, and submissiveness. But personality deviations in relatives of bipolar patients failed to be associated with the COMT $Val^{108/158}$Met polymorphism. Thus, characteristics shared by the relative groups are unrelated to the COMT gene. Instead the $Val^{108/158}$Met polymorphism of the COMT gene, and specifically the val allele, appears to be tied to elements of personality deviation (abnormally low narcissism, rejectionality, and stimulus seeking) that separate relatives of schizophrenia patients from relatives of bipolar patients and are perhaps specific to genetic liability for schizophrenia.

Being homozygous for the val allele predicts features that appear suggestive of psychosis-proneness in biological relatives of schizophrenia patients. Both deviantly low narcissism and abnormal receptivity to the ideas of others (i.e., low rejectionality) may suggest the presence of an underdeveloped self-concept. Although DAPP-BQ scores do not appraise clinical significance, these characteristics are phenomenologically similar to Schneiderian first-rank symptoms of made volition and passivity experiences proposed to be specific to schizophrenia (Schneider, 1959). Additionally, aspects of Schneiderian symptomatology have been shown

to be correlated in sibling pairs affected by schizophrenia and may be heritable (Loftus et al. 2000).

With respect to cognitive correlates of the COMT gene, Tunbridge et al. (2006) suggested that the COMT Val$^{108/158}$ Met polymorphism affects a functional trade-off between cognitive flexibility and stability. Specifically, that the val allele may be at a disadvantage in situations in which holding cognitive information stable is beneficial (e.g. working memory) and an advantage in tasks that require disengagement of cognitive states. Perhaps cognitive flexibility extends to self-perception. It is possible that val homozygote relatives of schizophrenia patients have elevated cognitive flexibility with a tendency toward permeable self-concepts and passivity. Additionally, reduced stimulus-seeking associated with the val allele is consistent with anhedonia evident in individuals at risk for psychosis and biological relatives of schizophrenia patients. Investigations have provided evidence for a relationship between dopamine and sensation-seeking traits perhaps affected by COMT (e.g., Tochigi et al. 2006; Stuettgen et al., 2005). We found relatives of schizophrenia patients as a group exhibit personality traits consistent with avoidant personality disorder (Bagge and Trull, 2003). Although avoidant personality disorder is not traditionally considered to be part of the schizophrenia spectrum of disorders, studies have shown avoidant personality disorder to be elevated in relatives of schizophrenia patients (e.g., Asarnow et al. 2001; Hans et al. 2004).

Relatives of bipolar patients had additional scale elevations, unshared with relatives of schizophrenia patients, that were consistent with hyperthymic temperament (i.e., affective lability, cognitive dysregulation, identity problems, insecure attachment, and self-harm). These 2003; Pukrop et al. 2001) and are broadly consistent with the clinical symptoms of bipolar disorder. Thus, the phenomenology that distinguishes schizophrenia and bipolar disorder appears to extend to individuals who carry genetic liability for the disorders. Although we did not find any associations between COMT polymorphisms and personality amongst relatives of bipolar disorder patients, this comparison may be underpowered, particularly with respect to detecting genotype effects. Thus, type II error cannot be ruled out. Future studies examining the effect of COMT on personality in biological relatives of bipolar disorder probands should include larger subject samples to test for the association.

Using personality as a phenotype may help to further illuminate unique and shared genetic liability for schizophrenia and bipolar disorder, as well as help clarify how specific genes interact with other elements of liability to produce psychopathology. In summary, we found COMT val homozygote relatives of schizophrenia patients had low scores on narcissism, rejection of ideas (i.e., rejectionality), and stimulus seeking in contrast to controls and met homozygote relatives of schizophrenia patients. Although relatives of bipolar patients showed scale elevations consistent with emotional dysregulation, the scores failed to be associated with COMT genotype. The present findings suggest that within relatives of schizophrenia patients the val allele may predispose an underdeveloped self-concept consistent with made volition and passivity experiences comprising first-rank symptoms of schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of Participants

	Relatives of Schizophrenia Patients	Relatives of Bipolar Patients	Nonpsychiatric Control Subjects
N	95	46	87
% female	66	54	48
Mean age (SD)	52.03 (12.9)	50.22 (15.8)	2.29 (15.4)
% Lifetime Axis I Disorder	26.3	32.6	4.6
% Lifetime MDD	20.0	21.7	0
% Lifetime BPD	1.1	0	0
% Lifetime Alcohol/Drug Dependence	5.3	2.2	3.4
% Lifetime Axis II Disorder	4.2	4.3	0
% Lifetime SCZ Spectrum Disorder	4.2	2.2	0

Note SD=Standard deviation; MDD=Major Depressive Disorder; BPD=Bipolar Disorder; SCZ Spectrum Disorder=DSM-IV Psychotic Disorders and Cluster A Personality Disorders.

Table 2

Mean Raw Scores and Standard Deviations on Dimensional Assessment of Personality Pathology – Basic Questionnaire (DAPP-BQ) scales for Relatives of Schizophrenia Patients, Relatives of Bipolar Patients, and Control Subjects.

	SCZ-rel Raw Score Mean (SD) (N=95)	BPD-rel Raw Score Mean (SD) (N=46)	Control Raw Score Mean (SD) (N=87)	F	p	η^2	ICC
Affective Lability	31.9 (10.08)	34.1 (10.65)[b‡]	29.9 (8.36)	2.73	.07	.03	.07
Anxiousness	31.9 (11.72)[a]	33.5 (12.85)[b‡]	28.5 (9.42)	3.51	.03	.03	.00
Callousness	25.9 (6.73)	26.6 (8.26)	27.9 (8.71)	.59	.55	.01	.00
Cognitive Dysregulation	22.9 (7.2)	24.5 (7.29)[b‡]	21.6 (5.15)	3.31	.04	.02	.00
Compulsivity	50.5 (8.83)	51.6 (9.75)	53.0 (9.7)	1.77	.17	.01	.30
Conduct Problems	22.2 (6.75)	23.6 (8.05)	22.6 (6.19)	.63	.53	.01	.00
Identity Problems	25.9 (10.35)	28.8 (11.93)[b‡]	23.6 (7.24)	4.60	.01	.04	.14
Insecure Attachment	28.1 (9.72)	30.2 (9.75)[b]	26.2 (7.98)	2.90	.06	.02	.15
Intimacy Problems	30.2 (10.15)	28.3 (9.19)	24.5 (9.35)	.31	.73	.00	.25
Narcissism	32.8 (10.24)[c‡]	37.1 (9.75)	34.8 (9.79)	2.26	.11	.02	.01
Passive-Aggressive Opp.	30.8 (10.5)[c‡]	35.2 (10.18)[b‡]	29.9 (7.72)	4.70	.01	.04	.03
Rejectionality	36.0 (9.55)[c]	39.8 (10.05)	37.8 (8.6)	1.99	.14	.02	.00
Restricted Expression	38.9 (10.95)[a]	37.1 (10.49)	35.8 (9.81)	4.05	.02	.02	.14
Self-Harm	13.8 (5.11)[c‡]	16.2 (8.66)[b‡]	12.6 (2.58)	6.43	.002[†]	.06	.02
Social Avoidance	32.4 (11.52)[a‡]	32.0 (13.36)[b‡]	27.2 (8.87)	6.32	.002[†]	.05	.02
Stimulus Seeking	31.6 (7.36)[a‡,c‡]	36.3 (9.51)	38.4 (9.31)	12.80	<.0005[†]	.12	.00
Submissiveness	35.4 (10.56)[a]	35.7 (9.39)[b]	32.2 (9.14)	2.91	.06	.03	.00
Suspiciousness	20.3 (6.18)	22.2 (7.77)	21.7 (7.16)	.69	.5	.01	.00

Note: Each DAPP-BQ scale has 16 items scored on a 5-point scale, with the exception of Suspiciousness and Self-Harm which have 14 and 12 items, respectively.

SCZ-rel=relatives of schizophrenia patients, BPD-rel=relatives of bipolar patients.

Results of a ANOVA with group and gender specified as the between subjects factors. The *F* statistic is for the group effect. η^2 represents the effect size of group from ANOVA computation. ICC = intraclass correlation reflecting family-level variance adjusted for probands diagnosis.

SD=Standard Deviation

[a]SCZ-rels differ from controls,

[b]BPD-rels differ from controls;

[c] SCZ-rels differ from BPD-rels

† =significant with threshold of $p \leq .003$ for tests across 18 DAPP-BQ scales

‡ =significant after Bonferroni correction

Table 3

DAPP-BQ Scores in Biological Relatives of Schizophrenia Patients by COMT Genotype and Controls for Scales Showing Val[108/158] met Polymorphism Effects.

	ICC	COMT Effect in ANOVA of SCZ-rel Effect Size partial η^2	SCZ-rel val/val Raw Score Mean (SD) N=22	SCZ-rel val/met Raw Score Mean (SD) N=42	SCZ-rel met/met Raw Score Mean (SD) N=18	Controls All Genotypes Raw Score Mean (SD) N=87
Narcissism	.07	.13	26.7 (6.42)^{a,b‡,c}	33.4 (11.9)	36.8 (8.77)	34.8 (9.8)
Rejectionality	.001	.10	32.3 (7.82) ^{b‡,c}	35.6 (9.95)^{d}	41.1 (8.94)	37.8 (8.6)
Stimulus Seeking	.13	.07	28.1 (7.53)^{a,c}	33.3 (6.92)^{c}	32.6 (7.4)^{c}	38.4 (9.31)

Note: : Each DAPP-BQ scale has 16 items scored on a 5-point scale, with the exception of Suspiciousness and Self-Harm which have 14 and 12 items, respectively.

SCZ-rel=biological relatives of schizophrenia patients, SD=Standard Deviation. η^2 represents the effect size of group from ANOVA computation. ICC = intraclass correlation reflecting family-level variance for unconditional mixed-model.

^{a}SCZ-rel val/val differ from SCZ-rel val/met,

^{b}SCZ-rel val/val differ from SCZ-rel met/met,

^{c}Different from controls,

^{d}SCZ rel val/met differ from SCZ-rel met/met.

‡=significant after Bonferroni correction.