DOPAMINE AND EMOTION PROCESSING IN SCHIZOTYPAL ANHEDONIA

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The undersigned, appointed by the dean of the Graduate School, have examined the thesis entitled

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Chapter 1: Emotion Processing in Anhedonia

Negative symptoms, such as anhedonia, are an important predictor of poor outcome in schizophrenia and increasingly are an important target for clinical interventions (Kirkpatrick, Fenton, Carpenter, & Marder, 2006). Anhedonia refers to a loss of self-reported pleasure (Meehl, 1962), including for both social and physical experiences (Chapman, Chapman, & Kwapil, 1995), and anhedonia is a prominent symptom in people with schizophrenia (e.g., Horan, Green, Kring, & Nuechterlien, 2006). At the same time, social anhedonia also predicts future schizophrenia-spectrum disorders (Gooding, Tallent, & Matts, 2005; Kwapil, 1998). Furthermore, there is evidence that negative symptoms like anhedonia can appear in the prodromal phase even before the emergence of psychotic symptoms (Hafner & an der Heiden, 2003). Hence, understanding the nature of anhedonia might provide evidence about the nature of the liability for schizophrenia (Lenzenweger, 1999). Previous research suggests a possible diminution of emotional experience in anhedonia (e.g., Kerns, 2006). The current research examined whether anhedonia in people at-risk for schizophrenia-spectrum disorders was associated with a decrease in two specific facets of emotional experience, valence and arousal. In addition, the current research examined two possible ways that emotion experience could be altered in anhedonia: (a) a generalized change in emotion; or (b) a change in the types of emotional situations typically experienced by people with anhedonia.

Although there is no agreed upon definition of emotion, emotions are often thought to be complex reactions to personally significant events that include

feelings as well as physiological and behavioral changes (VandenBos, 2006). Emotion research involves many important questions, such as what causes an emotion, what are its neurobiological correlates, and what are its consequences for information processing and behavior (LeDoux, 2000; Phelps, 2006). The current research specifically examined emotional experience and whether anhedonia is associated with changes in the subjective experience of emotion. According to a recent review of research and theoretical views of emotional experience (Barrett, Mesquita, Ochsner & Gross, 2007), emotional experience involves multiple features. One possible core feature of emotional experience is valence, or a sense of pleasure or displeasure. Another very common feature of emotional experience is arousal, or a sense of activation or deactivation (e.g., 'excited' is a high arousal emotion whereas 'serene' is a low arousal emotion). At the same time, it is thought that these features of emotional experience might interact with both the amount of attention given to affective feelings and the depth of conceptual knowledge used to process these feelings (Barrett et al., 2007; Frijda & Sundararajan, 2007; Lambie & Marcel, 2002). Therefore, emotional experience is thought to involve certain core affective features, such as valence and arousal, and that how these affective features are experienced depends upon attention and conceptual processing. The current study specifically focused on whether anhedonia is associated with changes in self-reported valence or arousal.

Some previous research suggests that anhedonia might be associated with changes in the experience of valence and arousal. For valence, some previous research suggests that anhedonia might be associated with decreased self-reported

positive affect. For instance, anhedonia has been typically measured using trait self-report measures largely assessing whether people tend to find particular experiences pleasurable or not (e.g., Chapman, Chapman, & Raulin, 1976). Moreover, anhedonia has been associated with decreased trait positive affect (Gooding, Davidson, Putnam & Tallent, 2002; including in people with schizophrenia, Horan & Blanchard, 2003) and with decreased extraversion (Kerns, 2006; Mason, 1995; Ross, Lutz, & Bailey, 2002; with one view of the nature of extraversion is that it largely reflects trait levels of positive affect; Lucas & Diener, 2001; Watson, Gamez, & Simms, 2005). In contrast, anhedonia has been only weakly associated with neuroticism (Kerns, 2006; Mason, 1995; Ross et al., 2002). One view of neuroticism is that it largely reflect trait levels of negative affect (Watson et al., 2005), suggesting that anhedonia might be weakly associated with increased negative affect. Hence, some previous anhedonia research suggests that it might be related to a reduction in positive affect and possibly to a small increase in negative affect. However, although anhedonia has been associated with trait measures of affect, some previous emotion research has found some dissociations between people's beliefs about how they typically feel as assessed by trait measures versus how they report feeling in current situations (Robinson & Clore, 2002). Hence, the current research examined whether people with anhedonia would also report changes in emotional experience for specific situations.

In addition to possible changes in the experience of valence, some previous research suggests that anhedonia could be related to changes in the

experience of emotional arousal (i.e., sense of activation or deactivation). For instance, it has been found that anhedonia is associated with an atypical left hemisphere bias on the chimeric faces task (Luh & Gooding, 1999). The typical right hemisphere bias on this task is thought to reflect right parietal functioning, with the right parietal area being associated with emotional arousal (Heller, 1994). At the same time, anhedonia has been associated with decreased scores on a questionnaire assessing the trait affect intensity (Kerns, 2006). It is possible that a decrease in trait affect intensity could reflect a decrease in the experience of high arousal emotions (for both positive emotions, e.g., 'excited' & 'alert', and negative emotions, e.g., 'stressed' & 'nervous'; Barrett & Russell, 1999). Therefore, it is possible that anhedonia might reflect a decreased experience of high arousal emotions, however to our knowledge this has not been examined in previous research.

Based on previous research, we examined whether anhedonia was associated with a decrease in positive affect, a small increase in negative affect, and with a decrease in high arousal emotions. In addition, in the current research we also examined the nature of any change of emotional experience in anhedonia. Although there are many possible ways that emotion experience could be altered, the current research focused on two general possibilities for how emotion experience might be changed in anhedonia. One possibility is that people with anhedonia report a generalized change in emotional experience. The second possibility is that people with anhedonia differ from other people in the types of emotion-eliciting situations they tend to experience. Importantly, these two

possibilities make different predictions regarding when reports of emotion experience should be altered for people with anhedonia. If people with anhedonia have a generalized change in emotional experience, then it would be expected to be found across situations and reporting formats. In contrast, if people with anhedonia differ in emotional experience because of the types of situations they tend to experience, then reports of their emotional experience should vary by the type of situation and also possibly by the type of reporting format.

In the current research, we examined five methodological factors that might reveal the specific types of situations and reporting formats where people with anhedonia might selectively report altered emotion experience. One methodological factor is whether emotions concern reactions to daily life situations or to lab stimuli. If people with anhedonia report decreased emotion experience because they are less likely to experience emotion-eliciting events, then they should report decreased emotion for the idiosyncratic real-world situations they experience, but they should not report decreased emotion for lab stimuli because with lab stimuli every participant responds to the exact same stimulus. Evidence for this type of dissociation between real-world versus lab stimuli has been found in people with schizophrenia. Although people with schizophrenia report decreased positive affect (and increased negative affect) in their daily lives (e.g., Myin-Germeys, Delespaul, & de Vries, 2000), accumulating evidence suggests that people with schizophrenia do not report decreased positive affect for lab stimuli (Burbridge & Barch, 2007; Horan et al., 2006; Kring, 1999). Previous research in people at possible risk for schizophrenia examining whether

physical anhedonia is associated with a reduction in positive affect for emotional stimuli in lab situations is very mixed (Berenbaum, Snowhite, & Oltmanns, 1987; Ferguson & Katkin, 1996; Fiorito & Simons, 1994; Fitzgibbons & Simons, 1992; Germans & Kring, 2000), while to our knowledge this has not been examined in social anhedonia.

A second methodological factor is whether emotions concern social versus non-social situations. For example, people with social anhedonia report not enjoying social situations (Eckblad, Chapman, Chapman, & Mishlove, 1982). It is possible that any decrease in positive affect for people with social anhedonia could be restricted to social situations. Moreover, given evidence that people with social anhedonia might have poorer quality social interactions (Collins, Blanchard, & Biondo, 2005; possibly due to reduced emotional expression; Aghevli, Blanchard, & Horan, 2003), any decrease in positive affect for social situations might be due to people with social anhedonia having fewer interactions with people that they are close to.

A third methodological factor is whether emotion reports are for retrospective or for current situations. Previous research has found some dissociations between how people remember feeling in previous situations versus how they actually report feeling in a current situation (Robinson & Clore, 2002). For example, perhaps people with anhedonia could have a memory bias and remember positive experiences as being less positive than they actually were (e.g., Horan et al., 2006, with a memory bias possibly developing due to experiencing

fewer positive situations). In contrast, people with anhedonia may not differ in current or "in the moment" reports of emotion.

A fourth methodological factor is whether emotion reports are for emotion intensity or for emotion frequency (Schimmack & Diener, 1997). People can vary in how intensely (or strongly) they experience emotions (e.g., tending to feel emotions like 'excited' or 'serene' weakly or strongly). At the same time, people can also vary in how frequently they experience emotions (e.g., tending to feel emotions like 'excited' or 'serene' rarely or quite often). If people with anhedonia experience more or less of a certain type of emotion-eliciting situation, it is possible that this could be reflected in a change only in emotion frequency but not intensity (e.g., experiencing more negative situations and therefore having more frequent negative emotions).

A fifth methodological factor is whether emotion experience is assessed through direct self-report or is assessed indirectly. Previous research has found evidence that self-reported emotional experience may not be commensurate with other indicators of emotions. Hence, people might report not experiencing an emotion even when they behaviorally appear to be emotional (e.g., Berenbaum & Irvin, 1996). Therefore, it would be helpful to assess emotion experience without directly asking participants to report their own emotions. For example, it has been found that people who on a questionnaire report reduced trait level affect intensity also report less emotional content and focus less on emotions in their descriptions of life events (e.g., describing what it would be like to have your house burn down; Larsen, Billings, & Cutler, 1996). However, if in anhedonia self-report is

not an accurate reflection of emotional experience, then it is possible that a decrease in self-reported emotion might not be accompanied by decreased content in their descriptions of what it is like to experience life events.

Overall, in two studies we examined whether anhedonia was associated with changes in facets of emotional experience. For valence, we examined whether anhedonia was associated with decreased positive affect and increased negative affect. For arousal, we examined whether anhedonia would be associated with decreased high arousal emotions. In addition, we used a variety of methods to characterize the nature of any change of emotional experience in anhedonia. We examined two possibilities for how emotional experience might be altered in anhedonia. One possibility is that anhedonia involves a generalized change in emotional experience, which predicts differences in emotions should be found across situations and reporting formats. In contrast, the second possibility is that anhedonia involves a change in the types of experiences that people tend to have, which should be selectively reflected in changes in emotional experience for one or more of the following: retrospective (but not current) emotions, daily life (but not lab) situations, social (but not non-social) situations, frequency (but not intensity) of emotions, and direct self-reports (but not verbal descriptions) of emotional experience.

Study One

In Study 1, we specifically examined social anhedonia. We did this because social anhedonia has been found to predict future schizophrenia-spectrum disorders (Gooding et al., 2005; Kwapil, 1998) and because few if any studies to

our knowledge have examined self-reports of emotional experience in social anhedonia. In Study 1, we used an extreme-groups approach (Preacher, Rucker, MacCallum, & Nicewander, 2005) that compared people with elevated social anhedonia to two other groups: a control group and a group with elevated levels of perceptual aberration and magical ideation (PerMag). We included the PerMag group in order to examine whether any changes in emotional experience would be specific to social anhedonia or would also be found in another group that is at increased risk of psychosis (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994).

Methods

Participants

Participants were college students attending a large Midwestern public university who received credit for an Introduction to Psychology course for their participation. They were selected from among a group of students (n = 4,165) who participated in departmental mass testing sessions in which they completed 15 items from the Revised Social Anhedonia Scale, seven items from the Perceptual Aberration Scale, and eight items from the Magical Ideation Scale. Individuals who scored either 2.0 standard deviations above or 0.5 standard deviations below the mass testing same-sex gender mean were recruited for an individual testing session. At the individual testing session, participants completed the full versions of these scales and participants for the current study were selected based on their scores for the full version of the scale, with means

and standard deviation cut-offs for the scales based on data obtained from a previous large sample study (Kerns & Berenbaum, 2000).

There were 40 people in the social anhedonia (SocAnh) group (27 females, mean age = 18.7, SD = 1.2; 35 Caucasian, 3 African-American, 2 Asian-American) who scored at least 1.96 SD above the same-sex mean on the Revised Social Anhedonia Scale. There were 30 people in the Control group (20 females, mean age = 18.6, SD = 1.1; 28 Caucasian, 1 African-American, 1 Asian-American) who scored less than 0.5 SD above the mean on the Revised Social Anhedonia, Perceptual Aberration, and Magical Ideation scales. There were 29 people in the PerMag group (17 females, mean age = 18.6, SD = 1.2; 26 Caucasian, 2 African-American, 1 Asian-American) who scored at least 1.96 SD above the same-sex sample mean on either the Perceptual Aberration or the Magical Ideation scale, or who had summed standardized Perceptual Aberration and Magical Ideation scores of 3 or higher (Chapman et al., 1994). Participants (n = 8) who scored high enough for both the SocAnh and the PerMag groups were excluded.

Psychosis-Proneness and Personality Questionnaires

Psychosis-Proneness Scales. Participants completed a 118-item true-false questionnaire composed of a random mixture of all items of three psychosis-proneness scales – the Revised Social Anhedonia Scale (Eckblad, Chapman, Chapman, & Mishlove, 1982), the Perceptual Aberration Scale (Chapman, Chapman, & Raulin, 1978), and the Magical Ideation Scale (Eckblad & Chapman, 1983) – as well as the Chapman Infrequency Scale (Chapman & Chapman, 1983), which measures careless or invalid responses. Following previous research (e.g.,

Chmielewski, Fernandes, Yee, & Miller, 1995), participants who endorsed three or more Infrequency Scale items were excluded. These scales have been used extensively in previous research (e.g., Edell, 1995; Horan, Blanchard, Gangstead, & Kwapil, 2004; Lenzenweger, 1999). High scorers on the Social Anhedonia scale are at increased risk for schizophrenia-spectrum disorders (Gooding et al., 2005; Kwapil, 1998) and high scorers on the Perceptual Aberration and Magical Ideation scales have been found to be at increased risk for future psychosis (Chapman et al., 1994).

Personality Traits. To examine whether any changes in emotion experience in anhedonia might be related to personality, the personality traits of Extraversion and Neuroticism were measured using the International Personality Item Pool (IPIP: Goldberg, 1999), with 10 items for both Extraversion (e.g., "Am the life of the party") and Neuroticism (e.g., "Get stressed out easily"). Responses are made with a 5-point scale indicating amount of agreement. Although we examined whether personality could statistically account for emotional changes in anhedonia, importantly it is unclear from previous research whether broad personality traits should be considered as the cause or the result of affective changes, making it uncertain whether they are a source of potential confounding (for methodological limitations of using statistical "controls" see Miller & Chapman, 2001).

Emotional Experience

Emotional experience was directly assessed in three different ways: the day reconstruction method (DRM), the situation rating task, and the picture rating

task. In all three assessments, following Barrett and Russell (1999), 16 different emotions were rated, including positive high arousal (happy, excited, alert, elated), positive low arousal (relaxed, contented, serene, calm), negative high arousal (stressed, nervous, upset, tense), and negative low arousal (lethargic, fatigued, sad, depressed). Hence, this allowed for the assessment of both emotional valence (positive versus negative) as well as emotional arousal (high versus low; in addition, at the end of the study, these emotion terms were used to assess current mood).

In addition, in all three assessments, to separately assess emotion frequency and emotion intensity, we followed the procedures used by Schimmack and Diener (1997). Emotions were rated on a scale from 0 to 6. Participants were told that they should first decide whether they experienced a particular emotion or not. They were told that if they did not experience that emotion that they should rate the emotion a 0. Hence, the measure of affect frequency is the proportion of all possible emotions not rated 0. Participants were told that if they had experienced the emotion, then they were told to rate how intensely they experienced that emotion from 1 to 6. Hence, the measure of intensity is the average of all emotions that were rated between 1 and 6.

The DRM was developed by Kahneman, Krueger, Schkade, Schwarz, and Stone (2004) as a one-time assessment of emotional experience that would share the advantages of experience sampling methods (e.g., reduced memory bias and therefore more likely to reflect actual emotional experience). On the DRM, people first reconstruct everything that happened to them on the previous day, from when

they woke up until when they went to bed. People divide up their day into discrete episodes (e.g., getting ready for school; being in class; going out to eat). After dividing up their day into episodes, then they rate how they felt during each episode. In addition, for each episode, people indicate if they were with anyone and who they were with (e.g., a friend, a significant other). This allows for an assessment of emotion in both social and nonsocial situations. It also allows for the assessment of emotion when interacting with people the participant is close to, defined as friends, significant others, and family. The DRM takes approximately 30-45 minutes to complete. On the DRM, the number of episodes that participants divide their previous day into can vary from person to person (e.g., in this study, range was from 5 to 29). The three groups did not differ in the mean number of episodes on the DRM that they rated, $p = .60$. In addition, as they were finishing the DRM, participants rated how typical their previous day was (from much worse, to typical, to much better). The groups did not differ significantly in how typical they rated the previous day, $p = .58$.

In addition to the DRM, participants also completed the situation rating task. This method has also been recommended by Kahneman et al. (2004) as a one-time assessment of emotional experience that shares some of the advantages of experience sampling methods. Participants were first asked to remember the last time they were in a particular situation (excluding the previous day). Then, after they remembered a specific occasion, they then rated how they felt in that situation. Participants rated 20 different positive, neutral, and negative situations (last time they took an exam, went to a sporting event, went to a movie, talked to

a friend on the phone, were in the car for more than 30 minutes, read a book, watched a TV program you usually like, watched news on TV, went shopping, talked to a relative, talked to someone you found attractive romantically, exercised, ate at a restaurant, went to a party, attended class, went to the library, went to a coffee shop, had a disagreement with a friend, heard a joke, and played with an animal/pet). Compared to the DRM, the situation rating task can involve less recent experiences; hence it is more susceptible to memory biases in people's ratings. However, one advantage of the situation rating task is that each participant rates their emotion over a broad range of experiences.

In addition to the DRM and the situation rating task, participants also completed a picture rating lab task. On this task, participants saw a picture from the International Affective Picture Set (IAPS; Lang, Bradley, & Cuthbert, 2005) for 10 seconds. Then they rated their emotional reaction to the picture. The picture rating lab task complements the DRM and the situation rating task in two ways. On the one hand, this task involves people's concurrent assessment of their emotional reactions. Hence, this assessment method eliminates any memory distortion in reporting emotional experience. On the other hand, every participant rates their emotional reactions to identical stimuli. Hence, any group differences cannot be due to differences in the events or stimuli that people experience. Participants rated 16 different IAPS pictures. The IAPS pictures used were the same ones selected by Barrett (2004) to assess a range of both emotional valence and emotional arousal. In the results section, results will be presented for level of positive affect reported for positive pictures and level of negative affect reported

for negative pictures. However, there were no significant between group differences for any of the other emotion ratings (all *p*'s > .45; e.g., the groups did not differ in level of positive affect for negative or neutral pictures).

Event Description Questionnaire

Emotional experience was indirectly assessed with the event description questionnaire (EDQ; Larsen et al., 1996; EDQ version 1 was used in the current study). On the EDQ, people are given 8 events that they need to describe, 4 positive and 4 negative, with the events varying in how strongly they elicit affect (e.g., having your house burn down; losing your favorite pen). On the EDQ, participants are given 90 seconds to describe each event. Participants are told to imagine what each experience is like and then write down a description that would inform another person who has never had the experience before know what it is like. Two ratings were made from the EDQ verbal descriptions. One, labeled *emotional content* (Larsen et al., 1996), was a count of the number of emotion-related terms within each description. The second, labeled *focus on feelings* (Larsen et al., 1996), was the degree to which people emphasized feelings versus emphasized facts in their description of the event, which was scored from 1 (extreme focus on facts; e.g., for having money problems: "Having money problems does not enable you to do very much. You have to rely a lot on what you already have. You can't spend any money that you have on anything that isn't of important use.") to 7 (extreme focus on feelings; e.g., for having money problems: "Anxiety, worry, this is a horrible feeling. It's a feeling of failure. You worry all of the time about people coming and taking away your possessions.").

Ratings were made by two research assistants who were blind to the hypotheses and to group membership. Interrater reliability using an intraclass correlation (Shrout & Fliess, 1979), treating the raters as random effects and the mean of the 2 raters as the unit of reliability was 0.97 for positive emotional content, 0.87 for positive focus on feelings, 0.97 for negative emotional content, and 0.90 for negative focus on feelings. Total scores for emotional content and focus on feelings were highly associated with each other (for positive descriptions, r = 0.88; for negative description, r = 0.94). Hence, a single positive event description and a single negative event description variable were created by summing standardized scores. In addition, the groups did not differ in the number of words in their descriptions, F (2, 96) = 0.39, p = .68; means and SDs for each group: SocAnh 33.5 (13.7), PerMag 32.9 (16.4), Control 35.1 (14.9; note also that the focus on feelings ratings are not based on the number of words produced).

Procedure and Data Analysis

Participants completed the study in the following order: EDQ, DRM, situation rating task, picture rating task, questionnaire measures, and current mood assessment. The EDQ was given first because pilot testing indicated that prior emotion ratings (e.g., on the DRM) could inadvertently increase the amount of emotional content provided on the EDQ (note also that because the DRM first involves reconstructing one's previous day, this means that there was an approximately 10 to 20 minute delay between completing the EDQ and making emotion ratings on the DRM). In addition, note that if current mood assessment is largely influenced by prior emotion rating tasks then (a) between-group results for

current mood and emotion rating tasks should be the same; and (b) current mood should statistically account for group differences in emotion rating tasks.

In analyzing the three emotion experience tasks (i.e., DRM, situation rating, and picture rating), data was analyzed using 2 (valence: positive versus negative) X 2 (arousal: high versus low) X 3 (task: DRM versus situation rating versus picture rating) X 3 (group: SocAnh versus Controls versus PerMag) mixed-model (three within-subjects factors and one between-subjects factor) ANOVA. If the SocAnh group differed from the other two groups in positive affect but not negative affect (or vice versa), this should be reflected in a significant valence by group interaction. Hence, significant valence by group interactions were followed up by ANOVAs including only positive affect and including only negative affect (i.e., arousal X task X group). At the same time, if the SocAnh group differed from the other groups in reports of emotion experience only for events in their daily lives but not for the picture rating lab task in which all participants saw the exact same stimuli, this should be reflected in a significant task by group interaction. Significant omnibus results were followed up with planned comparisons between (a) the SocAnh group and the Control group; and (b) the SocAnh group and the PerMag group. To control for the familywise error rate, for these planned comparisons we used a Bonferroni correction, with significance $p < .025$.

In reporting effect sizes, we used partial η^2 for omnibus tests and r for all other effect sizes (for r as an effect size, i.e., point-biserial correlation, see Rosenthal, 1991; note that r can be converted to d, with $r \geq 0.371$, $r \geq 0.243$, and

$r \geq 0.10$ corresponding to large, medium, and small effect sizes, respectively). Positive *r* effect sizes indicate the SocAnh group larger than the other groups (or the PerMag group larger than the Control group).

Results

Intensity of Emotion

For intensity of emotion ratings, as can be seen in Table 1, there was a significant interaction between valence and group, F (2, 96) = 6.04, p = .003, partial η^2 = .118. The interaction between group and valence reflects that there was a significant between-groups difference in an ANOVA for positive affect but not for negative affect: positive affect, F (2, 96) = 4.45, p = .014, partial η^2 = .083; negative affect, F (2, 96) = 0.27, p = .973, partial η^2 = .001. We next compared the SocAnh group with the other two groups on positive affect intensity. The SocAnh group reported significantly less intense positive affect than the Control group, t (68) = 3.51, p = .0008, r = -0.39, and the PerMag group, t (67) = 2.38, p = .02, r = -0.28 (note that the effect size difference between the PerMag group and the Control group was r = -0.10). For positive affect intensity, the interaction between task and group was not significant, F (2, 96) = 0.18, p = .84, partial η^2 = .004 (i.e., the SocAnh group reported decreased positive affect intensity on all three tasks; e.g., comparing SocAnh and Controls on positive affect intensity, between-groups effect sizes for the three tasks were r = -0.30, r = -0.33, and r = -0.27). No other effects involving group were significant (all p's > .35). For example, the interaction between group and arousal was not significant, F (2, 96) = 1.04, p = .36, partial η^2 = .024, as the SocAnh group did not selectively report decreased

high arousal emotions than controls (i.e., results were similar for high and low arousal emotions; e.g., the between-groups effect sizes between SocAnh and Controls for positive affect were r = -0.31 for high arousal and r = -0.34 for low arousal; for negative affect they were r = -0.02 for high arousal and r = 0.01 for low arousal).

Given that the SocAnh group reported decreased positive affect intensity for events in their daily lives, one possible explanation for this decrease is that the SocAnh group spends less time with people they are close to. To attempt to examine this, positive affect intensity ratings on the DRM were examined only for social situations where people were with either friends, significant others, or family. Overall, there was a significant between-groups difference in positive affect intensity, F (2, 96) = 3.33, p = .04, partial η^2 = .083, as even for these close relationships, the SocAnh group reported significantly decreased positive affect intensity than Controls, t (68) = 2.90, p = .005, r = -0.33, but they did not differ significantly from the PerMag group, t (67) = 1.36, p = .18, r = -0.16. In addition, the groups did not significantly differ in the number of situations interacting with people they were close to: F (2, 96) = 0.83, p = .44; means (and SDs) for each group: SocAnh 6.2 (3.1), PerMag 6.5 (3.0), Control 7.2 (3.6).

Another possible explanation for the decrease in positive affect intensity for daily experiences in the SocAnh group is that it is limited to social situations. If true, this would predict that the SocAnh group should not report decreased positive affect intensity when they are alone. As can be seen in Figure 1, there was a trend for a significant arousal by group interaction, F (2, 96) = 2.84, p =

.06, partial η^2 = .066. This trend for an interaction reflects that for situations when they were alone that the SocAnh group and Control groups differed on low arousal positive affect intensity, t (68) = 2.41, p = .019, r = -0.28, but not for high arousal positive affect intensity, t (68) = 0.24, p = .81, r = 0.03 (as the control group, as can be seen in Figure 1, reported decreased high arousal positive emotions, such as 'excited', when they were alone compared to when they were with others). In addition, the groups did not significantly differ in the number of situations when they were alone: F (2, 96) = 0.99, p = .37; means and SDs for each group: SocAnh 4.8 (3.2), PerMag 5.4 (3.1), Control 4.3 (2.0).

Frequency of Emotion

For frequency of emotion ratings, as can be seen in Table 2, there was a significant interaction between valence and group, F (2, 96) = 5.30, p = .0066, partial η^2 = .103. The interaction between group and valence reflects that there was a significant between-groups difference in an ANOVA for negative affect but not for positive affect: negative affect, F (2, 96) = 3.41, p = .037, partial η^2 = .067; positive affect, F (2, 96) = 1.21, p = .30, partial η^2 = .026. We next compared the SocAnh group with the other two groups on negative affect frequency. There was a trend for the SocAnh group to report significantly more frequent negative affect than the control group, t (68) = 2.24, p = .028, r = 0.26 (again, Bonferroni corrected significant p-value < .025). In contrast, the SocAnh and PerMag groups did not differ significantly on negative affect frequency, t (67) = 0.44, p = .66, r = -0.05 (note that the effect size difference between the PerMag group and the control group was r = 0.30). In addition, for negative affect frequency, there was

trend for a significant interaction between task and group, F (2, 96) = 0.18, p = .068, partial η^2 = .046. As can be seen in Table 2, this interaction reflects that the SocAnh group differed from controls in negative affect frequency in reporting on emotions for events in their daily lives, t (68) = 2.67, p = .01, r = 0.31 (note the effect size for the difference between PerMag and controls, r = 0.35); however, the SocAnh group did not differ from controls in negative affect frequency on the lab picture rating task, t (68) = 0.46, p = .65, r = 0.06 (note the effect size for the difference between PerMag and controls, r = 0.12). No other effects involving group were significant (all p's > .30). For example, the interaction between group and arousal was not significant, F (2, 96) = 1.03, p = .36, partial η^2 = .023, as the SocAnh group did not appear to report selectively fewer high arousal emotions than controls (i.e., results were similar for high and low arousal emotions; e.g., the between-groups effect sizes between SocAnh and controls for positive affect were r = -0.12 for high arousal and r = -0.13 for low arousal; for negative affect they were r = 0.22 for high arousal and r = 0.24 for low arousal).

Verbal Descriptions of Emotional Experience

To analyze verbal descriptions of emotion-eliciting events on the event description questionnaire, data was analyzed using a 2 (valence: positive versus negative) X 3 (group: SocAnh versus Controls versus PerMag) mixed-model ANOVA. Overall, there was a significant between-groups difference in the amount of emotional content, F (2, 96) = 3.70, p = .028, partial η^2 = .072. As can be seen in Table 3, this overall between-groups difference reflected that the SocAnh group provided significantly less emotional content and focused

significantly less on feelings than the PerMag group, t (67) = 2.76, p = .007, r = -0.32, and a trend for the SocAnh group to report less than the Control group, t (68) = 2.04, p = .045, r = -0.24. Given previous and current evidence that social anhedonia reflects decreased positive affect, we explored whether the SocAnh group would differ from controls for both positive events and negative events. The SocAnh group did provide less emotional content and focused less on feelings than the Control group for descriptions of positive events, t (68) = 2.41, p = .019, r = -0.28, but not for negative events, t (68) = 1.02, p = .31, r = -0.12.

Relationship between Personality, Current Mood, and Emotion Experience Ratings

As can be seen in Table 3 for personality, compared to Controls, the SocAnh group reported significantly lower levels of extraversion, t (68) = 7.51, p = .000001, r = -0.67, and higher levels of neuroticism, t (68) = 2.89, p = .005, r = 0.33. In addition, as can be seen in Table 3 for current mood, the SocAnh group tended to report lower positive affect, t (68) = 2.04, p = .045, r = -0.24, but significantly higher negative affect, t (68) = 2.41, p = .019, r = 0.28, than the control group. We next examined whether personality and current mood could statistically account for differences between the SocAnh and Control groups in positive affect intensity. For this analysis, we computed a single composite positive affect intensity score by averaging scores on the three emotion experience tasks. As can be seen in Table 4, in a hierarchical multiple regression, personality and current mood were entered first on Step 1. On Step 2, after statistically accounting for variance shared with personality and current mood,

categorical group membership (i.e., SocAnh vs. Control) still significantly predicted decreased positive affect intensity (in addition, statistically accounting for variance shared with positive affect frequency did not affect group differences in positive affect intensity).

Study Two

There were five main goals for Study 2. Study 1 found that people with elevated social anhedonia reported decreased positive affect intensity. However, in addition to social anhedonia, people with schizophrenia also report elevated physical anhedonia (Chapman et al., 1976). One main goal of Study 2 was to examine, in addition to social anhedonia, whether physical anhedonia would also be associated with decreased positive affect intensity.

A second goal of Study 2 was to examine whether current distress could statistically account for associations between anhedonia and positive affect intensity. Previous research has found evidence that self-reported pleasure is reduced in people currently under stress (e.g., final exam week; Berenbaum & Connelly, 1993). From this view, perhaps people with elevated anhedonia in Study 1 reported decreased positive affect intensity because they were currently under stress. Hence, Study 2 examined whether associations between anhedonia and positive affect intensity could be accounted for by current levels of self-reported depression or by reports of recent major or minor stressors.

A third goal of Study 2 was to further examine whether decreased positive affect intensity in anhedonia was not statistically accounted for by either perceptual aberration-magical ideation, personality, or current mood. In Study 1,

these other variables did not statistically account for decreased positive affect intensity in social anhedonia. However, some variables were measured categorically and other variables were measured dimensionally. Potentially the influence of one variable on another could be more clearly examined when they are all measured in a similar way (Kerns, 2006). In Study 2, we separately and dimensionally measured both anhedonia and perceptual aberration-magical ideation to further assess whether only anhedonia and not psychosis-proneness in general was associated with decreased positive affect intensity. At the same time, Study 2 further examined whether decreased positive affect intensity in anhedonia was not statistically accounted for either by personality or by current mood.

A fourth goal of Study 2 was to examine whether in a separate set of participants that anhedonia would again be associated with decreased self-reported positive affect intensity for lab stimuli. Study 1 found that people with elevated social anhedonia report decreased intensity of positive affect both for reports of real-world experiences as well as for responses to lab stimuli. In contrast, research on people with schizophrenia has generally not found decreased self-reported positive affect in response to lab stimuli (e.g., Burbridge & Barch, 2007). Therefore, Study 2 examined whether the finding of an association between anhedonia and decreased positive affect intensity for lab stimuli would replicate in a new sample.

A fifth goal of Study 2 was to examine whether anhedonia would be associated with decreased positive affect for lab stimuli using a dimensional design. An important advantage of dimensional designs is that they provide a less

biased estimate of the effect size for the association between two variables than an extreme-group design that selects groups from the extreme tails of the distribution (Preacher et al., 2005). In fact, it is possible that variation in control group selection could partially account for some of the variation in previous research on positive affect in physical anhedonia. Overall, two previous published studies did not find that physical anhedonia is associated with decreased positive affect for positive lab stimuli (Berenbaum, Snowhite, & Oltmanns, 1987; Germans & Kring, 2000). In contrast, three previous published studies did find a decrease in physical anhedonia (Ferguson & Katkin, 1996; Fitzgibbons & Simons, 1992; Fiorito & Simons, 1994). Importantly, the studies that did find a decrease in physical anhedonia probably selected a more extreme control group than the two studies that did not find a decrease. Hence, variation in whether anhedonia is associated with decreased positive affect for lab stimuli might be due to variation in the selection of the control group. Importantly, in Study 2 we measured anhedonia dimensionally and therefore provide an estimate of the association between anhedonia and positive affect that is less biased relative to an extreme-group design.

In Study 1, social anhedonia was measured categorically in an extreme-groups design. In Study 2, social and physical anhedonia were measured dimensionally. Potentially, each study design has pros and cons. Categorical designs might be a more accurate way of assessing schizotypy facets if they are truly categorical variables (Horan et al., 2004), some schizotypy measures were initially designed to measure the extreme end of the distribution which is focused

on in an extreme-groups design, and there is potentially much less information in the literature about the relationship between measures of schizotypy with other variables across the entire range of schizotypy scores. On the other hand, dimensional designs might allow for a more straightforward examination of the specificity of the association with a schizotypy facet when removing variance shared with other variables. At the same time, previous research has found some similar results for schizotypy facets whether measured dimensionally or categorically (e.g., Kerns, 2005; Kerns, 2006; Kerns & Becker, 2008; Martin & Kerns, manuscripts in preparation) and with large enough samples dimensional designs can still allow for a categorical analysis of data. Perhaps most importantly, as previously discussed, dimensional studies provide a less biased measure of effect size (Preacher et al., 2005). Overall, using both categorical and dimensional designs across multiple studies with their complementary strengths might be able to provide important converging evidence about schizotypy (Shadish, Cook, & Campbell, 2002).

Methods

Participants

Participants were 339 college students (187 females; mean age = 18.7, SD = 1.5; 89% Caucasian, 7% African-American, 2% Latino/Latina, 2% Asian-American) attending a large Midwestern public university who received credit for an Introductory Psychology course for their participation.

Questionnaire Measures

Psychosis-Proneness Scales. As in Study 1, participants completed the Revised Social Anhedonia Scale, the Perceptual Aberration Scale, the Magical Ideation Scale, and Chapman Infrequency Scale. In addition, in Study 2 they also completed the Physical Anhedonia scale (Chapman et al., 1976). Using standardized scores, we created a singe anhedonia score (summing level of social and physical anhedonia) and a single PerMag score (summing level of perceptual aberration and magical ideation). However, given than anhedonia scales tend to be only moderately correlated and have exhibited different associations with other variables in some previous research (e.g., Prince & Berenbaum, 1993), we also report results separately for social and physical anhedonia.

Personality Traits. As in Study 1, the personality traits of Extraversion and Neuroticism were measured using the International Personality Item Pool (IPIP: Goldberg, 1999).

Current Distress. Participants completed two measures to assess their current level of distress. One measure was the Beck Depression Inventory-Second Edition (Beck, Steer, & Brown, 1996), a frequently used measure of current depression and psychological distress. The second measure was the Undergraduate Stress Questionnaire (Crandall, Preisler, & Aussprung, 1992) which lists a number of stressors that could be experienced by undergraduate students that range from major to minor stressors (e.g., "death of a family member or friend"; "victim of a crime"; "property stolen"; "had a class presentation"; "got a traffic ticket"). Two measures of stress were calculated: (a) recent major stress, the frequency of major

stressors reported in the previous two weeks; and (b) recent minor stress, the frequency of minor stressors reported in the previous two weeks.

Emotional Experience

Participants completed the same picture rating task as in Study 1.

Procedure and Data Analysis

Participants completed the study in the following order: picture rating, questionnaire measures, and current mood assessment (note that the picture rating task was the last emotion experience task given in Study 1 but it was given first in Study 2). In data analysis, our primary focus was to examine two associations, whether (a) anhedonia or (b) PerMag scores would be associated with decreased positive affect intensity. In addition, in a hierarchical multiple regression, we examined whether anhedonia would significantly add to the prediction of positive affect intensity after statistically removing variance shared with other variables associated with anhedonia. Note that because use of extreme-groups designs (as in Study 1) inflates effect sizes (Preacher et al., 2005), estimates of the association between anhedonia and positive affect intensity in Study 2 were expected to be smaller than in Study 1.

Results

As can be seen in Table 5, as found in Study 1, anhedonia was significantly associated with decreased positive affect intensity on the picture rating task (anhedonia was associated with both high arousal positive emotions, r = -0.18, p = .001, and low arousal positive emotions, r =

-0.16, $p = .004$). At the same time, both social anhedonia ($r = -0.14$, $p = .01$) and physical anhedonia ($r = -0.20$, $p = .0002$) were significantly associated with decreased positive affect intensity (furthermore, if analyzed categorically, 28 people had elevated anhedonia and they also differed significantly from control participants in level of positive affect intensity, $p < .01$). In contrast to anhedonia, as can be seen in Table 5, PerMag scores were not associated with positive affect intensity. Instead, PerMag scores were significantly associated with increased negative affect intensity.

As can also be seen in Table 5, anhedonia was significantly associated with personality, current mood, and current levels of distress. Hence, we next examined whether these other variables, plus PerMag scores, could account for the association between anhedonia and positive affect intensity. In a hierarchical multiple regression, we first entered PerMag scores, personality, current mood, and current distress. After this, we then entered anhedonia. As can be seen in Table 6, in this analysis anhedonia still significantly predicted decreased positive affect intensity.

Discussion

The goal of this research was to examine self-reported emotional experience in anhedonia, in particular the facets of valence and arousal. In addition, this research examined whether anhedonia was associated with a generalized change in emotional experience or whether self-reported emotional experience varied by types of experiences or reporting format. For valence, in two studies, we found that anhedonia was associated with decreased positive affect

intensity. Moreover, decreased intensity appeared to be generalized across both situations and reporting formats. For example, in Study 1 there was a decrease of positive affect intensity in people's daily lives, consistent with a recent experience sampling study (Brown et al., 2007). Decreased intensity was found even in situations when people with social anhedonia were interacting with people they are close to. In addition, even for situations when they were alone people with elevated social anhedonia reported decreased positive affect intensity. At the same time, in both studies there was a decrease in positive affect intensity for lab stimuli. Hence, there was evidence of decreased positive affect intensity even when controlling for any differences in the types of situations experienced. Furthermore, the decreased intensity was for both retrospective and current reports of emotion, suggesting that the decrease for daily life situations probably cannot be entirely accounted for by poor memory for positive emotions, which is consistent with what has been found in schizophrenia (Horan et al., 2006). The decrease in Study 1 was for intensity but not for frequency of positive affect, providing some evidence that people with social anhedonia did not differ from controls in the number of positive events but in their reactions to events. In addition to self-reported emotion, in Study 1 anhedonia was associated with decreased emotional content and focus on feelings in verbal descriptions of what it is like to experience positive emotional events. Therefore, even when not directly asked to report their emotions, there was evidence that there is decreased positive affective content in the verbal behavior of people with anhedonia. Overall, the results of these two studies suggest that anhedonia in people at

possible risk for schizophrenia-spectrum disorders might be associated with a general decrease in the experience of positive affect intensity.

At the same time, there was evidence that decreased positive affect intensity might be specifically related to anhedonia. In both studies there was evidence that decreased positive affect intensity was associated with anhedonia but not with a general increased risk of psychosis-proneness, as perceptual aberration-magical ideation was not associated with positive affect in either study. Moreover, in both studies personality and current mood did not statistically account for the association between anhedonia and decreased positive affect intensity.

In contrast to positive affect, for negative affect there was evidence that anhedonia might be associated with an increased frequency of experiencing negative emotional situations and not with a generalized increase in the experience of negative emotions. In both studies, anhedonia was not associated with negative affect intensity. Instead, anhedonia was associated with increased frequency of negative emotions. However, the increase in frequency was only found for daily life situations but not for lab stimuli, suggesting that the increase in negative affect frequency might be related to people with anhedonia experiencing more frequent negative daily life events. At the same time, the increase in negative affect frequency did not appear to be specific to anhedonia, as this was also found in perceptual aberration-magical ideation. This suggests that psychosis-proneness or risk for psychopathology in general might be associated with increased reports of negative affect in daily life situations.

In contrast to valence, the current research did not find evidence that anhedonia is associated with a specific decrease in the experience of high arousal emotions. Instead, to the extent that anhedonia was associated with changes in high arousal emotions (e.g., a decrease in high arousal positive affect intensity), anhedonia was similarly associated with changes in low arousal emotions. Hence this study does not support the hypothesis that anhedonia reflects a decrease specifically in the emotional experience of arousal. Importantly, self-reported emotional arousal is not synonymous with either physiological measures of emotion or with self-reports of physiological processes (e.g., detecting heart rate changes; Barrett et al., 2007). Therefore, it is possible that anhedonia might be associated with some other aspect of emotional arousal. However, the current research did not find evidence that anhedonia was associated with a decrease specifically in the self-report of high arousal emotions.

Hence, based on the current research examining the facets valence and arousal, it appears that anhedonia is associated with decreased positive affect intensity. As mentioned previously, emotional experience is thought to involve certain core affective features, such as valence and arousal, and that how these affective features are experienced depends upon attention and conceptual processing (Barrett et al., 2007). Therefore, there are at least two possible explanations for the decrease in positive affect intensity in anhedonia. One explanation is that anhedonia reflects a decreased capacity to experience positive affect. The other explanation is that decreased positive affect intensity in

anhedonia reflects decreased attention to and conceptual processing of positive affect.

A decrease in the capacity to experience positive affect in anhedonia does seem generally consistent with the current finding of decreased positive affect intensity in anhedonia across a range of situations and reporting formats. On the other hand, a decrease in capacity might seem inconsistent with other research on positive affect for lab stimuli in people with schizophrenia. However, overall, previous research has found some evidence of a decrease in positive affect in people with schizophrenia, although the decrease may be quite small. For example, in 25 previous studies examining positive affect for lab stimuli, 20 of these studies reported numerically lower positive mood in people with schizophrenia (Cohen & Minor, in press), a difference that is significant in a vote counting meta-analysis using a sign test, $p = .004$ (Rosenthal, 1991). However, the effect size difference across these studies is quite small (r at least > -.16). However, it is possible that the effect size in people with schizophrenia might be at least somewhat larger if these studies focused specifically on people with anhedonia. For example, in the current research PerMag scores were not associated with decreased positive affect, consistent with the possibility that people with schizophrenia who do not have anhedonia may not report decreased positive affect after positive lab stimuli.

Although it is possible that people with anhedonia have a decreased capacity to experience positive affect, we think a more likely interpretation for the decrease in positive affect intensity in the current research is that it reflects a

decreased attention to and conceptual processing of positive affect. Hence, from this view, although people with anhedonia could experience pleasure to the same extent as controls, they are less likely to pay attention to or to conceptually elaborate their feelings and therefore less likely to experience them as specific positive emotions (Barrett et al., 2007; Frijda & Sundararajan, 2007; Lambie & Marcel, 2002). A decrease in attention to emotions in anhedonia is consistent with some previous anhedonia research. For example, anhedonia in people at possible risk for schizophrenia-spectrum disorders has been strongly associated with decreased scores on the attention to emotions questionnaire (Berenbaum et al., 2006; Kerns, 2006). At the same, in people with schizophrenia (n = 47) we have recently found that clinically rated anhedonia is also strongly negatively associated (r = -0.50) with the attention to emotions questionnaire (Becker, Cicero, & Kerns, 2007). Importantly, other research on the attention to emotions scale has found that it is specifically associated with attention to positive emotions (Gasper, 2006). At the same time, in the current Study 1 decreased positive affect content and decreased focus on feelings on the event description questionnaire also seems consistent with a decreased attention to and conceptual processing of positive emotions. Therefore, it is possible that the current finding of decreased positive affect intensity in anhedonia is related to decreased attention to and conceptual processing of positive affect.

A decrease in attention to and conceptual processing of positive affect also seems consistent with other research on motivation in schizophrenia. There is some evidence that people with schizophrenia report a decreased wanting but not

a decreased liking of stimuli (Gard, Kring, Gard, Horan, & Green, 2007). It is possible that decreased wanting and anticipation of positive stimuli could potentially contribute to decreased attention to and thinking about positive emotions. At the same time, it is possible that anhedonia might be associated with a generalized problem in the controlled processing of emotional, especially positive, stimuli. For example, we have recently found in two separate studies that social anhedonia is associated with poorer controlled processing of emotional stimuli (Martin & Kerns, 2008). Another possibility is that the length of stimulus processing could influence the depth of emotional processing (Frijda & Sundararajan, 2007), which could also influence whether controls are more likely to report an increase in positive affect compared to people with anhedonia. In fact, one study (Germans & Kring, 2000) that did not report a significant decrease in positive affect in people with elevated physical anhedonia used a shorter stimulus duration (6 sec) than the studies that have found a significant decrease in positive affect (≥ 10 sec; Ferguson & Katkin, 1996; Fiorito & Simons, 1994; Fitzgibbons & Simons, 1992; current Study 1 and 2). At the same time, another issue for future research is to examine the relationship between attention to and conceptualization of positive emotions and reports of emotional experience in people with anhedonia.

Research on people at-risk for schizophrenia-spectrum disorders can provide evidence about the nature of the liability for schizophrenia without many of the confounds involved in schizophrenia research (e.g., medication; Blanchard & Neale, 1992). An issue for future research is to further examine whether people

with schizophrenia report reduced intensity for specific positive emotions and whether it is related to decreased attention to emotions. At the same time, another issue for future research is to continue to compare similarities and differences between social and physical anhedonia. For example, future research could examine whether physical anhedonia is also associated with decreased positive affect intensity for people's daily experiences.

References

Aghevli, M. A., Blanchard, J. J., & Horan, W. P. (2003). The expression and experience of emotion in schizophrenia: a study of social interactions. *Psychiatry Research, 119*, 261-270.

Barrett, L. (2004). Feelings or words? Understanding the content in self-report ratings of experienced emotion. *Journal of Personality and Social Psychology, 87*, 266-281.

Barrett, L. F., Mesquita, B., Ochsner, K. N., & Gross, J. J. (2007). The experience of emotion. *Annual Review of Psychology, 58*, 373-403.

Barrett, L., & Russell, J. A. (1999). The structure of current affect: controversies and emerging consensus. *Current Direction in Psychological Science, 8*, 10-14.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.

Becker, T. M., Cicero, D. C., & Kerns, J. G. (2007). Disorganized speech, cognitive control deficits, and emotion traits in schizophrenia. Poster presented at the Society for Research in Psychopathology, Iowa City, IA, October, 2007.

Berenbaum, H., Boden, M. T., Baker, J. P., Dizen, M., Thompson, R. J., & Abramowitz, A. (2006). Emotional correlates of the different dimensions of schizotypal personality disorder. *Journal of Abnormal Psychology, 115*, 359-368.

Berenbaum, H., & Connelly, J. (1993). The effects of stress on hedonic capacity. *Journal of Abnormal Psychology, 102*, 474-481.

Berenbaum, H., & Irvin, S. (1996). Alexithymia, anger, and interpersonal behavior. *Psychotherapy and Psychosomatics, 65*, 203-208.

Berenbaum, H., Snowhite, R., & Oltmanns, T. F. (1987). Anhedonia and emotional responses to affect evoking stimuli. *Psychological Medicine, 17*, 677-684.

Blanchard, J. J., & Neale, J. M. (1992). Medication effects: conceptual and methodological issues in schizophrenia research. *Clinical Psychology Review, 12*, 345-361.

Brown, L. H., Silvia, P. J., Myin-Germeys, I., & Kwapil, T. R. (2007). When the need to belong goes wrong: the expression of social anhedonia and social anxiety in daily life. *Psychological Science, 18*, 778-782.

Burbridge, J. A., & Barch, D. M. (2007). Anhedonia and the experience of emotion in individuals with schizophrenia. *Journal of Abnormal Psychology, 116*, 30-42.

Chapman, L. J., & Chapman, J. P. (1983). *Infrequency scale.* Unpublished test.

Chapman, J. P., Chapman, L. J., & Kwapil, T. R. (1995). Scales for the measurement of schizotypy. In A. Raine & T. Lencz (Eds.), *Schizotypal Personality* (pp. 79-106). New York: Cambridge University Press.

Chapman, L. J., Chapman, J. P, Kwapil, T. R., Eckblad, M. & Zinser, M. C. (1994). Putatively psychosis-prone subjects 10 years later. *Journal of Abnormal Psychology, 103*, 171-183.

Chapman, L. J., Chapman, J. P., & Raulin, M. L. (1976). Scales for physical and social anhedonia. *Journal of Abnormal Psychology, 85*, 374-382.

Chapman, L. J., Chapman, J. P., & Raulin, M. L. (1978). Body-image aberration in schizophrenia. *Journal of Abnormal Psychology, 87,* 399-407.

Chmielewski, P. M., Fernandes, L. O., Yee, C. M., & Miller, G. A. (1995). Ethnicity and gender in scales of psychosis proneness and mood disorders. *Journal of Abnormal Psychology, 104*, 464-470.

Cohen, A. S., & Minor, K. S. (in press). Emotional experience in patients with schizophrenia revisited: Meta-analysis of laboratory studies. *Schizophrenia Bulletin*.

Collins, L. M., Blanchard, J. J., & Biondo, K. M. (2005). Behavioral signs of schizoidia and schizotypy in social anhedonics. *Schizophrenia Research, 78*, 309-322.

Crandall, C. S., Preisler, J. J., & Aussprung, J. (1992). Measuring life event stress in the lives of college students: the undergraduate stress questionnaire. *Journal of Behavioral Medicine, 15*, 627-662.

Eckblad, M., & Chapman, L. J. (1983). Magical ideation as an indicator of schizotypy. *Journal of Consulting and Clinical Psychology, 51,* 215-225.

Eckblad, M., Chapman, L. J., Chapman, J. P., & Mishlove, M. (1982). *The Revised Social Anhedonia Scale.* Unpublished test.

Edell, W. S. (1995). The psychometric measurement of schizotypy using the Wisconsin Scales of Psychosis-Proneness. In G. A. Miller (Ed.), *The*

behavioral high-risk paradigm in psychopathology (pp.1-46). New Work: Springer-Verlag.

Ferguson, M. L., & Katkin, E. S. (1996). Visual perception, anhedonia, and emotion. *Biological Psychology, 42*, 131-145.

Fiorito, E. R., & Simons, R. F. (1994). Emotional imagery and physical anhedonia. *Psychophysiology, 31*, 513-521.

Fitzgibbons, L., & Simons, R. F. (1992). Affective response to color-slide stimuli in subjects with physical anhedonia: A three-systems analysis. *Psychophysiology, 29*, 613-620.

Frijda, N. H., & Sundararajan, L. (2007). Emotion refinement: a theory inspired by Chinese poetics. *Perspectives on Psychological Science, 2*, 227-241.

Gard, D. E., Kring, A. M., Gard, M. G., Horan, W. P., & Green, M. F. (2007). Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. *Schizophrenia Research, 93*, 253-260.

Gasper, K., & Bramesfeld, K. D. (2006). Should I follow my feelings? How individual differences in following feelings influence affective well-being, experience, and responsiveness. *Journal of Research in Personality, 40*, 986-1014.

Germans, M. K., & Kring, A. M. (2000). Hedonic deficit in anhedonia: support for the role ofapproach motivation. *Personality and Individual Differences, 28*, 659-672.

Goldberg, L. R. (1999). A broad-bandwidth, public domain, personality inventory measuring the lower-level facets of several five-factor models. In I.

Mervielde, I. Deary, F. De Fruyt, & F. Ostendorf (Eds.), *Personality Psychology in Europe, Vol. 7* (pp. 7-28). Tilburg, The Netherlands: Tilburg University Press.

Gooding, D. C., Davidson, R. J., Putnam, K. M., & Tallent, K. A. (2002). Normative emotion-modulated startle response individuals at risk for schizophrenia-spectrum disorders. *Schizophrenia Research, 57*, 109-120.

Gooding, D. C., Tallent, K. A., & Matts, C. W. (2005). Clinical status of at-risk individuals 5 years later: further validation of the psychometric high-risk strategy. *Journal of Abnormal Psychology, 114*, 170-175.

Hafner, H., & an der Heiden, W. (2003). Course and outcome of schizophrenia. In S. R. Hirsch & D. R. Weinberger (Eds.), *Schizophrenia, Second Edition* (pp. 101-141). Malden, MA:Blackwell.

Heller, W. (1994). Neuropsychological mechanisms of individual differences in emotion, personality, and arousal. *Neuropsychology, 7*, 476-489.

Horan, W. P., & Blanchard, J. J. (2003). Neurocognitive, social, and emotional dysfunction in deficit syndrome schizophrenia. *Schizophrenia Research, 65*, 125-137.

Horan, W. P., Blanchard, J. J., Gangstead, S. W., & Kwapil, T. R. (2004). The psychometric detection of schizotypy: Do putative schizotypy indicators identify the same latent class? *Journal of Abnormal Psychology, 113*, 339-357.

Horan, W. P., Green, M. F., Kring, A. M., & Nuechterlein, K. H. (2006). Does anhedonia in schizophrenia reflect faulty memory for subjectively experienced emotions? *Journal of Abnormal Psychology, 115*, 496-508.

Kahneman, D., Krueger, A. B., Schkade, D. A., Schwarz, N., & Stone, A. A. (2004). A survey method for characterizing daily life experience: the day reconstruction method. *Science, 306*, 1776-1780.

Kerns, J. G. (2005). Positive schizotypy and emotion processing. *Journal of Abnormal Psychology, 114*, 392-401.

Kerns, J. G. (2006). Schizotypy facets, cognitive control, and emotion. *Journal of Abnormal Psychology, 115*, 418-427.

Kerns, J. G., & Becker, T. M. (2008). Communication disturbances, working memory, and emotion in people with elevated disorganized schizotypy. *Schizophrenia Research, 100*, 172-180.

Kerns, J. G., & Berenbaum, H. (2000). Aberrant semantic and affective processing in people at-risk for psychosis. *Journal of Abnormal Psychology, 109,* 728-732.

Kirkpatrick, B., Fenton, W. S., Carpenter, W. T. Jr., & Marder, S. R. (2006). The NIMH-MATRICS consensus statement on negative symptoms. *Schizophrenia Bulletin, 32*, 214-219.

Kring, A. M. (1999). Emotion in schizophrenia: old mystery, new understanding. *Current Directions in Psychological Science, 8*, 160-163.

Kwapil, T. R. (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *Journal of Abnormal Psychology, 107*, 558-565.

Lambie, J. A., & Marcel, A. J. (2002). Consciousness and the varieties of emotion experience: a theoretical framework. *Psychological Review, 109*, 219-259.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2005). *International affective picture system (IAPS): affective ratings of pictures and instruction manual. Technical Report A-6.* University of Florida, Gainesville, FL.

Larsen, R. J., Billings, D. W., & Cutler, S. E. (1996). Affect intensity and individual differences in informational style. *Journal of Personality, 64*, 185-207.

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience, 23*, 155-184.

Lenzenweger, M. F. (1999). Schizophrenia: refining the phenotype, resolving endophenotypes. *Behaviour Research and Therapy, 37*, 281-295.

Lucas, R. E., & Diener, E. (2001). Understanding extraverts' enjoyment of social situations: the importance of pleasantness. *Journal of Personality and Social Psychology, 81*, 343-356.

Luh, K. E., & Gooding, D. C. (1999). Perceptual biases in psychosis-prone individuals. *Journal of Abnormal Psychology, 108*, 283-289.

Martin, E. A., & Kerns, J. G. (2008). Social anhedonia and increased emotional but not cognitive conflict. Poster to be presented at the Society for Research in Psychopathology, Pittsburgh, PA, September, 2008.

Mason, O. (1995). A confirmatory factor analysis of the structure of schizotypy. *European Journal of Personality, 9*, 271-281.

Meehl, P. E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist, 17*, 827-838.

Miller, G. A., & Chapman, J. P. (2001). Misunderstanding analysis of covariance. *Journal of Abnormal Psychology, 110*, 40-48.

Myin-Germeys, I., Delespaul, P. A. E. G., & deVries, M. W. (2000). Schizophrenia patients are more emotionally active than is assumed based on their behavior. *Schizophrenia Bulletin, 26*, 847-854.

Phelps, E. A. (2006). Emotion and cognition: insights from studies of the human amygdala. *Annual Review of Psychology, 57*, 27-53.

Preacher, K. J., Rucker, D. D., MacCallum, R. C., & Nicewander, W. A. (2005). Use of the extreme groups approach: a critical reexamination and new recommendations. *Psychological Methods, 10*, 178-192.

Prince, J. D., & Berenbaum, H. (1993). Alexithymia and hedonic capacity. *Journal of Research in Personality, 27*, 15-22.

Robinson, M. D., & Clore, G. L. (2002). Belief and feeling: evidence for an accessibility model of emotional self-report. *Psychological Bulletin, 128*, 934-960.

Rosenthal, R. (1991). *Meta-analytic procedures for social research*. Thousand Oaks, CA: Sage.

Ross, S. R., Lutz, C., J., & Bailey, S. E. (2002). Positive and negative symptoms of schizotypy and the five-factor model: a domain and facet level analysis. *Journal of Personality Assessment, 79*, 53-72.

Schimmack, U., & Diener, E. (1997). Affect intensity: separating intensity and frequency in repeatedly measured affect. *Journal of Personality and Social Psychology, 73*, 1313-1329.

Shadish, W. R., Cook, T. D., Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference*. Houghton Mifflin: New York.

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: Uses in assessing rater reliability. *Psychological Bulletin, 86,* 420-428.

VandenBos, G. R. (2006). *APA Dictionary of Psychology*. Washington, DC: Amercian Psychological Association.

Watson, D., Gamez, W., & Simms, L. J. (2005). Basic dimensions of temperament and their relation to anxiety and depression: a symptom-based perspective. *Journal of Research in Personality, 39*, 46-66.

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Table 1

Intensity of Positive and Negative Affect by Arousal Level and by Task in Study 1

Measure	SocAnh	PerMag	Control
Day Reconstruction Method			
PA, High Arousal	2.80 (0.87)	3.23 (0.96)	3.16 (0.61)
PA, Low Arousal	2.72 (0.82)	2.93 (1.09)	3.23 (0.80)
NA, High Arousal	2.37 (0.99)	2.43 (0.83)	2.41 (0.87)
NA Low Arousal	2.73 (0.77)	2.29 (0.94)	2.52 (0.73)
Situation Rating Task			
PA, High Arousal	3.54 (0.71)	3.90 (0.87)	4.04 (0.67)
PA, Low Arousal	3.25 (0.70)	3.48 (0.91)	3.71 (0.85)
NA, High Arousal	2.85 (0.77)	2.95 (0.77)	2.93 (0.76)
NA Low Arousal	2.64 (0.76)	2.65 (0.86)	2.65 (0.79)
Picture Rating Task			
PA, High Arousal	3.73 (0.98)	3.95 (0.94)	4.23 (0.95)
PA, Low Arousal	3.54 (0.93)	3.95 (0.84)	4.06 (1.01)
NA, High Arousal	3.89 (1.10)	4.06 (1.22)	3.90 (1.12)
NA Low Arousal	3.47 (1.01)	3.59 (1.12)	3.63 (1.14)

Table 2

Frequency of Positive and Negative Affect by Arousal Level and by Task in Study 1

Measure	SocAnh	PerMag	Control
Day Reconstruction Method			
PA, High Arousal	0.59 (0.23)	0.68 (0.18)	0.62 (0.25)
PA, Low Arousal	0.67 (0.26)	0.73 (0.20)	0.72 (0.23)
NA, High Arousal	0.47 (0.27)	0.51 (0.28)	0.34 (0.21)
NA Low Arousal	0.45 (0.25)	0.44 (0.27)	0.31 (0.24)
Situation Rating Task			
PA, High Arousal	0.74 (0.17)	0.80 (0.12)	0.76 (0.17)
PA, Low Arousal	0.76 (0.16)	0.79 (0.15)	0.77 (0.19)
NA, High Arousal	0.47 (0.25)	0.50 (0.20)	0.33 (0.20)
NA Low Arousal	0.40 (0.25)	0.42 (0.21)	0.29 (0.23)
Picture Rating Task			
PA, High Arousal	0.72 (0.21)	0.79 (0.18)	0.73 (0.26)
PA, Low Arousal	0.78 (0.19)	0.83 (0.15)	0.79 (0.23)
NA, High Arousal	0.72 (0.22)	0.77 (0.25)	0.73 (0.24)
NA Low Arousal	0.52 (0.21)	0.53 (0.22)	0.49 (0.23)

Table 3

Event Description Questionnaire, Personality, and Current Mood in Study 1

Measure	SocAnh	PerMag	Control
Event Description Questionnaire			
Positive Emotional Content	1.9 (0.84)	2.5 (1.30)	2.4 (1.16)
Positive Focus on Feeling	3.3 (1.06)	4.0 (1.28)	3.9 (1.16)
Positive Event Description	-0.34 (0.83)	0.26 (1.15)	0.20 (1.01)
Negative Emotional Content	1.9 (0.92)	2.5 (0.96)	2.1 (1.07)
Negative Focus on Feeling	3.4 (1.24)	4.2 (1.25)	3.7 (1.30)
Negative Event Description	-0.26 (0.97)	0.37 (0.98)	-0.02 (1.06)
Personality			
Extraversion	2.56 (0.86)	3.62 (0.91)	3.82 (0.46)
Neuroticism	3.12 (0.88)	3.04 (0.76)	2.52 (0.83)
Current Mood			
Positive Affect	1.7 (1.04)	1.9 (1.15)	2.2 (1.01)
Negative Affect	1.9 (1.22)	2.1 (1.37)	1.3 (0.73)

Table 4

Summary of Hierarchical Regression Analyses for Variables Predicting Positive Affect Intensity in Study 1 (n = 70)

Variable	B	SE B	β
Step 1			
Extraversion	.14	.15	.16
Neuroticism	-.11	.13	-.14
Current Positive Affect	.27	.12	.28*
Current Negative Affect	.12	.12	.15
Step 2			
Extraversion	.09	.15	.07
Neuroticism	-.05	.12	-.04
Current Positive Affect	.21	.12	.25*
Current Negative Affect	.17	.11	.20
Group (SocAnh vs. Control)	-.54	.21	-.36**

Note. $R^2 = .21$ for Step 1, $p < .05$; $\Delta R^2 = .09$ for Step 2, $p < .01$.

* $p < .05$. ** $p < .01$.

Table 5

Correlations between Psychosis-Proneness Scores and Individual Differences in Study 2

Measure	Anhedonia	PerMag
Picture Rating Intensity		
Positive	-.20**	.03
Negative	-.08	.11*
Personality		
Extraversion	-.34**	.03
Neuroticism	.18**	.24**
Current Mood		
Positive	-.16**	.01
Negative	.12*	.25**
Current Distress		
Beck Depression Inventory	.31**	.43**
Recent Major Stress	.06	.12*
Recent Minor Stress	.09	.41**

* $p < .05$. ** $p < .01$.

Table 6

Summary of Hierarchical Regression Analyses for Variables Predicting Positive Affect

Intensity in Study 2 (n = 339)

Variable	B	SE B	β
Step 1			
Extraversion	.11	.05	.12*
Neuroticism	.12	.06	.12
Current Positive Affect	.25	.05	.26**
Current Negative Affect	.18	.06	.19**
Beck Depression Inventory	-.11	.07	-.11
PerMag	-.02	.06	-.02
Step 2			
Extraversion	.07	.05	.08
Neuroticism	.11	.06	.12
Current Positive Affect	.23	.05	.25**
Current Negative Affect	.17	.06	.18**
Beck Depression Inventory	-.08	.07	-.08
PerMag	-.01	.06	-.01
Anhedonia	-.17	.06	-.16**

Note. $R^2 = .12$ for Step 1, $p < .001$; $\Delta R^2 = .03$ for Step 2, $p < .01$.

* $p < .05$. ** $p < .01$.

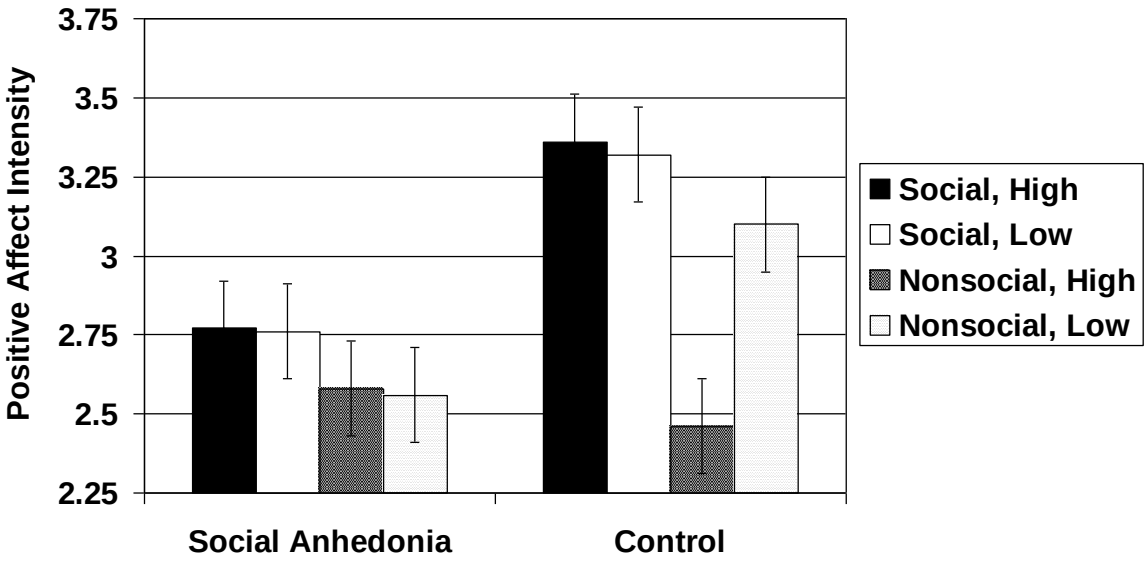
3.75
3.5
3.25
3
2.75
2.5
2.25
Positive Affect Intensity
Social Anhedonia
Control
Social, High
Social, Low
Nonsocial, High
Nonsocial, Low

Figure Caption

Figure 1. Positive affect intensity for high arousal emotions and low arousal emotions and for social and nonsocial situations in the Social Anhedonia and Control groups on the Day Reconstruction Method in Study 1.

Chapter 2: Anhedonia as a Phenotype for the Val158Met Polymorphism of COMT in First-Degree Relatives of People with Schizophrenia

Introduction

Determining which schizotypy phenotypes relate to specific genes is important for developing a working model of psychosis proneness tied to the genetics of schizophrenia (Meehl, 2001; Horan et al., 2004; Lenzenweger et al., 2006). The $Val^{158}Met$ polymorphism of the catechol-O-methyltransferase (COMT) gene has been associated with various phenotypes in schizophrenia patients (Bilder et al., 2004) but has yet to be thoroughly tested for associations with schizotypy phenotypes in individuals who carry genetic liability for schizophrenia (e.g., first-degree biological relatives of schizophrenia patients).

The COMT gene encodes an enzyme involved in the inactivation of catecholamines (dopamine, adrenaline, and noradrenaline) and incorporates codon 158 of the chromosomal region 22q11 (Dunham et al., 1992). The $Val^{158}Met$ polymorphism influences variation in enzyme availability—with activity three to four times lower for the met allele than for the val allele (Lotta et al., 1995; Lachman et al., 1996) and appears associated with D_1 receptor availability in the human cortex (Slifstein et al., 2008). Evidence suggests an association between the val allele (i.e., less catecholomine activity) and the diagnosis of schizophrenia (Wonodi et al., 2003), decreased performance on cognitive tasks (Bilder et al., 2002; MacDonald et al., 2007), and decreased efficiency of prefrontal cortex (Egan et al., 2001). Nonetheless, in studies of schizophrenia the met allele has been related to impaired shifting of a response rule based on feedback (Nolan et

al., 2004), reduced ability to sustain smooth pursuit eye movements in the brief absence of a target (Thaker et al., 2004), greater vulnerability to visual backward masking effects (Goghari & Sponheim, 2008), and increased low frequency electroencephalography activity over frontal brain regions during resting state (Venables et al., in press). It is also important to note that the region of the genome where COMT resides has been associated with both schizophrenia and bipolar disorder (Badner & Gershon, 2002) with some studies pointing to an association between bipolar disorder and the met allele (Li et al., 1997; Mynett-Johnson et al., 1998). The met allele at codon 158 has also been associated with anxiety in women, panic disorder, and sensitivity to pain in adults (Enoch et al., 2003; Woo et al., 2004; Zubieta et al., 2003). Thus, the role of $Val^{158}Met$ polymorphism of the COMT gene in psychopathology is unclear. It appears the polymorphism may exert varying effects on different forms of psychopathology depending on the allele and the mental disorder.

Reviews of the literature show that when investigators have employed a diagnosis of schizophrenia, phenotype associations with the COMT polymorphism are variable. Although Fan et al. (2002) found family-based association studies to provide evidence for the val allele to be related to schizophrenia, a recent meta-analysis failed to show such an association (Glatt et al., 2003). Glatt and colleagues suggested that the association of the COMT polymorphism with schizophrenia may be most evident in individuals of European ancestry; however, a recent analysis of large samples of subjects with European ancestry failed to yield association of schizophrenia with the COMT

Val^{158}Met polymorphism (Sanders et al., in press). On the other hand, a study of Irish families with a high density of schizophrenia provided evidence that the val allele of the polymorphism contributes to genetic risk of schizophrenia (Chen et al., 2004).

Several studies have investigated schizotypal characteristics as phenotypes for the COMT Val^{158}Met polymorphism. Avramopoulos et al (2002) reported that the val allele was associated with high schizotypy scores in a male normative sample. Stefanis et al., (2004) replicated these results and found that the val allele was specifically related to negative and disorganization dimensions of schizotypy. More recently, these investigators showed that in the general population the relationship between negative schizotypy and cognitive deficits was moderated by the val allele (Smyrnis et al., 2007). Schurhoff et al. (2007) studied relatives of schizophrenia and bipolar patients and found the presence of the val allele to be associated with independent dimensions of negative and positive schizotypy. Within the context of these variable findings, only an association of the val allele of the COMT polymorphism with negative schizotypy has been replicated. Thus, aspects of negative schizotypy such as anhedonia may be tied to the Val^{158}Met polymorphism. Investigators have yet to specifically examine individuals who carry genetic liability for schizophrenia for associations between the elements of schizotypy and the COMT polymorphism, or employ measures that comprehensively characterize the phenomenology of schizotypy that has been associated with liability for schizophrenia.

Social and physical anhedonia are constructs central to "negative schizotypy" (Blanchard et al., 2000, Gooding & Braun, 2004). It has been shown that high scores on the Social Anhedonia Scale (SAS) predict vulnerability to psychosis in college and community populations (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994; Kwapil, 1998). Social anhedonia is also separable from elements of "positive schizotypy" such as magical ideation (Horan et al., 2007). The SAS and Physical Anhedonia Scale (PAS) extensively assess anhedonia and indifference to social and physical experiences, and may serve as sensitive measures for detecting genetic effects related to schizophrenic phenomenology. Kendler et al. (1996) found that the SAS differentiated relatives of individuals with schizophrenia from controls in a large community adult sample. Earlier, Katsanis et al. (1990) successfully differentiated relatives of schizophrenia patients and controls with the PAS. Moreover, physical anhedonia scores tend to be higher in family members of schizophrenia patients with severe anhedonic symptoms (Berenbaum & McGrew, 1993; Fanous et al., 2001). In bipolar disorder physical anhedonia has failed to be associated with increased familial risk for the condition (Etain et al., 2007).

The Schizotypal Personality Questionnaire (SPQ: Raine, 1991) is a brief measure that assesses all nine criteria of DSM-III-R Schizotypal Personality Disorder and functions as a useful screen for the disorder (Raine, 1991). Thus far it has served as the primary phenotypic measure in studies associating schizotypy with the Val^{158}Met COMT polymorphism. Higher scores on the Interpersonal factor of the SPQ have been associated with poorer sustained attention (Chen,

1997) and greater spatial working memory deficit (Park & McTigue, 1997) perhaps suggesting an association with cognitive functions involving frontal cortex. Although it may be considered an aspect of the Interpersonal factor, anhedonia is not expressly measured by the SPQ. Thus, additional instruments that specifically assess anhedonia may prove to be useful in examining the role of the COMT gene in risk for schizophrenia.

We hypothesized that the SAS and PAS measure aspects of the schizotypy phenotype associated with genetic liability for schizophrenia and the $Val^{158}Met$ polymorphism of the COMT gene. The goals of the study were to 1) examine the specificity of anhedonia to liability for schizophrenia as compared to bipolar disorder, 2) test whether anhedonia was increased in relatives possessing the val allele of the COMT polymorphism, and 3) investigate whether associations of anhedonia with the val allele were diagnostically specific to schizophrenia.

Materials and Methods

Participants

Subjects were 94 first-degree relatives of schizophrenia ($N = 79$) or schizoaffective disorder ($N = 15$) patients, 45 first-degree relatives of bipolar patients, and 85 healthy nonpsychiatric control participants. Data were gathered within the context of a family study in which patients with schizophrenia, schizoaffective disorder, or bipolar disorder were recruited from the Minneapolis VA Medical Center, community outpatient programs, and a county mental health clinic. First-degree biological relatives were identified through interviews with patients and invited by letter and telephone to participate. We identified potential

nonpsychiatric control participants through posting announcements at community libraries, fitness centers, the Minneapolis VA Medical Center, and in newsletters for veterans and fraternal organizations. Staff excluded potential control subjects with personal or family histories of psychotic symptoms or affective disorder as defined by the DSM-IV. Patients, relatives, and control subjects were excluded for histories of substance dependence but were not excluded for past alcohol dependence, as long as they had not abused alcohol in the past month.

Relatives and control subjects completed the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First et al., 1996), the Structured Interview for Schizotypy (SIS; Kendler et al., 1989), and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First et al., 1997) when indicated by item endorsements on the SCID-II Personality Questionnaire (Ekselius et al., 1994). Lifetime Axis I and II diagnoses for subjects were determined by doctoral-level psychologists and trained advanced graduate students through a consensus process consistent with published guidelines (Leckman et al., 1982) which involved review of SCID-I, SCID-II, SIS, medical history, and family informant material. See Sponheim et al. (2004) for complete description of exclusion criteria, recruitment, and assessment procedures. All participants completed an informed consent process, and the Minneapolis VA Medical Center and University of Minnesota Institutional Review Boards approved the study protocol. For the 53 relatives who were unable to travel for in-person assessments, questionnaires were mailed to them after they had completed informed consent procedures by telephone and a mailed consent form had

returned with their signature. These individuals completed SCID-I assessment via telephone and collected buccal swab specimens from themselves after being instructed to follow printed guidelines. Participants returned buccal swabs and completed questionnaires by U.S. Postal Service.

Questionnaires

Relatives and control subjects completed the SPQ (Raine, 1991), a 74-item true-false questionnaire that measures interpersonal, cognitive-perceptual, and disorganized schizotypal characteristics with nine subscales: constricted affect, suspiciousness, no close friends, social anxiety, odd beliefs, odd behavior, odd speech, unusual perceptual experiences, and ideas of reference. While the many scales of the SPQ may provide a detailed characterization of schizotypy, and the SPQ total score has been shown to possess good internal reliability with a coefficient alpha of .91 (Raine, 1991), reliabilities for individual SPQ subscales have been reported below .70 (Calkins, Curtis, Grove, & Iacono, 2004; Kerns, 2007). The SPQ has shown good criterion and discriminant validity for the detection of schizotypal personality. Fifty-five percent of individuals in a normed sample who scored in the top 10% of SPQ total scores had a DSM-III-R diagnosis of schizotypal personality disorder as assessed by the SCID-I. In addition, the SPQ has low correlations with scales that assess psychosis-proneness not included in criteria for schizotypal personality (.18 to .19 with Anhedonia, and .27 to .37 with Psychoticism) (Raine, 1991).

All participants also completed the "Survey of Attitudes and Experiences" which included a pseudo-random mixture of the true-false questions from the

Revised Social Anhedonia Scale (SAS; Eckblad et al., 1982), the Revised Physical Anhedonia Scale (PAS; Eckblad and Chapman, 1983), the Magical Ideation Scale (Chapman et al., 1976), the Perceptual Aberration Scale (Chapman et al., 1978), the Chapman Infrequency Scale (to measure careless responding; Chapman & Chapman, 1983) as well as the L and K Scales from the Minnesota Multiphasic Personality Inventory-2 (to measure defensiveness; MMPI-2; Butcher et al., 2001). The Chapman scales have shown good reliability across schizophrenia and control groups with a Cronbach α's of >.7 (ie. recently Kerns, 2006, Horan et al., 2008). Subjects were excluded from analyses if answers to items on a schizotypy scale were missing. No more than seven subjects were excluded from analyses of any given measure.

COMT Genotyping

We determined the COMT Val^{158}Met genotype for each individual by a restriction fragment length polymorphism technique. Whole blood specimens were collected on FTA Matrix specimen collection cards.[1] Punches from the FTA blood cards were then prepared for PCR analysis according to Whatman FTA protocol. The washed punch was used directly for PCR amplification. Amplification was carried out as described by Bergman-Jungestrom and Wingren (2001). PCR reactions were initially denatured at 94^{o} Celsius for 3 minutes followed by 39 cycles of denaturation at 93 ^{o} C for 45 seconds, annealing at 55^{o} C

[1] As described under *Participants*, for those relatives who were unable to travel buccal swab specimens were collected by participants via printed instruction and sent back to the study with the questionnaires. DNA was isolated from buccal swabs and then subjected to the same procedures as DNA isolated from whole blood in order to characterize the Val^{158}Met polymorphism.

for 1 minute and extension at 72° C for 1 minute with a final 4 minute extension at 72° C. The PCR products were digested with NlaIII (New England Biolabs) for 3 hours at 37° C followed by incubation at 60° C for 20 minutes to denature the enzyme. The digestion was then separated by polyacrylamide gel electrophoresis and the digestion products visualized by staining with ethidium bromide. The COMT val allele has a G at position 1947 yielding a 114 base pair fragment after digestion with NlaIII, whereas the COMT met allele has an A at this position, which allows digestion of the 114 base pair fragment into two products of 96 and 18 base pairs. Genotypes were called by two independent and trained technicians. If it was difficult to determine genotype from gels the specimen was again amplified and submitted to electrophoresis. Discordance was resolved by first running an additional gel and if further disagreement or uncertainty was noted, it was resolved by a doctoral-level molecular biologist. Later we completed genotyping of specimens using a Sequenom MassArray platform that yielded complete agreement with genotypes determined through electrophoresis.

Sample Characteristics

Not all relatives and control subjects were genotyped. Thirteen relatives of schizophrenia patients and seven relatives of bipolar patients failed to provide usable specimens. Specimens were not initially gathered from control participants, hence only 35 recently studied individuals provided useable specimens. Table I reports demographic information regarding genotyped and non-genotyped participants from the three subject groups. Table II presents demographic characteristics and rates of lifetime psychopathology for each

participant group by COMT genotype. All participant groups were in Hardy-Weinburg Equilibrium (relatives of schizophrenia patients, X^2 =.02, df = 2, p = .99; relatives of bipolars, X^2 =.24, df = 2, p = .89; controls, X^2 = .53, df = 2, p = .77). Analyses of the total sample revealed differences in gender across groups (X^2 = 6.54, p <.05) with a higher ratio of female to male relatives for schizophrenia patients as compared with controls. Relative and control groups differed in age. Within each of the relative groups age was not significantly correlated with any of the measures found to be associated with group differences (e.g., For PAS and constricted affect in relatives of schizophrenia patients, r = .04, p = .71, and r = .15, p = .15, respectively. For SAS in relatives of bipolar patients, r = -.15, p = .33). Age was positively correlated with constricted affect within the control group (r = .28, p = .01).[2]

Insert Tables I and II about here

Of 94 relatives of schizophrenia and schizoaffective patients, 21 were determined to have a history of either Major Depressive Disorder or Depressive Disorder Not Otherwise Specified. Nine of the 45 relatives of bipolar patients had a history of such a disorder. In order to rule out the influence of vulnerability to

[2] For scales failing to differentiate groups, age was correlated with the disorganized factor in controls (r = -.23, p = .04), odd speech and unusual perceptual experiences in relatives of schizophrenia patients (r = .25, p = .02; r = .24, p = .02, respectively), and magical ideation (r = -.38, p = .01), odd behavior (r = -.36, p = .02), odd speech (r = -.34, p = .02), the cognitive perceptual factor (r = -.40, p = .01), and the disorganized factor (r = -.38, p = .01) in relatives of bipolar patients.

depression on schizotypy indices we carried out several one-way analysis of variances (ANOVAs) with lifetime mood disorder as the fixed factor (present, absent) and schizotypy variables (e.g. social anhedonia) as the dependent variables, within each relative group. No analysis for either relative group revealed an effect of lifetime mood disorder on schizotypy indices with the exception of a trend toward relatives of bipolar disorder participants with a history of mood disorder having increased Interpersonal factor scores compared to those without such a history ($F_{1,39} = 3.72$, $p = .06$).

Statistical Analysis

Because of non-normal distribution within groups, a logarithmic transformation of the schizotypy variables was performed. To determine whether the groups of relatives showed elevation on schizotypy indices we carried out separate repeated measures ANOVAs for each set of schizotypy measures (one for the three SPQ factors, and one for the four Chapman scales) specifying subject group (schizophrenia relative, bipolar relative, control) and gender (male, female) as between subjects factors and scale as a within subjects factor. We carried out a similar repeated measures ANOVA on the validity scales (L, K, and Chapman Infrequency Scale) to determine whether groups or genders were discrepant in their overall tendency to endorse questionnaire items. After determining group, gender, and group by gender interactions for the entire sample, we conducted repeated measures ANOVAs for individuals with available genotype data to test for effects of the COMT Val^{158}Met polymorphism on selected sets of measures that had yielded elevated schizotypy scores for relatives. For these analyses we

specified genotype (val/val, val/met, met/met), group (relative, control), and gender as between-subject factors. When ANOVA's yielded significant effects, pairwise comparisons were computed to detail group differences.

Results

Schizotypal Phenotypes in Biological Relatives of Schizophrenia and Bipolar Disorder Patients

Table III presents means and standard deviations of the SPQ factors and Chapman scale indices for the two groups of relatives and the control group, as well as statistics for group comparisons. Analysis of the SPQ factors yielded a nearly significant effect of group across all factors ($F_{2,191} = 2.842$, $p = .06$). There were no interactions of scale and group (Greenhouse-Geisser [*GG*] $F_{3.8, 213.8} = 1.11$, $p = .35$), and scale and gender (*GG* $F_{1.9, 213.8} = .251$, $p = .77$) indicating that regardless of gender the relatives and controls did not vary in their differences across all SPQ factors of schizotypy. Because differences have been found previously between relatives and controls on the Interpersonal factor (Grove et al., 1991; Calkins et al., 2004), exploratory univariate tests of each factor were examined. Only the Interpersonal factor demonstrated an effect of group (see Table III) with relatives of schizophrenia patients having higher scores than controls. Effect sizes indicated that the relatives of schizophrenia patients were the most elevated on the factor although relatives of bipolar patients tended toward high scores. There were no group differences on the Cognitive-Perceptual and Disorganization factors of the SPQ. Univariate tests also failed to show group differences in total SPQ score.

To detail how the three groups compared on specific elements of the Interpersonal factor we carried out separate ANOVAs for each factor subscale. Analyses of specific subscales revealed that groups differed only in constricted affect ($F_{2,191} = 4.77$, $p = .01$) with relatives of schizophrenia patients (*M[SD]* = 1.55[1.67]) having higher scores than controls, (*M[SD]* = 1.06[1.28]), $p = .002$, and relatives of bipolar patients (*M[SD]* =1.48[1.95]) failing to differ from controls, $p = .16$.

Univariate tests with gender as the fixed factor showed an effect of gender on the Interpersonal factor only within the relatives of schizophrenia patients ($F_{1,84} = 4.802$, $p = .031$). Due to the difference between genders in this group, each gender was compared with same-gendered control participants in scores on the constricted affect subscale. Male relatives of schizophrenia patients had significantly higher constricted affect scores (*M[SD]* = 2.32[1.70]) than male controls (*M[SD]* = 1.30[1.37]), $p = .02$, while female relatives of schizophrenia patients (*M[SD]* = 1.14[1.52]) did not differ from female controls (*M[SD]* = .80[1.13]), $p = .24$. When age was entered into the ANOVA group difference in constricted affect remained, $p = .05$.

Insert Table III about her

Analysis of the four Chapman scales yielded a nearly significant group effect ($F_{2,178} = 2.515$, $p = .08$) and a scale-by-group interaction (*GG* $F_{4.9,\ 432.4} =$ 2.08, $p = .07$) with a significant interaction of scale and gender (*GG* $F_{2.4,\ 432.4} =$

5.32, $p = .003$). These effects indicated that groups and genders tended to vary in their differences across Chapman scales of psychosis-proneness. Since evidence suggests that relatives of schizophrenia patients predominantly exhibit anhedonia (Katsanis et al., 1990, Kendler et al., 1996) we tested each Chapman scale for group differences. ANOVAs for each Chapman scale yielded group effects for the SAS and PAS (see Table III). Both relatives of schizophrenia patients and relatives of bipolar patients had elevated scores on the SAS compared to controls. Only relatives of schizophrenia patients had higher PAS scores than controls. Inspection of effect sizes revealed that relatives of schizophrenia patients deviated most strongly from control subjects on measures of anhedonia although both groups of relatives tended to have elevated scores.

Follow-up analyses comparisons were carried out to detail gender differences on the Chapman scales and because of gender differences previously noted on the measures of psychosis proneness (i.e, Miller & Burns, 1995). Both male and female relatives of schizophrenia patients had higher scores on the SAS (*M[SD]*= 10.59[7.02], 7.45[4.95], respectively) than same-gendered controls (*M[SD]* = 7.54[6.54], 5.54[4.49]; $p = .006$ and .03, respectively), but male relatives of schizophrenia patients also had elevated SAS scores compared to female relatives of schizophrenia patients (t [80] = 2.23, $p = .03$). Male relatives of schizophrenia patients had elevated PAS scores (*M[SD]* = 15.89[7.89]) compared to same-gendered controls (*M[SD]* = 12.03[6.07]; t [65] = 2.16, $p = .03$) and female relatives of schizophrenia patients (*M[SD]* = 12.13[4.47]; t [79] = 2.11, $p = .04$). Only male relatives of bipolar patients showed elevated scores on

the SAS compared to same-gendered controls (p = .04 for males; p = .43 for females). Male relatives of bipolar patients had significantly higher scores on the SAS compared to female relatives of bipolar patients (*M[SD]* = 10.00[6.65], 6.17[5.41], respectively; t[40] = 3.04, p = .004). Male relatives of bipolar patients also had significantly higher scores on the PAS compared to same-gendered controls (*M[SD]* = 15.94[7.04], *M[SD]* = 12.03[6.07], respectively; t[55] = 2.02, $p < .05$) and female relatives (10.82[7.27]; t[38] = 2.60, p = .01). Neither the relatives of schizophrenia patients nor the relatives of bipolar disorder patients were elevated on Scales of Magical Ideation or Perceptual Aberration. The two genders in the control group did not differ on any of the Chapman scales (range of p values = .13 to .98),

Analyses of L, K, and Chapman Infrequency validity scales yielded an interaction of group and scale (*GG* $F_{2.7, 259}$ = 4.94, p = .004) but no interaction of group, scale, and gender (*GG* $F_{2.7,5.3}$ = .51, *ns*) indicating that groups differed in response biases but this was not influenced by gender. Follow-up ANOVAs for each scale revealed that compared to controls, K scale scores were lower in relatives of schizophrenia patients (p = .02) and relatives of bipolar patients (p = .008). Lower K scores in the relatives of schizophrenia patients are consistent with the two groups admitting to more psychopathology than controls and the relative groups not adopting a defensive response, as has been suggested in other family studies (Katsanis et al., 1990). There were no effects involving group for the Infrequency and L scales.

Schizotypal Phenotypes Evident in COMT Val Homozygote Relatives of Schizophrenia Patients

Because constricted affect, social anhedonia, and physical anhedonia most strongly characterized relatives of schizophrenia patients, we sought to determine whether these indices served as phenotypes for the Val^{158}Met polymorphism of the COMT gene in the first-degree biological relatives of schizophrenia patients. The subset of subjects with genotype data was submitted to analyses of genotype effects[3] [4].

Table IV presents means and standard deviations of relatives of schizophrenia patients and controls by COMT genotype on the Chapman scales and subscales of the SPQ Interpersonal factor. A repeated measures ANOVA of the four subscales of the SPQ Interpersonal factor failed to yield any effects involving COMT genotype indicating that elevated scores of relatives of schizophrenia patients on SPQ subscales were not associated with the Val^{158}Met polymorphism. Analysis of the four Chapman scales yielded an interaction of group, scale, and genotype (*GG* $F_{5.23, 206.6} = 3.82$, $p = .002$) and a trend toward an interaction of group, scale, and gender (*GG* $F_{2.61, 206.6} = 2.43$, $p = .07$). There

[3] Note that for analyses involving genotype, a maximum of three subjects were excluded due to missing data on one or more of the schizotypy measures. At least seven subjects were included in genotypes for relatives of schizophrenia and controls.

[4] T-tests were performed to examine differences within groups between genotyped and non-genotyped participants on each measure. Differences between genotyped and non-genotyped participants were found only within the control group, with genotyped participants showing significantly lower 'no close friends', 'odd behavior', and 'suspiciousness' subscale scores than non-genotyped individuals ($t_{1,81} = -2.548$, $p = .013$; $t_{1,81} = -2.178$, $p = .032$; $t_{1,82} = -2.825$, $p = .002$, respectively). No significant differences were found within groups for any of the Chapman measures.

were no other effects involving genotype or gender, indicating that gender distribution did not account for the observed interaction involving group and genotype.

To determine how group differences on each scale contributed to the interaction of group, scale and genotype, we examined the relatives of schizophrenia patients and controls by carrying out an ANOVA for each Chapman scale with group and genotype as the between subjects factors. There was an interaction of group and genotype for the PAS ($F_{2,90} = 3.43$, $p = .04$). The val-homozygote relatives of schizophrenia patients had elevated PAS scores compared to met homozygote relatives of schizophrenia patients ($t[33] = 2.07$, $p = .05$; $d = .70$) and a trend toward higher PAS scores than val/met relatives of schizophrenia patients ($t[55] = 1.9$, $p = .06$, $d = .55$). The three genotypes for the control subjects failed to differ from one another in PAS scores. When the COMT genotype groups for relatives of schizophrenia patients were contrasted with the entire group of controls to determine which allele was associated with abnormal elevations of anhedonia, val homozygote relatives of schizophrenia patients had higher PAS scores ($t[94] = 3.191$, $p = .003$, $d = .73$), while the other genotypes failed to differ from control subjects (val/met relatives and controls, $t[113] = 1.02$, $p = .30$, $d = .21$; met/met relatives and controls, $t[91] = .274$, $p = .79$, $d = .08$). Although the follow-up ANOVA for the SAS failed to yield a genotype effect ($F_{2,90} = .582$, $p = .56$) the val homozygote relatives of schizophrenia patients differed from the mean score of the control subjects on the SAS ($t[99] = 1.975$, $p = .05$, $d = .51$). The val/met genotypes showed a trend, and

the met/met genotypes failed to differ from controls (val/met relatives and controls, $t[116] = 1.87$, $p = .06$, $d = .38$; met/met relatives and controls, $t[93] = 1.29$, $p = .20$, $d = .41$). The Figure depicts social and physical anhedonia scores for relatives of schizophrenia patients in contrast with the control group mean. The val allele was associated with greater scores in the relatives.

Insert Figure 1 and Table IV about here

Diagnostic Specificity of the Anhedonia Phenotype for COMT.

Availability of the relatives of bipolar patients allowed for examination of whether the association between anhedonia and the val allele of the COMT polymorphism in relatives of schizophrenia patients was evident for another heritable disorder shown to be associated with the locus. Because relatives of bipolar disorder patients had elevated SAS scores compared to controls we carried out a repeated measures ANOVA of the Chapman scales[5]. Although the analysis failed to yield any effects involving genotype we carried out an ANOVA for each Chapman scale, with group and genotype as the between subjects factors, to fully test the specificity of the anhedonia phenotype to the val allele in relatives of schizophrenia patients. There was no group-by-genotype interaction for any of the four Chapman scales. Follow-up ANOVA of PAS scores failed to yield a genotype effect ($F_{2,32} = .521$, $p = .60$) and differences between the genotypes were small or failed to indicate a clear association with the COMT polymorphism in

[5] Because a small number of relatives of bipolar patients of specific genders and genotypes were available we did not include gender as a factor in this analysis.

the relatives of bipolar patients (val/val compared to val/met, d = .49; val/val compared to relatives, d = .22; val/met compared to met/met, d = -.24). Differences between the genotypes and the control group on the PAS were also small or not consistent with a direct association with the gene (val homozygotes, d = .59; val/met, d = .15, met/met, d = .35). Thus, PAS scores of relatives of bipolar patients were largely unrelated to COMT genotype. A similar analysis for SAS scores failed to yield a genotype effect ($F_{2,34}$ = .83, p = .45). Effect sizes for differences between genotypes were all modest or inconsistent with an association with SAS scores in the relatives of bipolar patients (val/val compared to val/met, d = - .54; val/val compared to met/met, d = -.36; val/met compared to met/met, d = .24). Differences between each genotype in the relatives of bipolar patients and the control group were also inconsistent with genotype being associated elevations on the SAS (val/val to controls, d = .02; val/met to controls, d = .56; met/met to controls, d = .38). No genotypes showed significant elevations in scores on the Magical Ideation and Perceptual Aberration scales relative to other genotypes within the relatives of bipolar patients or in contrast with the controls.[6]

Finally, inspection of Table II revealed that schizophrenia spectrum pathology was only evident in relatives of schizophrenia patients with the val allele. An aggregation of schizophrenia spectrum conditions in val homozygote relatives of schizophrenia patients is evidence that the val allele of the Val^{158}Met

[6] Examination of individual PAS scores for the val homozygote relatives of bipolar patients revealed that one relative had a score of 41 which drove the effect. When this person was excluded the mean PAS score for the val homozygote relatives of bipolar patients fell to 11.2 (1.9) and the mean score was no longer significantly elevated (p =.39).

polymorphism may be associated with increased pathology. Schizophrenia spectrum disorders in relatives of bipolar patients were rare and failed to be associated with the val allele.

Discussion

Of several schizotypy phenotypes we found anhedonia was most evident in first-degree biological relatives of schizophrenia patients and that physical anhedonia was associated with the Val^{158}Met polymorphism of the COMT gene. The relatives of schizophrenia patients as a group reported increased anhedonia, but the val homozygote relatives showed the greatest levels of social and physical anhedonia as assessed by the Chapman scales. Relatives of schizophrenia patients also had elevated scores on the Interpersonal Factor of the SPQ suggestive of social difficulties and concerns, but the factor failed to be associated with the Val^{158}Met polymorphism. Although first-degree biological relatives of bipolar disorder patients had elevated social anhedonia the COMT polymorphism failed to be associated with the schizotypy phenotype in this group. Social anhedonia may not be specific to first-degree relatives of schizophrenia patients; however, the association of physical anhedonia with the COMT gene may be unique to schizophrenia amongst severe mental disorders. The increase of physical anhedonia in biological relatives of schizophrenia patients substantiates anhedonia as an indicator of predisposition to psychosis. The absence of increased physical anhedonia in bipolar relatives may be due to anhedonia in relatives of people with mood disorders being less stable and related to state depression. There is

evidence that more trait-like anhedonic characteristics are evident in schizophrenia as compared to depression (Blanchard, Horan, & Brown, 2001).

Because of its possible effects on regulation of prefrontal and striatal catecholamines the Val^{158}Met polymorphism has been proposed to be causally related to frontal cortical dysfunction, deficits in executive function, and impaired working memory in schizophrenia (Tunbridge et al., 2006). Studies have documented an association of the COMT polymorphism with indices of prefrontal dysfunction in first-degree biological relatives of schizophrenia, (Egan et al., 2001; Callicot et al., 2003) but a clear tie to schizophrenia was absent in other investigations (Goldberg et al., 2003; Rosa et al., 2004). The present finding of the COMT polymorphism as related to a schizotypy phenotype provides evidence that the biological effects of the COMT gene may be relevant to the pathophysiology of schizophrenia. The balance of dopamine in prefrontal and striatal regions has been considered in etiologic formulations of schizophrenia (Weinberger et al., 1988; Meyer-Lindenberg et al., 2002; McIntosh, 2006) and may relate to schizotypal characteristics evident in individuals who carry genetic liability for the condition. For example, Siessmeier et al (2006) found that a tendency to differentiate positive from neutral visual stimuli was positively correlated with the size of ventral striatum in healthy controls. Also, administration of COMT antagonist tolcapone in mice inhibits stress-induced anhedonia-related behavior (Moreau et al., 1994) suggesting that greater availability of dopamine reduces anhedonic responses.

Meehl proposed that primary hypohedonia is a heritable element of pleasure impairment that reflects genetic predisposition for schizophrenia (for a discussion see Meehl, 2001). Recent work has provided evidence that aspects of anhedonia assessed by the SAS and PAS function as latent taxa (Blanchard et al., 2000; Horan et al., 2004) that are abnormally prevalent in individuals who carry genetic liability for schizophrenia (Glatt et al., 2007; Kendler et al., 1996; Clementz et al., 1991; Katsanis et al., 1990). The present study provides the first evidence that anhedonia is associated with a candidate gene for schizophrenia in biological first-degree relatives of schizophrenia patients. Similarly, we observed schizophrenia spectrum disorders to only be present in relatives of schizophrenia patients who carried the val allele. Perhaps COMT can be considered a schizogene akin to the descriptions of Meehl (ie. Archives of General Psychiatry, 1989).

Previous investigations that show varied associations of schizotypy phenotypes with the COMT polymorphism have included subjects from the general population (Avramopoulos et al., 2002; Stefanis et al., 2004; Ma et al., 2007), compared genotypes within relatives of schizophrenia and bipolar disorder as one group, without distinguishing between schizophrenia and bipolar disorder (Schurhoff et al., 2007), or used a schizotypy measure not expressly measuring psychosis-proneness (Ma et al., 2007; Schurhoff et al., 2007; Avramopoulos et al., 2002) thus limiting the conclusions one can draw about characteristics of schizotypy and genetic liability for schizophrenia. The present study yielded evidence that the SAS and PAS may more sensitively measure anomalies in

biological relatives of schizophrenia patients. Other studies have found that of schizotypy factors derived from the SPQ, only the Interpersonal factor reveals anomalies in biological relatives (Grove et al., 1991; Calkins et al., 2004). But it appears that anhedonia, and not the broader construct of interpersonal functioning, is associated with the influence of the val allele of the COMT polymorphism in families affected by schizophrenia. The present results also suggest that anhedonia may be evident in relatives of bipolar patients but that it is largely independent of the Val^{158}Met polymorphism of the COMT gene. Thus, although anhedonia is observed in relatives of schizophrenia and bipolar patients, and the COMT gene has been associated with both disorders, the relationship between anhedonia and the COMT polymorphism appears to be only evident in relatives of schizophrenia patients.

Given the limited sample size of the relatives of bipolar patients the present findings regarding diagnostic specificity need to be replicated in a larger sample of relatives. Future studies of COMT gene would also benefit from inclusion of multiple SNPs relevant to dopamine transmission to further explore the role of dopamine genes in predisposing an individual to schizotypy and schizophrenia. Ideally, these studies would compose their samples with similar proportions of the two genders. Nevertheless, the present study provides support for a link between the val allele of the COMT gene and anhedonic characteristics in individuals who carry genetic liability for schizophrenia.

References

Avramopoulos, D., Stefanis, N. C., Hantoumi, I., Smyrnis, N., Evdokimidis, I., & Stefanis, C. N. (2002). Higher scores of self reported schizotypy in healthy young males carrying the COMT high activity allele. *Molecular Psychiatry, 7*(7), 706-711.

Badner, J. A., & Gershon, E. S. (2002). Meta-analysis of whole-genome linkage scans of bipolar disorder and schizophrenia. *Molecular Psychiatry, 7*(4), 405-411.

Berenbaum, H., McGrew, J. (1993) Familial resemblance of schizotypic traits. *Psychological Medicine* 23(2), 327-33.

Bergman-Jungestrom, M., & Wingren, S. (2001). Catechol-O-Methyltransferase (COMT) gene polymorphism and breast cancer risk in young women. *British Journal of Cancer, 85*(6), 859-862.

Bilder, R. M., Volavka, J., Czobor, P., Malhotra, A. K., Kennedy, J. L., Ni, X., et al. (2002). Neurocognitive correlates of the COMT Val(158)Met polymorphism in chronic schizophrenia. *Biological Psychiatry, 52*(7), 701-707.

Bilder, R.M., Volavka, J., Lachman, H.M., Grace, A.A. (2004) The catechol-O-methyltransferase polymorphism: relations to the tonic-phasic dopamine hypothesis and neuropsychiatric phenotypes. *Neuropsychopharmacology*. 29(11), 1943-61.

Blanchard, J.J., Gangestad, S.W., Brown, S.A., Horan, W.P. (2000) Hedonic capacity and schizotypy revisited: a taxometric analysis of social anhedonia. *Journal of Abnormal Psychology,* 109(1), 87-95.

Blanchard, J.J., Horan, W. P., Brown, S.A. (2001). Diagnostic differences in social anhedonia: a longitudinal study of schizophrenia and major depressive disorder. *Journal of Abnormal Psychology*,110(3),363-71.

Calkins, M.E., Curtis, C.E., Grove, W.M., Iacono, W.G. (2004) Multiple dimensions of schizotypy in first degree biological relatives of schizophrenia patients. *Schizophrenia Bulletin,* 30(2), 317-25.

Callicott, J.H., Mattay, V.S., Verchinski, B.A., Marenco, S., Egan, M.F., Weinberger, D.R. (2003) Complexity of prefrontal cortical dysfunction in schizophrenia: more than up or down. *American Journal of Psychiatry.* 160(12), 2209-15.

Chapman, L. J., & Chapman, J. P. (1983). *Infrequency Scale.* Unpublished test.

Chapman, L. J., Chapman, J. P., & Raulin, M. L. (1978). Body-image aberration in schizophrenia. *Journal of Abnormal Psychology, 87,* 399–407.

Chapman, L. J., Chapman, J. P., Kwapil, T. R., Eckblad, M., & Zinser, M. C. (1994). Putatively psychosis-prone subjects 10 years later. *Journal of Abnormal Psychology, 103*(2), 171-183.

Chapman, L. J., Chapman, J. P., & Raulin, M. L. (1976). Scales for physical and social anhedonia. *Journal of Abnormal Psychology, 85*(4), 374-382.

Chen, X., Wang, X., O'Neill, A.F., Walsh, D., Kendler, K.S. (2004) Variants in the catechol-o-methyltransferase (COMT) gene are associated with

schizophrenia in Irish high-density families. *Molecular Psychiatry, 9*(10), 962-7.

Chen, Z. Y., Jing, D., Bath, K. G., Ieraci, A., Khan, T., Siao, C. J., et al. (2006). Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. *Science, 314*(5796), 140-143.

Cohen J. (1977). Statistical power analysis for the behavioural sciences, Revised Edition. *New York: Academic Press*.

Drabant, E. M., Hariri, A. R., Meyer-Lindenberg, A., Munoz, K. E., Mattay, V. S., Kolachana, B. S., et al. (2006). Catechol O-methyltransferase val(158)met genotype and neural mechanisms related to affective arousal and regulation. *Archives of General Psychiatry, 63*(12), 1396-1406.

Dunham, I., Collins, J., Wadey, R., & Scambler, P. (1992). Possible role for COMT in psychosis associated with velo-cardio-facial syndrome. *Lancet, 340*(8831), 1361-1362.

Eckblad, M., & Chapman, L. J. (1983). Magical ideation as an indicator of schizotypy. *Journal of Consulting and Clinical Psychology, 51,* 215–225.

Eckblad, M., Chapman, L. J., Chapman, J. P., & Mishlove, M. (1982). *The Revised Social Anhedonia Scale.* Unpublished test.

Ekselius, L, Lindstrom, E, von Knorring, L, Bodlund, O, Kullgren, G. (1994) SCID II interviews and the SCID Screen questionnaire as diagnostic tools for personality disorders in DSM-III-R. *Acta Psychiatrica Scandinavica,* 90(2), 120-3.

Egan, M. F., Goldberg, T. E., Gscheidle, T., Weirich, M., Rawlings, R., Hyde, T. M., et al. (2001). Relative risk for cognitive impairments in siblings of patients with schizophrenia. *Biological Psychiatry, 50*(2), 98-107.

Egan, M.F., Goldberg, T.E., Kolachana, B.S., Callicott, J.H., Mazzanti, C.M., Straub, R.E., Goldman, D., Weinberger, D.R. (2001) Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia. *Proceedings of the National Academy of Sciences USA,* 98(12), 6917-22.

Enoch, M. A., Xu, K., Ferro, E., Harris, C. R., & Goldman, D. (2003). Genetic origins of anxiety in women: a role for a functional catechol-O-methyltransferase polymorphism. *Psychiatric Genetics, 13*(1), 33-41.

Etain, B., Roy, I., Henry, C., Rousseva, A., Schurhoff, F., Leboyer, M., & Bellivier, F. (2007). No evidence for physical anhedonia as a candidate symptom or an endophenotype in bipolar affective disorder. *Bipolar Disorders,* 9(7), 706-12.

Fan, J.B., Chen, W.Y., Tang, J.X., Li, S., Gu, N.F., Feng, G.Y., Breen, G., St.Clair, D., & He, L. (2002). Family-based association studies of COMT gene polymorphisms and schizophrenia in the Chinese population. *Molecular Psychiatry,* 7(5), 446-7.

Fanous, A., Gardner, C., Walsh, D., Kendler, K.S. (2007) Relationship between positive and negative symptoms of schizophrenia and schizotypal symptoms in nonpsychotic relatives. *Archives of General Psychiatry,* 58(7), 669-73.

Glatt, S.J., Faraone, S.V., Tsuang, M.T. (2003) Association between a functional catechol O-methyltransferase gene polymorphism and schizophrenia: meta-analysis of case-control and family-based studies. *American Journal of Psychiatry*, 160(3), 469-76.

Glatt, S.J., Chayavichitsilp, P., Depp, C., Schork, N.J., Jeste, D.V. (2007) Successful aging: from phenotype to genotype. *Biological Psychiatry,* 62(4), 282-93.

Gooding, D.C., Braun, J.G. (2004) Visuoconstructive performance, implicit hemispatial inattention, and schizotypy. *Schizophrenia Research,* 68(2-3), 261-9.

Goldberg, T.E., Egan, M.F., Gscheidle, T., Coppola, R., Weickert, T., Kolachana, B.S., Goldman, D., Weinberger, D.R. (2003) Executive subprocesses in working memory: relationship to catechol-O-methyltransferase Val158Met genotype and schizophrenia. *Archives of General Psychiatry,* 60(9), 889-96.

Grove, W. M., Lebow, B. S., Clementz, B. A., Cerri, A., Medus, C., & Iacono, W. G. (1991). Familial prevalence and coaggregation of schizotypy indicators: a multitrait family study. *Journal of Abnormal Psychology, 100*(2), 115-121.

Gruzelier, J. H. (1996). The factorial structure of schizotypy: Part I. Affinities with syndromes of schizophrenia. *Schizophrenia Bulletin, 22*(4), 611-620.

Hashimoto, K. (2007). BDNF variant linked to anxiety-related behaviors. *Bioessays, 29*(2), 116-119.

Horan, W.P., Blanchard, J.J., Gangestad, S.W., Kwapil, T.R. (2004) The psychometric detection of schizotypy: do putative schizotypy indicators identify the same latent class? *Journal of Abnormal Psychology,* 113(3), 339-57.

Horan, W.P., Brown, S.A., Blanchard, J.J. (2007) Social anhedonia and schizotypy: the contribution of individual differences in affective traits, stress, and coping. *Psychiatry Research,* 149(1-3), 147-56.

Horan, W.P., Reise, S.P., Subotnik, K.L., Ventura, J., Nuechterlein, K.H. (2008) The validity of psychosis proneness scales as vulnerability indicators in recent-onset schizophrenia patients. *Schizophrenia Research*, 100(1-3), 224-36.

Katsanis, J, Iacono, WG, Beiser, M. (1990) Anhedonia and perceptual aberration in first-episode psychotic patients and their relatives. *Journal of Abnormal Psychology,* 99(2), 202-6.

Kendler, K.S., Lieberman, J.A., Walsh, D. (1989) The Structured Interview for Schizotypy (SIS): a preliminary report. *Schizophrenia Bulletin,* 15(4), 559-71.

Kendler, K. S. (2005). "A gene for...": the nature of gene action in psychiatric disorders. *American Journal of Psychiatry, 162*(7), 1243-1252.

Kendler, K. S. (2005). Psychiatric genetics: a methodologic critique. *American Journal of Psychiatry, 162*(1), 3-11.

Kendler, K. S., Thacker, L., & Walsh, D. (1996). Self-report measures of schizotypy as indices of familial vulnerability to schizophrenia. *Schizophrenia Bulletin, 22*(3), 511-520.

Kerns, J. G. (2006). Schizotypy facets, cognitive control, and emotion. *Journal of Abnormal Psychology, 115*(3), 418-27.

Kwapil, T. R. (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *Journal of Abnormal Psychology, 107*(4), 558-565.

Lachman, H., Morrow, B., Shprintzen, R., Veit, S., Parsia, S., Faedda, G., et al. (1996). Association of codon 108/158 catechol-O-methyltransferase gene polymorphism with the psychiatric manifestations of velo-cardio-facial syndrome. *American Journal of Medical Genetics,* 67(5), 468-472.

Leckman, J.F., Sholomskas, D., Thompson, W.D., Belanger, A., Weissman, M.M. (1982) Best estimate of lifetime psychiatric diagnosis: a methodological study. *Archives of General Psychiatry* 39(8), 879-83.

Lenzenweger, M.F. (2006) Schizotaxia, schizotypy, and schizophrenia: Paul E. Meehl's blueprint for the experimental psychopathology and genetics of schizophrenia. *Journal of Abnormal Psychology,* 115(2), 195-200.

Li, T., Vallada, H., Curtis, D., Arranz, M., Xu, K., Cai, G., Deng, H., Liu, J., Murray, R., Liu, X., Collier, D.A.(1997). Catechol-O-methyltransferase Val158Met polymorphism: frequency analysis in Han Chinese subjects and allelic association of the low activity allele with bipolar affective disorder. *Pharmacogenetics.* 7(5), 349-53.

Lotta, T., Vidgren, J., Tilgmann, C., Ulmanen, I., Melen, K., Julkunen, I., et al. (1995). Kinetics of human soluble and membrane-bound catechol O-methyltransferase: a revised mechanism and description of the thermolabile variant of the enzyme. *Biochemistry, 34*(13), 4202-4210.

Ma, X., Sun, J., Yao, J., Wang, Q., Hu, X., Deng, W., et al. (2007). A quantitative association study between schizotypal traits and COMT, PRODH and BDNF genes in a healthy Chinese population. *Psychiatry Research,* 153(1), 7-15.

MacDonald, A.W., Carter, C., Flory, J. D., Ferrell, R. E., Manuck, S.B. (2007) COMT Val^{158}Met and executive control: a test of the benefit of specific deficits to translational research. *Journal of Abnormal Psychology*, 116(2), 306-12.

McIntosh, A. M., Baig, B. J., Hall, J., Job, D., Whalley, H. C., Lymer, G. K., et al. (2007). Relationship of Catechol-O-Methyltransferase Variants to Brain Structure and Function in a Population at High Risk of Psychosis. *Biological Psychiatry,* 61(10),1127-34.

Meehl, P.E. (1962) Schizotaxia, schizotypy, schizophrenia. *American Psychologist* 17, 827–838.

Meehl, P.E. (1989) Schizotaxia revisited. *Archives of General Psychiatry*, 46(10), 935-44.

Meehl, P.E. (2001) Primary and secondary hypohedonia. *Journal of Abnormal Psychology,* 110(1), 188-93.

Meyer-Lindenberg, A., Miletich, R.S., Kohn, P.D., Esposito, G., Carson, R.E., Quarantelli, M., Weinberger, D.R., Berman, K.F. (2002) Reduced prefrontal activity predicts exaggerated striatal dopaminergic function in schizophrenia. *Nature Neuroscience,* 5(3), 267-71.

Miller, L.S., & Burns, S.A. (1995). Gender differences in schizotypic features in a large sample of young adults. *Journal of Nervous and Mental Disease,* 183(10), 657-61.

Mishlove, M., & Chapman, L. J. (1985). Social anhedonia in the prediction of psychosis proneness. *Journal of Abnormal Psychology, 94*(3), 384-396.

Mynett-Johnson, L. A., Murphy, V. E., Claffey, E., Shields, D. C., & McKeon, P. (1998). Preliminary evidence of an association between bipolar disorder in females and the catechol-O-methyltransferase gene. *Psychiatric Genetics, 8*(4), 221-225.

Park, S., & McTigue, K. (1997). Working memory and the syndromes of schizotypal personality. *Schizophrenia Research, 26*(2-3), 213-220.

Raine, A. (1991) The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophrenia Bulletin,* 17(4), 555-64.

Schurhoff, F., Szoke, A., Chevalier, F., Roy, I., Meary, A., Bellivier, F., et al. (2007). Schizotypal dimensions: An intermediate phenotype associated with the COMT high activity allele. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 144*(1), 64-68.

Shadish, W. R. (2002). Revisiting field experimentation: field notes for the future. *Psychological Methods, 7*(1), 3-18.

Siessmeier, T., Kienast, T., Wrase, J., Larsen, J.L., Braus, D.F., Smolka, M.N., Buchholz, H.G., Schreckenberger, M., Rosch, F., Cumming, P., Mann, K., Bartenstein, P., Heinz, A. (2006) Net influx of plasma 6-[18F]fluoro-L-DOPA (FDOPA) to the ventral striatum correlates with prefrontal processing of affective stimuli. *European Journal of Neuroscience.* 24(1), 305-13.

Smyrnis, N., Avramopoulos, D., Evdokimidis, I., Stefanis, C.N., Tsekou, H., Stefanis, N.C. (2007). Effect of schizotypy on cognitive performance and its tuning by COMT val158 met genotype variations in a large population of young men. *Biological Psychiatry,* 61(7), 845-53.

Sponheim, S. R., Iacono, W. G., Thuras, P. D., & Beiser, M. (2001). Using biological indices to classify schizophrenia and other psychotic patients. *Schizophrenia Research, 50*(3), 139-150.

Sponheim, S. R., Steele, V. R., & McGuire, K. A. (2004). Verbal memory processes in schizophrenia patients and biological relatives of schizophrenia patients: intact implicit memory, impaired explicit recollection. *Schizophrenia Research, 71*(2-3), 339-348.

Stefanis, N. C., Van Os, J., Avramopoulos, D., Smyrnis, N., Evdokimidis, I., Hantoumi, I., et al. (2004). Variation in catechol-o-methyltransferase val158 met genotype associated with schizotypy but not cognition: a population study in 543 young men. *Biological Psychiatry, 56*(7), 510-515.

Tochigi, M., Otowa, T., Hibino, H., Kato, C., Otani, T., Umekage, T., et al. (2006). Combined analysis of association between personality traits and three functional polymorphisms in the tyrosine hydroxylase, monoamine oxidase A, and catechol-O-methyltransferase genes. *Neuroscience Research, 54*(3), 180-185.

Tunbridge, E., Harrison, P., Weinberger, D. (2006). Catechol-o-methyltransferase, cognition, and psychosis: Val158Met and beyond. *Biological Psychiatry,* 60(2), 141-51.

Weinberger, D., Berman, K., Chase, T. (1988). Mesocortical dopaminergic function and human cognition. *Annual N Y Academy of Sciences,* 537, 330-8.

Weinberger, D. R. (2002). Biological phenotypes and genetic research on schizophrenia. *World Psychiatry, 1*(1), 2-6.

Wonodi, I., Stine, O. C., Mitchell, B. D., Buchanan, R. W., & Thaker, G. K. (2003). Association between Val108/158 Met polymorphism of the COMT gene and schizophrenia. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 120*(1), 47-50.

Woo, J. M., Yoon, K. S., Choi, Y. H., Oh, K. S., Lee, Y. S., & Yu, B. H. (2004). The association between panic disorder and the L/L genotype of catechol-O-methyltransferase. *Journal of Psychiatric Research, 38*(4), 365-370.

Wuthrich, V. M., & Bates, T. C. (2006). Confirmatory factor analysis of the three-factor structure of the schizotypal personality questionnaire and chapman schizotypy scales. *Journal of Personality Assessment, 87*(3), 292-304.

Zubieta, J., Heitzeg, M., Smith, Y., Bueller, J., Xu, K., Xu, Y., Koeppe, R., Stohler, C., Goldman, D. (2003) COMT val158met genotype affects mu-opioid neurotransmitter responses to a pain stressor. *Science,* 299(5610), 1240-3.

ANHEDONIA AS A PHENOTYPE FOR COMT IN RELATIVES OF SCHIZOPHRENIA PATIENTS

Table I

Demographic Characteristics of Participant Groups: Genotyped, Non-Genotyped, and Total Sample

	Group								
	Relatives of SC Patients			Relatives of BPD Patients			Nonpsychiatric Controls		
	G	NG	Total	G	NG	Total	G	NG	Total
N	81	13	94	38	7	45	30	55	85
% female	68	62	67	53	71	56	50	47	48
Mean age (SD)	50(12)[b]	63(12)	52(13)[a]	50(17)	50(12)	50(16)[c]	39(12)	44(17)	42(15)

Note: SC = Schizophrenia (79 relatives) or schizoaffective disorder (15 relatives); BPD = Bipolar disorder**;** G = Genotyped subjects; NG = Non-genotyped subjects (subjects without genotype information)

[a] $p < .001$; comparing relatives of SC and control group

[b] $p < .005$; comparing genotyped and non-genotyped relatives within group

[c] $p < .01$; comparing relatives of BPD and control group

Table II

Demographic Characteristics of Genotyped Individuals by Group and Genotype

	Group								
	Relatives of SC Patients			Relatives of BPD Patients			Nonpsychiatric Controls		
	Val/Val	Val/Met	Met/Met	Val/Val	Val/Met	Met/Met	Val/Val	Val/Met	Met/Met
N	22	41	18	6	20	12	9	13	8
Mean Age (SD)	53(9)[a]	48(10)	49(12)[b]	51(10)[b]	51(20)	45(15)	36(13)	44(9)	34(13)
% Female	71	60	64	83	47	36	44	69	25
% Siblings	64	73	83	50	35	50	n/a	n/a	n/a
% Parents	36	24	11	50	40	33	n/a	n/a	n/a
% Offspring	0	2	6	0	25	17	n/a	n/a	n/a
%Lifetime DSM Axis I Dis.	32	37	33	67	40	50	0	0	0
% Major Depression	23	29	33	67	20	50	0	0	0
% Alcohol Dependence	4	5	11	0	0	0	0	0	0
% Bipolar Disorder	0	2	0	0	0	0	0	0	0
% Anxiety Disorder[1]	4	7	0	17	15	17	0	0	0
% Lifetime DSM Axis II Dis[2].	24	0	0	0	0	22	0	0	0
% Lifetime SCZ Spect. Dis.	24	3	0	0	6	0	0	0	0

Note SC = Schizophrenia or schizoaffective disorder; BPD = Bipolar disorder; DSM = Diagnostic and Statistical Manual; Dis = Disorder ; SCZ Spect. Dis. = DSM-IV Psychotic Disorders and Cluster A Personality Disorders

[a] $p < .005$; compared with controls of same genotype.

[b] $p < .05$; compared with controls of same genotype.

[1] Two individuals in the nonpsychiatric control group were given a diagnosis of a lifetime anxiety disorder (one had Panic Disorder, and one had a history of PTSD) but neither of these controls were genotyped.

[2] Axis II disorders were not assessed for 22 relatives of schizophrenia patients and 13 relatives of bipolar disorder patients because they did not travel to the study site. The percentages reflect the proportion of individuals with genotype data affected for whom Axis II diagnoses were available.

Table III.

Means, Standard Deviations, and Univariate Test Statistics for Chapman Scales and SPQ Factors using Total Sample

	Rels of SC	[1]d	Rels of BPD	[2]d	Controls	(df) F	p
SPQ							
Total Score	14.4 (11.2)	.35	14.8 (14.2)	.17	10.2 (7.1)	$(_{2,196})$ 2.24	.11
Interpersonal Factor	7.6 (6.2)[b]	.38	7.0 (7.7)	.11	4.9 (4.7)	$(_{2,191})$ 4.40	.01
Cognitive-Perceptual Factor	4.3 (4.9)	.08	4.9 (6.2)	.16	3.2 (2.6)	$(_{2,191})$ .60	.55
Disorganization Factor	3.9 (3.3)	.17	4.2 (4.1)	.10	3.0 (2.4)	$(_{2,191})$ 1.62	.20
Chapman Scales							
Social Anhedonia Scale (SAS)	8.6 (5.9)[a]	.44	7.9 (6.2)[b]	.31	6.6 (5.7)	$(_{2,178})$ 6.88	.001
Magical Ideation Scale	2.6 (2.7)	.03	2.9 (3.9)	-.10	2.3 (2.0)	$(_{2,178})$ .04	.97
Perceptual Aberration Scale	1.7 (2.5)	.16	1.9 (3.1)	.11	1.2 (1.3)	$(_{2,178})$ .15	.87
Physical Anhedonia Scale (PAS)	13.4 (6.1)[b]	.33	13.1 (7.5)	.15	11.7 (6.1)	$(_{2,178})$ 3.33	.04
Validity Scales							
Chapman Infrequency Scale	2.3 (.6)	.00	2.4 (.7)	.15	2.3 (.6)	$(_{2,195})$ .36	.70
MMPI-2 L Scale	4.3(2.1)	.29	3.6 (1.9)	-.05	3.7 (2.1)	$(_{2,195})$ .81	.45
MMPI-2 K Scale	17.4 (4.6)[b]	-.42	16.9 (4.9)[a]	-.51	19.2 (4.0)	$(_{2,195})$ 4.54	.01

Note. Effect sizes and test statistics are based on logarithmically transformed scores for each schizotypy measure in order to correct for non-normal distributions. Validity scales were not log transformed. Rels of SC = Relatives of schizophrenia patients; Rels of BPD = relatives of bipolar disorder patients; Controls = Nonpsychiatric control subjects.

[1] effect size (Cohen, 1977) for differences between relatives of schizophrenia patients and controls.

[2] effect size (Cohen, 1977) for differences between relatives of bipolar patients and controls.

[a] different from controls $p < .01$

[b] different from controls $p < .05$

Table IV.

Means and Standard Deviations for Relatives of Schizophrenia Patients and Controls Subjects by COMT Val[158]Met Genotype

	Relatives of SC Patients			Nonpsychiatric Controls		
	Val/Val	Val/Met	Met/Met	Val/Val	Val/Met	Met/Met
Chapman Scales						
Social Anhedonia	9.1 (6.9)[a]	8.5 (6.4)	7.5 (4.3)	4.5 (4.2)	5.6 (2.7)	5.5 (3.0)
Physical Anhedonia	15.2 (5.3)[a,b]	12.5 (5.4)	11.9 (6.0)	10.6 (6.0)	9.1 (4.3)	14.1 (6.6)
Magical Ideation Scale	1.8 (2.1)	3.2 (3.2)	2.2 (1.3)	2.2 (1.8)	1.5 (1.4)	1.5 (1.5)
Perc. Aberration Scale	1.0(1.3)	2.1 (2.9)	2.2 (3.2)	1.1 (1.1)	1.0 (1.0)	.4 (.7)
SPQ Interpersonal Factor Subscales						
No Close Friends	2.1 (2.8)	1.7 (2.3)	1.6 (1.8)	.3 (.7)	1.2 (2.0)	.3 (.5)
Constricted Affect	1.6 (1.8)	1.4 (1.7)	1.9 (1.7)	.6 (.9)	.7 (1.3)	.8 (.7)
Excessive Social Anxiety	2.4 (2.1)	3.3 (2.8)	3.3 (2.2)	2.0 (1.8)	1.7 (1.2)	1.1 (1.4)
Suspiciousness	1.0 (1.3)	1.0 (1.4)	1.2 (1.4)	.4 (.7)	.3 (.5)	.3 (.5)

a = significantly different controls of same genotype, $p < .05$

b = significantly different from met/met relatives of schizophrenia patients, $p < .05$

SC = First-degree relatives of schizophrenia patients.

Perc. = Perceptual

ANHEDONIA AS A PHENOTYPE FOR COMT IN RELATIVES OF SCHIZOPHRENIA PATIENTS

Figure 1.

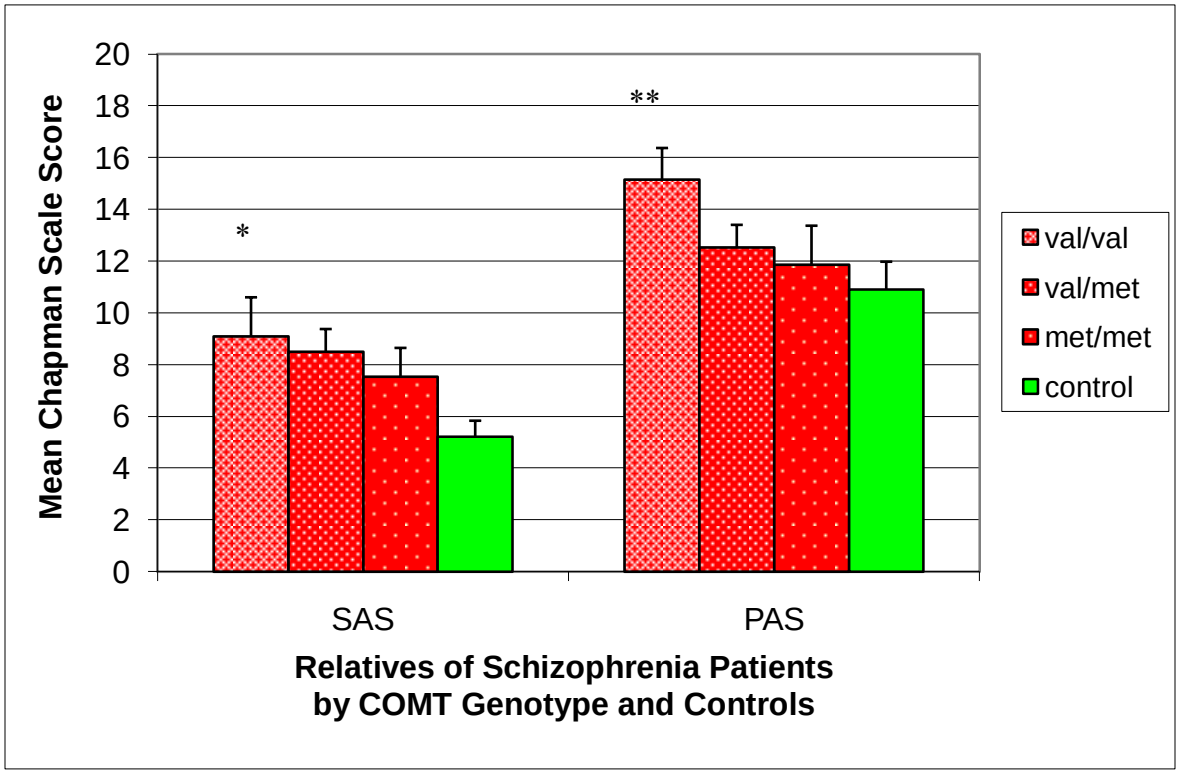

Figure Caption

Figure 1.

Social Anhedonia Scale (SAS) and Physical Anhedonia Scale (PAS) scores in nonpsychiatric control participants and first-degree biological relatives of schizophrenia patients by COMT Val^{158}Met genotype. Error bars represent standard errors of the mean.

** $p < .005$ for difference with control subjects.

* $p \leq .05$ for difference with control subjects.