DIFFERENTIATING PSYCHOSIS RISK AND MANIA RISK SCALES AND
THEIR ASSOCIATIONS WITH SPONTANEOUS EYE BLINK RATE

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THEIR ASSOCIATIONS WITH SPONTANEOUS EYE BLINK RATE

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I dedicate this thesis to my family for their love and support.

To my mom, who knows me best

To my dad, for the stories and life lessons

To my sister, Amanda, the original subject

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Abstract

Psychosis risk and mania risk scales are strongly correlated, and both psychosis and mania are linked to alterations in striatal dopamine. However, previous research has not examined whether measures of psychosis and mania risk form distinct factors or whether they are differentially related to other measures of psychopathology risk or to a measure reflecting increased striatal dopamine. In the current study with undergraduate students ($N = 596$), participants completed both psychosis risk and mania risk scales as well as scales assessing related psychopathology (i.e., negative and disorganized schizotypy; self-reported manic-like episodes). Additionally, I measured spontaneous eye blink rate (sEBR), which has been consistently associated with striatal dopamine levels. As expected, psychosis risk and mania risk factors were strongly correlated (factor correlation = .73). However, a two-factor confirmatory factor analytic model with psychosis risk and mania risk as separate factors fit significantly better than a one-factor risk model. Additionally, after removing shared variance, only psychosis risk was positively associated with both negative and disorganized schizotypy measures, and only mania risk was significantly related to self-reported manic-like episodes. Furthermore, psychosis risk and mania risk were differentially associated with sEBR. Specifically, psychosis risk was associated with *decreased* sEBR, and mania risk was associated with *increased* sEBR. Overall, these results suggest that psychosis risk and mania risk can be distinguished as separate factors and that they might be differentially associated with striatal dopamine measure.

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Differentiating Psychosis Risk and Mania Risk Scales and Their Associations with Spontaneous Eye Blink Rate

Psychosis involves symptoms such as delusions and hallucinations, whereas mania involves distinct periods of dramatically elevated moods and concomitant changes in behavior (American Psychiatric Association, 2013). There are a number of self-report scales that attempt to assess either psychosis or mania risk, and there are multiple reasons that researchers use these scales. First, it has long been thought that research on these risk scales might help us understand the nature of psychosis and mania risk (e.g., Barrantes-Vidal, Grant, & Kwapil, 2015; Debbané et al., 2015; Eckblad & Chapman, 1986). Additionally, it has been thought that research on these scales might help us understand extreme variation in common personality traits that might be present in personality disorders (Krueger & Markon, 2014; Schalet, Durbin, & Revelle, 2011; Watson, Stasik, Ro, & Clark, 2013). Finally, researchers and clinicians attempting to assess people at clinical high risk often use these scales as screening instruments to initially identify people in need of an additional in-depth risk assessment (Kline & Schiffman, 2014). Hence, research further examining the construct validity of psychosis and mania risk scales could be useful for several reasons. A potentially critical gap in research on these scales is that previous research has rarely examined whether psychosis and mania risk scales can be differentiated from each other (Prete et al., 2015). Thus, the current research examined whether psychosis and mania risk scales formed distinct factors in a confirmatory factor analysis, whether these factors were differentially related to other measures of psychopathology risk, and whether these factors were differentially related to a measure reflecting increased striatal dopamine.

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There are several reasons why it is important to examine whether psychosis and mania risk scales can be differentiated. First, there is evidence that psychosis and mania risk scales are highly correlated. For instance, several studies examining correlations in the general population ($N = 1095$; Claridge et al., 1996), in college students ($Ns = 515$, 657, & 625; Applegate, El-Deredy, & Bentall, 2009; Eckblad & Chapman, 1986; Schuldberg, 1990) or in a sample of artists ($N = 100$; Nelson & Rawlings, 2010) have found correlations ranging from .43 to .64, with these correlations being close to or in the range for how strongly psychosis risk scales correlate with each other (e.g., Cicero & Kerns, 2010a; 2010b). Second, there is evidence that elevated psychosis risk scores might predict future manic episodes about as strongly as they do future psychotic disorders (Chapman et al., 1994). Third, there is evidence that mania risk also predicts increased future psychotic-like experiences (Kwapil et al., 2000; Walsh, DeGeorge, Barrantes-Vidal, & Kwapil, 2015). Hence, although it was expected in the current research that psychosis and mania scales would be differentiated, the strong associations between psychosis and mania risk suggest that it is important to empirically examine this relationship directly. In fact, there is evidence in previous research that some psychosis risk scales could not be easily differentiated from another related risk construct (i.e., dissociation; Cicero & Kerns, 2010b), further arguing for the need to directly examine whether psychosis and mania risk scales could be differentiated.

Another reason why it is important to examine whether psychosis and mania risk scales can be differentiated is that in addition to these risk scales being highly correlated, there is also a long line of evidence demonstrating that psychotic and manic disorders are highly related. For instance, psychotic and mood disorders are highly comorbid, with a

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majority of individuals with so-called non-affective psychotic disorders experiencing mood episodes less than 50% of the time (American Psychiatric Association, 2013). Similarly, about half of all people with Bipolar Disorder also present with psychotic symptoms during their illness (Dunayevich & Keck, 2000). Furthermore, many individuals are diagnosed with schizoaffective disorder because they have at least one period where they only experience psychosis plus an extensive history of experiencing mood episodes (American Psychiatric Association, 2013). Consistent with this extensive comorbidity between psychosis and mania, family history studies have found that genetic risk for psychotic disorders predicts increased risk for Bipolar Disorder and vice versa (e.g., Lichtenstein et al. 2009). In addition, a recent GWAS study found a large overlap between common alleles related to non-affective psychotic disorders (i.e., Schizophrenia) and Bipolar Disorder (genetic correlation $r = .68$; Cross-Disorder Group of the Psychiatric Genomics Convention, 2013). Given this evidence, some have argued that the categorical distinction between non-affective psychotic disorders and Bipolar Disorder may not be valid (e.g., Craddock, O'Donovan, & Owen, 2005). In fact, an argument could be made that the disorder most closely related to non-affective psychosis is Bipolar Disorder. Given the extensive relationships between psychosis and mania, this makes it even more important to directly examine whether psychosis and mania risk scales can be differentiated.

A final reason why it might be important to examine whether psychosis and mania risk scales can be differentiated is that both psychosis and mania have been linked to the same neurobiological mechanism: striatal dopamine. For instance, medication that blocks dopamine D₂ receptors, with D₂ receptors most prevalent in the striatum (Hisahara

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& Shimohama, 2011), is the only effective medication for psychosis (Seeman, 2010) and is also at least as effective as any other medication for the treatment of acute mania (Scherk, Pajonk, & Leucht, 2007). Further, increased striatal dopamine is the best-established neurobiological correlate of psychosis (e.g., Howes et al., 2012). In addition, mania is associated with alterations in the Behavioral Activation System (BAS; Alloy et al., 2012; Johnson, Edge, Holmes, & Carver, 2013), which has long been linked to striatal dopamine (Beaver et al., 2006; Lawrence & Brooks, 2014). Hence, potentially an important issue in differentiating psychosis and mania risk scales is to examine whether psychosis and mania risk are differentially associated with a measure related to striatal dopamine levels.

A physiological measure that has been consistently associated with striatal dopamine levels is spontaneous eye blink rate (sEBR). It is thought that the brain has a spontaneous blink generator (e.g., to help maintain eye moisture), with some evidence that the spinal trigeminal complex might be involved (Kaminer, Powers, Horn, Hui, & Evinger, 2011). The striatum/basal ganglia is known to regulate spinal trigeminal complex activity, suggesting that striatal dopamine levels could then affect sEBR. Consistent with this, a long line of animal and human research has found evidence that striatal dopamine functioning is related to sEBR, with decreased dopamine being associated with a decrease in sEBR and increased dopamine being associated with an increase in sEBR (Cavanagh, Masters, Bath, & Frank, 2014; Slagter, Georgopoulou, & Frank, 2015). For instance, Parkinson's Disease, which involves decreased striatal dopamine, is associated with decreased sEBR (Karson, 1983). In contrast, there is evidence that sEBR is increased in people with psychotic disorders (Karson, Dykman, &

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Paige, 1990; Kleinman et al., 1984). Furthermore, animal evidence has consistently found that striatal dopamine manipulations affect sEBR (Groman et al., 2014; Kleven & Koek, 1996). Therefore, if psychosis and mania risk scales are differentially associated with striatal dopamine levels, then it might be expected that these scales would be differentially associated with sEBR.

Thus, the current research examined whether psychosis and mania risk scales could be differentiated from each other. If they could, then it would be expected that even though psychosis and mania risk scales might be strongly correlated, that they would still form distinct factors in a confirmatory factor analysis. In the current research, I examined whether a 2-factor psychosis risk and mania risk model fit significantly better than a 1-factor model that included all psychosis and mania risk scales.

If psychosis and mania risk scales could be differentiated from each other, then it would also be expected that these risk scales would be differentially associated with other scales reflecting psychopathology risk and symptoms. In particular, one expectation is that only psychosis risk scales would be associated with other measures of schizotypy. Schizotypy refers to traits that reflect symptoms of schizophrenia but in a diminished form (Raine, 2006), with research suggesting at least three distinct general facets of schizotypy—positive/psychosis risk (i.e., scales measuring delusion-like and hallucination-like experiences reflecting psychosis risk), negative, and disorganized (Kerns, 2006). Studies have found that both negative and disorganized schizotypy are positively correlated with psychosis risk (e.g., Cicero & Kerns, 2010b). On the other hand, at least one study has found that a mania risk scale was not associated with a measure of negative schizotypy (Applegate, El-Deredy, & Bentall, 2009). In the current

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study, it was expected that after removing shared variance that only psychosis risk would be associated with measures of negative and disorganized schizotypy.

In contrast, another expectation is that after removing shared variance that only mania risk would be associated with measures of self-reported prior experience of manic-like episodes. Consistent with this, mania risk scales have been found to not only predict future Bipolar Disorder but to also identify people with a previous history of hypomanic or manic episodes. However, to my knowledge previous research has not examined whether after removing shared variance that only mania risk but not psychosis risk would be associated with measures of prior manic-like episodes.

Finally, if psychosis and mania risk scales could be differentiated from each other, then it would also be expected that these risk scales would be differentially associated with sEBR. Again, previous research and theory suggest that both psychosis risk and mania risk might be associated with an increase in striatal dopamine. However, there are also reasons to think that psychosis risk scales might be associated with a *decrease* in striatal dopamine. There is evidence that striatal dopamine is only increased during acute psychotic episodes, but that striatal dopamine may not be increased when not in an acute psychotic episode (Laruelle, Abi-Dargham, Gil, Kegeles, & Innis, 1999). Further, psychosis risk scales do not directly assess current symptoms but instead enquire about trait levels of psychotic-like beliefs and experiences. Finally, there is evidence that if anything, psychotic disorders might be associated with low levels of trait striatal dopamine (Maia & Frank, 2017). For instance, there is consistent evidence that psychotic disorders and genetic risk for psychotic disorders are associated with decreased activation in the limbic striatum (meta-analysis by Radua et al., 2015), which is consistent with

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psychosis risk being associated with decreased trait dopamine. Hence, if psychosis and mania risk scales can be differentiated from each other, then it might also be expected that these risk scales would be differentially associated with sEBR, with psychosis risk being associated with decreased sEBR and mania risk being associated with increased sEBR.

METHODS

Participants

Participants ($N = 639$) were undergraduates at University of Missouri enrolled in an Introduction to Psychology course. Participants ($n = 23$) who scored 3 or greater on a 13-item infrequency scale (Chapman & Chapman, 1986), which measures careless and invalid responding (e.g., I cannot remember a time when I talked with someone who wore eyeglasses). In addition, one participant with invalidly fast questionnaire responses and noted by research assistants as not paying attention as well as participants ($n = 4$) who exhibited very poor performance on a very simple cognitive task (accuracy $< 65\%$ on a task involving deciding whether two cards were the same or different) were also excluded. Lastly, 15 participants were excluded for not completing all questionnaire measures; as can be seen in Table 1, this resulted in a final sample size of 596 participants.

Measures

Psychosis Risk Questionnaires. Participants completed five different psychosis risk questionnaires. The Perceptual Aberration Scale (PerAb; Chapman, Chapman, & Raulin, 1978; $\alpha = .81$ in current study; note that questionnaire reliabilities were uniformly high in the current study, with all α 's $\geq .80$) is a 35-item true/false scale that assessed perceptual distortions about one's body. A second questionnaire was the Magical Ideation Scale (MagicId; Eckblad & Chapman, 1983; $\alpha = .81$), a 30-item true/false scale that assessed "beliefs in forms of causation that by conventional standards are invalid" (Eckblad & Chapman, 1983; p. 215). Individuals scoring high on PerAb and MagicId scales have been found to be at increased risk for a future psychotic disorder (Chapman et

al., 1994). The third was the Cardiff Anomalous Perceptions Scales (CAPS; Bell, Halligan, & Ellis, 2006; $\alpha = .89$), a 32-item yes/no scale that assessed psychosis experiences, olfactory and gustatory experiences, and temporal lobe disturbance experiences. For items that participants endorsed as having experienced, participants then also rated frequency, distress, and intrusiveness on a five-point Likert-scale. Previous studies have looked at the CAPS using four scores separately: number of items endorsed, sum of distress ratings for items endorsed, sum of intrusiveness ratings for items endorsed, and sum of frequency ratings for items endorsed. In the current study, all of these 4 scores were strongly correlated with each other, $r_s \geq .93$. Hence, I created a single composite CAPS score by standardizing and averaging these four scores together. The CAPS has been found to be highly correlated with other psychosis risk scales (e.g., O-Life Unusual Experiences Subscale $r = .57$; Peters Delusions Inventory $r = .60$; Launay-Slade Hallucinations Scale $r = .65$), and it has been found that inpatients with psychosis scored significantly higher compared to a sample from the general population (Bell et al., 2006). The fourth questionnaire was the Positive Symptoms subscale of the Prodromal Questionnaire-Likert (PQ-Likert Pos; $\alpha = .91$; Loewy, Johnson, & Cannon, 2007), a 45-item scale that assessed the occurrence, frequency (5-point Likert scale, from 0 to Daily), and distress (true/false) of psychotic-like beliefs and experiences. PQ-Likert Pos frequency and distress scores were highly correlated with each other, $r = .82$. Hence, I created a single composite PQ-Likert Pos score by averaging standardized frequency and distress scores. The PQ-Likert Pos has been found to significantly predict interview assessment of probable high imminent risk of psychotic disorder onset (Loewy, Bearden, Johnson, Raine & Cannon, 2005). The last psychosis scale was the Psychoticism

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Personality Traits Domain from the Personality Inventory for *DSM-5* (PID-5; Krueger, Derringer, Markon, Watson, & Skodol, 2012; $\alpha = .95$). The Psychoticism Domain subscale consisted of 33 Likert-rated items (0 = Very False or Often False to 3 = Very True or Often True), which assessed psychoticism facets related to eccentricity, perceptual dysregulation, and unusual experiences. A previous study found that a group with psychotic disorder scored significantly higher on the PID-5 Psychoticism Domain subscale compared to a control group, with the Psychoticism Domain also being moderately correlated with current psychotic symptom severity (Bastiaens et al., 2017).

Mania Risk Questionnaires. Participants also completed two mania risk questionnaires: the General Behavior Inventory 10-Item Mania Scale (GBI; Youngstrom, Frazier, Demeter, Calabrese, & Findling, 2008) and the Hypomanic Personality Scale (HPS; Eckblad & Chapman, 1986). The GBI 10-Item Mania Scale ($\alpha = .84$) consisted of Likert-rated items (0 = Never/Hardly Ever to 3 = Very Often), which assessed both hypomanic and biphasic behaviors (i.e., behaviors fluctuating between depression and hypomania). The 10 items used in the current research were from the larger original version of the GBI (Depue, Krauss, Spoont, & Arbisi, 1989), with these 10 items found to best discriminate pediatric Bipolar Disorder in youth up to age 17 (Youngstrom, Frazier, Demeter, Calabrese, & Findling, 2008) and found to correlate highly with the original GBI ($r = .95$).

The HPS ($\alpha = .86$) is a 48-item true/false scale that was constructed to identify individuals who were predisposed to experience episodes of hypomanic euphoria as well as to develop Bipolar Disorder. Eckblad and Chapman (1986) reported that the overwhelming majority of people scoring high on the HPS had a history of hypomanic

episodes but without a history of manic episodes. In a 13-year follow-up study of individuals, who scored high on the HPS, 25% of the high scoring group met criteria for Bipolar Disorder compared to 0% of controls (Kwapil et al., 2000). Consistent with most previous research using this scale (e.g., Fulford, Feldman, Tabak, McGillicuddy, & Johnson, 2013; Kwapil et al., 2000, Walsh, DeGeorge, Daniella, Barrantes-Vidal, & Kwapil, 2015), the HPS total score was used in the main analyses.

Negative and Disorganized Schizotypy Traits. To examine convergent and discriminant associations of psychosis and mania risk scales, participants also completed measures of negative and disorganized schizotypy. To assess negative schizotypy, participants completed the Revised Social Anhedonia Scale (SocAnh; $\alpha = .82$; Eckblad, Chapman, Chapman, & Mishlove, 1982) as well as the PQ-Likert Negative Symptoms subscale (PQ-Likert Neg; $\alpha = .89$; Loewy, Johnson, & Cannon, 2007). SocAnh is a 40-item true/false scale that assessed lack of social contact and lack of social pleasure and has been found to predict future onset of non-psychotic schizophrenia-spectrum disorders (Gooding et al., 2005; Kwapil, 1998). The PQ-Likert Neg is a 19-item Likert scale that assessed the frequency of (5-point Likert scale, from 0 to Daily) and distress (true/false) associated with negative symptoms. To assess disorganized schizotypy, participants completed the PQ Disorganized Symptoms subscale (PQ-Likert Disorg; $\alpha = .80$; Loewy et al., 2007), a 13-item measure that assessed the frequency of (5-point Likert scale, from 0 to Daily) and distress (true/false) associated with disorganized symptoms. To account for both symptoms endorsed and distress, PQ-Likert Neg and PQ-Likert Disorg scores were calculated by summing their respective standardized frequency and distress scores.

Manic-Like Episode Questionnaires. To further examine convergent and discriminant associations of psychosis and mania risk scales, participants also completed two questionnaires that assessed previous manic-like episodes: the WHO Composite International Diagnostic Interview 3.0 (CIDI; Kessler et al., 2006) and the Mood Disorder Questionnaire (MDQ; Hirschfeld et al., 2000). The CIDI is a yes/no interview that assessed to what extent people reported previous manic-like episodes. For the purposes of this study, participants completed the interview on the computer as a questionnaire. This measure first asks about whether the participant experienced periods of euphoria or irritability. If the participant responded yes, then the participant was asked whether they experienced any of up to nine symptoms during those periods (e.g., “Did you spend so much more money than usual that it caused you to have financial trouble?”). Participants who then endorsed at least six items were considered at moderate risk for having had a manic-like episode/meeting criteria for a Bipolar Disorder (although note that this scale has not been used in previous research with undergraduate college students). This measure has been shown to have good concordance with the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID), an established interview measure of bipolar-spectrum disorders, with the scale detecting 67% – 96% of true cases and with a predictive value of 31% – 52% (Kessler et al., 2006).

Participants also completed the MDQ, a true/false scale that assesses past manic-like episodes. On the MDQ, participants first reported whether they had experienced any of 13 manic-like symptoms (e.g., “you got much less sleep than usual and found you didn’t really miss it?”). Then individuals rated whether several of these symptoms had occurred during the same time period. Finally individuals were asked whether any

symptoms had caused problems for them. The MDQ has been shown to have high specificity (.90) and high sensitivity (.73) in an outpatient population diagnosed with a mood disorder (Hirschfeld et al., 2000). In contrast, it has been shown to have high specificity (.97) but *low* sensitivity (.28) in a general population (Hirschfeld et al., 2003). In particular, it has been suggested that the MDQ's requirement that manic symptoms cause impairment might prevent the MDQ from effectively detecting Bipolar II Disorder because Bipolar II involves hypomanic episodes that do **not** cause significant impairment (Miller, Johnson, Kwapil, & Carver, 2011; note that in contrast, Bipolar I is defined as involving manic episodes that do cause significant impairment; American Psychiatric Association, 2013). Consistent with this, in the validation study of the MDQ in a general population (Hirschfeld et al., 2003), the authors found unexpectedly lower rates of Bipolar II Disorder, compared to Bipolar I Disorder, in their sample. Thus in the current study, in line with previous studies (e.g., Hirschfeld et al., 2000; Hirschfeld et al., 2003), manic-like episodes were indicated both by endorsing at least 7 of the 13 items and by indicating that several of these symptoms had occurred during the same time period. However, based on previous research, I omitted the requirement that these symptoms cause impairment. Overall, it was expected that mania risk would be more associated than psychosis risk with evidence of previous manic-like episodes.

General Distress and Current Mood. Participants also completed measures related to general distress and current mood to examine: (a) whether current distress or mood was differentially associated with psychosis or mania risk and (b) whether differences in current general distress or mood could possibly account for relationships between psychosis and mania risk with the other questionnaires and with sEBR. General

distress was assessed with the PQ-Likert General Symptoms subscale (PQ-Likert Gen; $\alpha = .88$; Loewy et al.; 2007), a 15-item measure that assessed the frequency of (5-point Likert scale, from 0 to Daily) and distress (true/false) associated with psychological distress (e.g., depression-like symptoms) and problems in role functioning. A PQ-Likert Gen score was obtained by summing standardized frequency and distress scores. Current mood (Barrett & Russell, 1999) was assessed with a 16-item Likert-rated scale (0 = Not at All to 6 = Extremely Strongly). The scale consisted of 8 positive items (e.g., happy, excited, calm; $\alpha = .77$) and 8 negative items (e.g., upset, depressed; $\alpha = .81$). Total scores for positive mood and negative mood were used in analyses.

Spontaneous Eye Blink Rate. To measure trait dopamine (Slagter, Gerogopoulou, & Frank, 2015), sEBR was measured by videotaping participants as they looked at a fixation cross on a blank poster board for six minutes in accordance with a well-validated procedure of sEBR data collection (Colzato, Slagter, van den Wildenberg, & Hommel, 2009; Chermahini & Hommel, 2010). sEBR was calculated as the average number of blinks across the six minutes. As Barbato and colleagues (2000) have found that dopamine levels increase after 5:00 P.M., sEBR data were not collected past 5:00 P.M. Additionally, as contacts could irritate the eyes and result in increased blink rates, all participants with contacts were asked to wear their glasses during the current study.

From these video recordings, research assistants calculated the participants' sEBR. As this study did not use electrooculography (EOG) to measure sEBR, the first author of this article piloted the reliability of video assessment ratings on 10 undergraduates. Participants' blink rates were simultaneously measured with EOG and video recordings. My ratings of video recorded sEBR were reliable ($ICC = 1.00$) and virtually identical to

EOG recordings. Furthermore, 20 research assistants were trained to rate sEBR by rating a subset of 10 participant videos, and the research assistants reached a high level of interrater reliability with my ratings ($ICC = .94$). During the data collection phase of the study, videos that were deemed difficult to rate were rated by multiple research assistants. If the ratings between the two research assistants varied by more than 10 blinks across the 6 minutes, the data ($n = 2$) were not included in the analyses. Note that if I divided up the sEBR into six 1-minute intervals, these six scores exhibited a high level of reliability ($\alpha = .97$).

Procedure

The duration of the study was 90 minutes. All questionnaire and task measures were administered in E-Prime 2.0 (Psychology Software Tools, 2012). Upon arrival to the study and after obtaining informed consent, participants first completed the current mood questionnaire and then sEBR data was obtained. Following this, participants completed the questionnaires in the current study in two different blocks. In the first questionnaire block, participants completed the measures in the following order: (1) Wisconsin Schizotypy Scales (consisting of a mixture of PerAb, MagicId, SocAnh, and infrequency scale items); (2) GBI; (3) CAPS; and (4) HPS. In the second questionnaire block, participants completed the measures in the following order: (1) PQ-Likert (consisting of a mixture of PQ-Likert Pos, PQ-Likert Neg, PQ-Likert Disorg, and PQ-Likert General Symptoms); (2) MDQ; (3) PID-5; and (4) CIDI. Note again that questionnaire scale internal reliabilities for the psychosis and mania risk scales in the current study were uniformly high (all α s $> .80$). Additionally, in the current study participants completed several computerized behavioral tasks, in particular multiple

versions of the Weather Prediction Task (WPT), which was previously found to be associated with psychosis risk (Karcher, Martin, & Kerns, 2015). In this study, I did not find an association between psychosis risk and WPT performance. However, performance on the WPT, which can be a challenging and effortful task, was quite poor in the current study. The WPT should produce a clear and strong learning effect over time; however in the current study a learning effect was virtually absent (current study accuracy by task quartile 55%, 60%, 61%, & 61%; in contrast, accuracy by quartile in Karcher et al., 2015: 59%, 69%, 72%, & 76%; similarly in Gluck et al., 2002: accuracy near 50% accuracy in Quartile 1 versus > 70% accuracy by Quartile 4). Thus, it is unclear whether the current WPT data provide a valid test of whether WPT performance is associated with either psychosis risk or mania risk. Complete details of WPT task administration and all WPT results are included in the Supplemental Materials and Results.

Analyses

Data were analyzed with a series of structural equation models using Mplus 7 (Muthén & Muthén, 1998-2015). First, I determined the best-fitting structural equation model involving psychosis risk and mania risk scales. The manifest variable that loaded highest on each latent variable was included first in the model, which set the standardized factor loadings to be equal to one. As all of the manifest variables were continuous and distributions were non-normal, MLR estimators were used to fit the model. MLR are maximum likelihood parameter estimates with robust standard errors and a chi-square test statistic that is robust to non-normality. Model fit was evaluated using three test statistics: the comparative fit index (CFI), Tucker-Lewis index (TLI), and the root mean

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square error of approximation (RMSEA). Chi-square difference tests of model comparisons were done using the Satorra-Bentler scaled chi-square (Satorra & Bentler, 2010). Lastly, to examine differential validity of psychosis risk and mania risk, I used structural equation modeling to examine psychosis risk and mania risk factors as joint predictors of other variables (e.g., sEBR). Given sizable sex differences on multiple scales, consistent with previous research I standardized all measures within sex (e.g., Bell, Halligan, & Ellis, 2006; Eckblad & Chapman, 1986; Kerns, 2006).

RESULTS

Factor Structure of Psychosis Risk and Mania Risk

As can be seen in Table 2, as expected, the psychosis risk measures were highly correlated with each other, the mania risk measures were also highly correlated with each other, and at the same time all correlations between the psychosis risk and mania risk measures were moderate to large in size. Next, I used confirmatory factor analyses to examine if psychosis risk and mania risk could be distinguished as two distinct factors. Model 1 included a single general risk factor with all psychosis risk scales (i.e., CAPS, PerAb, MagicId, PQ-Likert Pos, and PID-5) and all mania risk scales (i.e., GBI and HPS) loading on just one factor. Model 1 did not provide an adequate fit, $\chi^2(14, N = 596) = 140.97, p < .001$, CFI = .91, TLI = .86, RMSEA = .12. As can be seen in Figure 1, Model 2 included two factors with psychosis risk and mania risk scales loading on separate factors. In contrast to the single factor Model 1, the two factor Model 2 provided a more adequate fit, $\chi^2(13, N = 596) = 92.64, p < .001$, CFI = .96, TLI = .93, RMSEA = .09, with Model 2 providing significantly better fit than Model 1, $\chi^2(1, N = 596) = 65.68, p < .01$.

Associations between Risk Factors with Symptoms and Mood

Next, I examined whether the distinct psychosis risk and mania risk factors were differentially associated with other self-reported symptom measures and with self-reported current mood. As can be seen in Table 3, as expected, only psychosis risk was positively associated with both negative schizotypy (including social anhedonia) measures and with a disorganized schizotypy measure. I further examined whether common-method variance could account for some of these associations with psychosis

risk. In particular, note that the PQ-Likert subscales were highly correlated with each other (r s ranging from .75 to .82). Hence, I repeated these analyses after removing the PQ-Likert Pos scale from the model, finding similar results (associations with psychosis risk & mania risk: for PQ-Likert Neg .48 & .15; for PQ-Likert Disorg .57 & .07) Hence only psychosis risk but not mania risk was associated with negative and disorganized schizotypy. In contrast, as can be seen in Table 3, for self-reported manic episodes, only the mania risk factor was significantly associated with reporting manic-like episodes on both the CIDI and the MDQ. Hence, there was evidence that only the mania risk factor, but not the psychosis risk factor, was associated with manic-like episodes.

For current general distress (i.e., PQ-Likert Gen), both psychosis and mania risk were associated with increased current general symptoms (note that if I removed PQ-Likert Pos, associations were .21 & .40 for psychosis risk & mania risk, respectively; both $ps < .001$). For current mood, neither psychosis risk nor mania risk were associated with current positive mood. However, only mania risk was significantly associated with increased current negative mood. In addition, note that current mood was associated with negative and disorganized schizotypy and with self-reported manic-like episodes. However, after removing shared variance with current mood, associations between psychosis and mania risk with schizotypy facets and manic-like episodes were very similar.

Associations between Risk Factors and Spontaneous Eye Blink Rate

Next, I examined whether psychosis risk and mania risk were differentially associated with sEBR. As can be seen in Table 3, I found that psychosis risk was significantly associated with *decreased* sEBR. In contrast, mania risk was significantly

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associated with *increased* sEBR. Hence, psychosis risk and mania risk were differentially associated with sEBR. Further, note that current mood was not associated with sEBR.

DISCUSSION

Psychosis and mania risk scales have been used in research and in clinical practice to identify individuals at risk for psychotic or mania disorders. However, few studies have examined whether these scales can be differentiated from each other, even though previous research has found that (1) psychosis and mania risk scales are often highly correlated; (2) psychotic and manic disorders are highly related; (3) and both psychosis and mania might be related to the same neurobiological mechanism, striatal dopamine. In the current study, I found evidence that psychosis and mania risk scales form two distinct risk factors. In addition, psychosis and mania risk were also differentially related to other measures of psychopathology and current mood as well as to a measure related to striatal dopamine (i.e., sEBR). Thus, this study provides novel evidence that psychosis risk and mania risk can be differentiated from each other.

If psychosis and mania risk scales can be differentiated from each other, then it would be expected that these scales would form distinct factors in a confirmatory factor analysis. In the current study, as predicted, psychosis and mania risk scales were moderately to highly correlated with each other, and distinct psychosis and mania risk factors were highly associated with each other. However in a confirmatory factor analyses, a two-factor risk model with separate psychosis and mania risk factors did fit significantly better than a one-factor risk model. Little previous research has examined whether psychosis and mania risk scales form separate factors. One previous study reported evidence of distinct psychosis and mania risk scale factors (Prete et al., 2015), however there could be questions about whether that study truly assessed a mania risk factor (e.g., arguably only one mania risk scale amongst an otherwise heterogeneous mix

of negative affect scales). In any event, the current study provides novel evidence that psychosis risk and mania risk scales form distinct factors.

Although the current study found novel evidence for distinct factors, future research could continue to examine whether psychosis and mania risk factors are distinct. For instance, although the current research found a two-factor model fit significantly better than a one-factor model, the two-factor model did not meet all possible criteria for a well-fitting model (e.g., RMSEA < .06; Hu & Bentler, 1999). I suspect that part of the reason for this is that the psychosis risk scales used in this study might ultimately load onto more than one separate but highly correlated psychosis risk factors. Consistent with this, previous research has found that psychosis risk scales do form multiple factors. For instance, Cicero and Kerns (2010a) found that unusual beliefs and experiences, measured with the same Magical Ideation and Perceptual Aberration scales used in the current research, loaded on a factor distinct both from a referential thinking factor and from a paranoia factor. Potentially consistent with this, both the psychosis risk Prodromal Questionnaire-Likert (i.e., PQ-Positive) and the PID-5 used in the current study refer to a range of psychosis risk items including unusual beliefs and experiences, referential thinking, and paranoid ideation. Therefore, one issue for future research is to examine whether a model that involves distinct psychosis risk factors as well as a mania risk factor would meet criteria for a well-fitting model. Another issue for future research would be to examine whether mania risk might also be comprised of distinct sub-factors (Schalet et al., 2011). Lastly, future research could examine whether psychosis and mania risk scales form distinct factors in treatment-seeking populations.

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In addition to the two-factor psychosis and mania risk model fitting better than a single-factor model, the separate psychosis and mania risk factors were also differentially related to measures of psychopathology and current mood as well as to a measure of striatal dopamine (i.e., sEBR). Some of the specific associations for the psychosis risk factor after removing shared variance with mania were as expected. For instance, psychosis risk was thought to be at least moderately to strongly associated with other traits thought to reflect increased risk for schizophrenia-spectrum disorders (i.e., schizotypy). Consistent with this, I found that only psychosis risk, but not mania risk, was associated with both negative schizotypy and disorganized schizotypy. Hence, after removing shared variance, only psychosis risk but not mania risk was associated with other schizotypy facets.

In addition, psychosis risk and mania risk were also differentially associated with sEBR, with psychosis risk associated with decreased sEBR and mania risk associated with increased sEBR. The association between psychosis risk and decreased sEBR is consistent with the hypothesis that psychosis risk scales would be associated with decreased tonic striatal dopamine. Although increased striatal dopamine has been found in psychotic disorders (Howes et al., 2012), there is evidence that striatal dopamine increases only during acute psychotic episodes (Laruelle, Abi-Dargham, Gil, Kegeles, & Innis, 1999; Shotbolt et al., 2011). Further, despite this episodic increase, recent evidence has suggested that psychotic disorders might be associated with low levels of trait striatal dopamine (Maia & Frank, 2017). Hence, the current results provide novel evidence that scales that assess trait level psychosis risk are associated with a decrease in a biomarker related to striatal dopamine.

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There are several ways that future research could further examine whether psychosis risk is associated with decreased striatal dopamine. Most directly, future research could examine whether psychosis risk scales are related to striatal dopamine levels assessed using PET brain imaging. Interestingly, at least one study has measured striatal dopamine release in healthy participants and examined correlations with schizotypy traits thought to be related to schizophrenia-spectrum disorders (using the Schizotypal Personality Questionnaire), including measures of psychosis risk (Woodward et al., 2011). That study found evidence that schizotypy, specifically disorganized schizotypy, was associated with increased striatal dopamine release. On the surface, these results seem inconsistent with the current results. However, that previous PET study examined *phasic* dopamine release, whereas in the current study sEBR presumably reflects decreased tonic dopamine levels (Slagter, Georgopoulou, & Frank, 2015). Overall, the results of the current study and of Woodward et al. (2011) are consistent with the suggestion that psychotic disorders might involve a combination of both decreased tonic dopamine levels but increased spontaneous phasic dopamine release (Maia & Frank, 2017). Note also that there are striatal dopamine mechanisms that are consistent with decreased tonic and increased phasic dopamine (e.g., decreased tonic dopamine resulting in decreased activation of presynaptic dopamine autoreceptors that normally attempt to reduce phasic dopamine release; Grace, 2016). This suggests that an important issue in future research might be to directly examine how psychosis risk is associated with both tonic dopamine levels and phasic dopamine release in the same study. In addition, future research could examine other indicators related to sEBR and dopamine,

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such as performance on behavioral tasks (Cavanagh, Masters, Bath, & Frank, 2014; Groman et al., 2014; Slagter, Georgopoulou, & Frank, 2015).

In contrast to psychosis risk, mania risk had a different pattern of associations with other variables. Although mania risk as expected was not associated with other facets of schizotypy, mania risk was associated with self-reported manic-like episodes on both the CIDI and the MDQ. Hence, as expected, only mania risk measures were associated with a measure of previous manic-like episodes, consistent with previous research (Eckblad & Chapman, 1986; Kwapil et al., 2000). This result is also interesting given that psychosis risk has been found to predict future risk of manic-like episodes (Chapman et al., 1994). The current research suggests that the association between psychosis risk measures and future manic-like episodes might have been the result of variance shared between psychosis and mania risk scales.

In addition, mania risk showed a very different association with sEBR than psychosis risk. In particular, in contrast to psychosis risk, which was associated with decreased sEBR, mania risk was associated with increased sEBR. This is consistent with the hypothesis that mania risk might be associated with increases in striatal dopamine (Beaver et al., 2006; Lawrence & Brooks, 2014). To date, only two studies have examined the relationship between mania and sEBR, and the results have been mixed. In a small sample study on individuals with Bipolar II Disorder with a seasonal affective course, Depue and colleagues (1990) found that this group exhibited elevated sEBR compared to a healthy control group. However, a recent study examining sEBR in individuals diagnosed with Bipolar I Disorder found that there was no difference in sEBR between the Bipolar I Disorder group and the healthy control group at baseline and

during a reward task (Peckham & Johnson, 2016). However, note that participants in the Depue et al. (1990) study were unmedicated. In contrast, in Peckham and Johnson (2016) more than 40% were taking antipsychotic medication that profoundly block D₂ receptors in the striatum and could have obscured possible associations with sEBR. Hence, the results from the current study are consistent with previous research on unmedicated Bipolar Disorder and provide novel evidence that mania risk scales are associated with an increase in a biomarker related to tonic striatal dopamine. Further, in the current study I only found that mania risk was associated with sEBR after removing variance shared with psychosis risk. Hence, the current study suggests that in the general population that it is the variance that is unique to mania risk and that is not shared with psychosis risk that is associated with sEBR and possibly with increased tonic dopamine.

Future research could further examine the relationship between mania risk and striatal dopamine. Firstly, studies could more directly examine if there is an increase in striatal dopamine in mania risk. Currently, no study has directly assessed striatal dopamine levels (i.e., using PET brain imaging) across the different phases of Bipolar Disorder (i.e., euthymia, hypomania, and mania) or in individuals at risk of developing a bipolar-spectrum disorder. In general, it is thought that mania is associated with increased dopamine levels (Ashok et al., 2017; Cousins, Butts, & Young, 2009); however, it is unknown if this increase is specific to a certain phase or if it is present in individuals at risk for mania. Secondly, to further investigate the relationship between mania and increased striatal dopamine levels, future studies could concurrently examine the relationship between mania and both tonic and phasic dopamine levels.

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In summary, this study provided novel evidence demonstrating that not only can psychosis risk and mania risk be discriminated from each other, but also that these risk factors were differentially associated with other measures of psychopathology, mood, and striatal dopamine. These results suggest that though psychosis and mania risk may have much in common, they show differential patterns, which can help us better understand risk for each of these disorders. Future research could further examine if psychosis and mania risk measures might form even more than two factors. Additionally, future research could further examine the relationship between psychosis and mania risk with both tonic dopamine levels and phasic dopamine release (Grace, 2016; Peckham & Johnson, 2016).

References

- Anderson, J. L., Sellbom, M., Bagby, R. M., Quilty, L. C., Veltri, C. O. C., Markon, K. E., & Krueger, R. F. (2013). On the convergence between PSY-5 domains and PID-5 domains and facets: Implications for assessment of *DSM-5* personality traits. *Assessment*, 20(3), 286-294.
- Alloy, L. B., Bender, R. E., Whitehouse, W. G., Wagner, C. A., Liu, R. T., Grant, D. A.,... Abramson, L. Y. (2012). High Behavioral Approach System (BAS) sensitivity, reward responsiveness, and goal-striving predict first onset of bipolar spectrum disorders: A prospective behavioral high-risk design. *Journal of Abnormal Psychology*, 121(2), 339-351.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.
- Applegate, E., El-Deredy, W., & Bentall, R. P. (2009). Reward responsiveness in psychosis-prone groups: Hypomania and negative schizotypy. *Personality and Individual Differences*, 47(50), 452-456.
- Ashok, A. H., Marques, T. R., Jauhar, S., Nour, M. M., Goodwin, G. M., Young, A. H., ... Howes, O. D. (2017). The dopamine hypothesis of bipolar affective disorder: The state of the art and implications for treatment. *Molecular Psychiatry*. Advanced online publication.
- Ashton, M. C., Lee, K., de Vries, R. E., Hendrickse, J., & Born, M. P. (2012). The maladaptive personality traits of the Personality Inventory for *DSM-5* (PID-5) in relation to the HEXACO personality factors and schizotypy/dissociation. *Journal of Personality Disorders*, 26(5), 641-659.

- Barrantes-Vidal, N, Grant, P., & Kwapil, T. (2015). The role of schizotypy in the study of the etiology of schizophrenia spectrum disorders. *Schizophrenia Bulletin*, 41(Suppl 2), 8408-8416.
- Barbato, G., Ficca, G., Muscettola, G., Fichele, M., Beatrice, M., & Rinaldi, F. (2000). Diurnal variation in spontaneous eye-blink rate. *Psychiatry Research*, 93(2), 145-151.
- Bastiaens, T., Smits, D., De Hert, M., Thys, E., Bryon, H., Sweers, K., ... Claes, L. (2017). The relationship between the Personality Inventory for the *DSM-5* (PID-5) and the psychotic disorder in a clinical sample. *Assessment*, 1-9.
- Beaver, J. D., Lawrence, A. D., Ditzhuijzen, Davis, M. H., Woods, A., and Calder, A. J. (2006). Individual differences in reward drive predict neural responses to images of food. *The Journal of Neuroscience*, 26(19), 5160-5166.
- Bell, V., Halligan, P. W., & Ellis, H. D. (2006). The Cardiff Anomalous Perceptions Scale (CAPS): A new validated measure of anomalous perceptual experience. *Schizophrenia Bulletin*, 32(2), 366-377.
- Bell, V., Halligan, P. W., Pugh, K. & Freeman, D. (2011) Correlates of perceptual distortions in clinical and non-clinical populations using the Cardiff Anomalous Perceptions Scale (CAPS): Associations with anxiety and depression and a re-validation using a representative population sample. *Psychiatry Research*, 189, 451-457.
- Cavanagh, J. F., Masters, S. E., Bath, K., Frank, M. J. (2014). Conflict acts as an implicit cost in reinforcement learning. *Nature Communications*, 5, 5394.
- Chapman, L. J., & Chapman, J. P. (1986). Infrequency scale for personality measures

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

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. (1978). Body-image aberration in schizophrenia. *Journal of Abnormal Psychology, 87*, 399-407.

Cicero, D. C., & Kerns, J. G. (2010a). Multidimensional factor structure of positive schizotypy. *Journal of Personality Disorders, 24*(3), 327-343.

Cicero, D. C., & Kerns, J. G. (2010b). Can disorganized and positive schizotypy be discriminated from dissociation? *Journal of Personality, 78*(4), 1239-1270.

Chermahini, S. A., & Hommel, B. (2010). The (b)link between creativity and dopamine: Spontaneous eye blink rates predict and dissociate divergent and convergent thinking. *Cognition, 115*, 458-465.

Claridge, G., McCreery, C., Mason, O., Bentall, R., Boyle, G., Slade, P., & Popplewell, D. (1996). The factor structure of “schizotypal” traits: A large replication study. *British Journal of Clinical Psychology, 35*(Pt. 1), 103-115.

Colzato, L. S., Slagter, H. A., van den Wildenberg, W., & Hommel, B. (2009). Closing one's eyes to reality: Evidence for a dopaminergic basis of psychoticism from spontaneous eye blink rates. *Personality and Individual Differences, 46*, 377-380.

Cousins, D. A., Butts, K., & Young, A. H. (2009). The role of dopamine in bipolar disorder. *Bipolar Disorders, 11*(8), 787-806.

Craddock, N., O'Donovan, M. C., & M.J. Owen. (2005). The genetics of schizophrenia and bipolar disorder: Dissecting psychosis. *Journal of Medical Genetics, 42*(3), 193-204.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Cross-Disorder Group of the Psychiatric Genomics Consortium. (2013). Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nature Genetics*, 45, 984-994.
- Debbané, M., Eliaz, S., Badoud, D., & Schultze-Lutter, F. (2015). Developing psychosis and its risk states through the lens of schizotypy. *Schizophrenia Bulletin*, 41(Suppl. 2), S396-S407.
- Depue, R. A., Krauss, S., Spoont, M. R., & Arbisi, P. (1989). General Behavior Inventory identification of unipolar and bipolar affective conditions in a nonclinical university population. *Journal of Abnormal Psychology*, 98(2), 117-126.
- 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. (1986). Development and validation of a scale for hypomanic personality. *Journal of Abnormal Psychology*, 95, 214-222.
- Eckblad, M. L., Chapman, L. J., Chapman, J. P., & Mishlove, M. (1982). *The revised social anhedonia scales*. (Available from L.J. Chapman, Department of Psychology, 1202 West Johnson Street, University of Wisconsin, Madison, WI 53706).
- Fulford, D., Feldman, G., Tabak, B. A., McGillicuddy, M., & Johnson, S. (2013). Positive affect enhances the association of hypomanic personality and cognitive flexibility. *International Journal of Cognitive Therapy*, 6(1), 1-16.
- 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(1), 170-175.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Grace, A. A. (2016). Dysregulation of the dopamine system in the pathophysiology of schizophrenia and depression. *Nature Reviews Neuroscience*, 17, 524-532.
- Groman, S. M., James, A. S., Seu, E., Tran, S., Clark, T. A., Harpster, S. N., ... Jentsch, J. D. (2014). In the blink of an eye: Relating positive-feedback sensitivity to striatal dopamine D2-like receptors through blink rate. *Journal of Neuroscience*, 34(43), 14443-14454.
- Hirschfeld, R. M. A. (2002). The Mood Disorder Questionnaire: A simple, patient-rated screening instrument for Bipolar Disorder. *Primary Care Companion to The Journal of Clinical Psychiatry*, 4(1), 9-11.
- Hirschfeld, R. M. A., Holzer, C., Calabrese, J. R., Weissman, M., Reed, M., Davies, M., ... Hazard, E. (2003). Validity of the Mood Disorder Questionnaire: A general population study. *American Journal of Psychiatry*, 160, 178-180.
- Hirschfeld, R. M., Williams, J. B., Spitzer, R. L., Calabrese, J. R., Flynn, L., Keck, P. E., ... Zajecka, J. (2000). Development and validation of a screening instrument for bipolar spectrum disorder: The Mood Disorder Questionnaire, *The American Journal of Psychiatry*, 157(11), 1873-1875.
- Hisahara, S., & Shimohama, S. (2011). Dopamine receptors and Parkinson's Disease. *International Journal of Medicinal Chemistry*, 1-16.
- Howes, O. D., Fusar-Poli, P., Bloomfield, M., Selvaraj, S., & McGuire, P. (2012). From the prodrome to chronic schizophrenia: the neurobiology underlying psychotic symptoms and cognitive impairments. *Current Pharmaceutical Design*, 18, 459-465.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Hu, Li-tze, & Bentler, P. M. (2009). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling, 6*(1), 1-55.
- Johnson, S. L., Edge, M. D., Holmes, M. K., & Carver, C. S. (2012). The Behavioral Activation System and mania. *Annual Review of Clinical Psychology, 8*, 243-267.
- Kaminer, J., Powers, A. S., Horn, K. G., Hui, C., & Evinger, C. (2011). Characterizing the spontaneous blink generator: An animal model. *Journal of Neuroscience, 31*(31), 11256-11267.
- Karcher, N. R., Martin, E. A., & Kerns, J. G. (2015). Examining associations between psychosis risk and performance of striatum-related behavioral tasks. *Journal of Abnormal Psychology, 124*(3), 507-518.
- Karson, C. N. (1983). Spontaneous eye-blink rates and dopaminergic systems. *Brain, 106*, 643-653.
- Karson, C. N., Dykman, R. A., & Paige, S. R. (1990). Blink rates in schizophrenia. *Schizophrenia Bulletin, 16*(2), 345-354.
- Kegeles, L. S., Abi-Dargham, A., Frankle, G., Gil, R., Cooper, T. B., Slifstein, M., ... Laruelle, M. (2010). Increased synaptic dopamine function in associative regions of the striatum in schizophrenia. *Archives of General Psychiatry, 67*(3), 231-239.
- Kerns, J. G. (2006). Schizotypy facets, cognitive control, and emotion. *Journal of Abnormal Psychology, 115*, 418-427.
- Kessler, R. C., Akiskal, H. S., Angst, J., Guyer, M., Hirschfeld, R. M. A., Merikangas, K. R., & Stand, P. E. (2006). Validity of the assessment of bipolar spectrum disorders in the WHO CIDI 3.0. *Journal of Affective Disorders, 96*, 259-269.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Kleinman, J. E., Karson, C. N., Weinberger, D. R., Freed, W. J., Berman, K. F., & Wyatt, R. J. (1984). Eye blinking and cerebral ventricular size in chronic schizophrenic patients. *American Journal of Psychiatry*, 141(11), 1430-1432.
- Kleven, M. S., & Koek, W. (1996). Differential effects of direct and indirect dopamine agonists on eye blink rate in cynomolgus monkeys. *The Journal of Pharmacology and Experimental Therapeutics*, 279, 1211-1219.
- Kline, E., & Schiffman, J. (2014). Psychosis risk screening: A systematic review. *Schizophrenia Research*, 158(1-3), 11-18.
- Krueger, R. F., Derringer, J., Markon, K. E., Watson, D., & Skodol, A. E. (2012). Initial construction of a maladaptive personality trait model and inventory for *DSM-5*. *Psychological Medicine*, 42, 1879-1890.
- Krueger, R. F., & Markon, K. E. (2014). The role of the *DSM-5* Personality Trait Model in moving toward a quantitative and empirically based approach to classifying personality and psychopathology. *Annual Review of Clinical Psychology*, 10, 477-501.
- Kwapil, T. R. (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *Journal of Abnormal Psychology*, 107(4), 558-565.
- Kwapil, T. R., Barrantes-Vidal, N., & Silvia, P. J. (2008). The dimensional structure of the Wisconsin Schizotypy Scales: Factor identification and construct validity. *Schizophrenia Bulletin*, 34(3), 444-457.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Kwapil, T. R., Miller, M. B., Zinser, M. C., Chapman, L. J., Chapman, J., & Eckblad, M. (2000). A longitudinal study of high scorers on the Hypomanic Personality Scale. *Journal of Abnormal Psychology, 109*(2), 222-226.
- Laruelle, Abi-Dargham, Gil, Kegeles, & Innis. (1999). Increase dopamine transmission in schizophrenia: Relationship to illness phases. *Biological Psychiatry, 46*(1), 56-72.
- Lawrence, A. D., & Brooks, D. J. (2014). Ventral striatal dopamine synthesis capacity is associated with individual differences in behavioral disinhibition. *Frontiers in Behavioral Neuroscience, 8*(86), 1-6.
- Lichtenstein, P., Yip, B. H., Björk, C., Pawitan, Y., Cannon, T. D., Sullivan, P. F., & Hultman C. M. (2009). Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: A population-based study. *Lancet, 373*(9659), 234-239.
- Loewy, R. L., Bearden, C. E., Johnson, J. K., Raine, A., & Cannon, T. D. (2005). The prodromal questionnaire (PQ): Preliminary validation of a self-report screening measure for prodromal and psychotic syndromes. *Schizophrenia Research, 79*, 117-125.
- Loewy, R. L., Johnson, J. K., & Cannon, T. D. (2007). Self-report of attenuated psychotic experiences in a college population. *Schizophrenia Research, 93*(1-3), 144-151.
- Maia, T. V., & Frank, M. J. (2017). An integrative perspective on the role of dopamine in schizophrenia. *Biological Psychiatry, 81*(1), 52-66.
- Muthén, L. K., & Muthén, B. O. (1998-2015). Mplus User's Guide. Seventh Edition. Los Angeles, CA: Muthén & Muthén.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

- Nelson, B. & Rawlings, D. (2010). Relating schizotypy and personality to the phenomenology of creativity. *Schizophrenia Bulletin*, 36(2), 388-399.
- Peckham, A. D. & Johnson, S. L. (2016). Spontaneous eye-blink rate as an index of reward responsivity: Validation and links to Bipolar Disorder. *Clinical Psychological Science*, 4(3), 451-463.
- Prete, A., Corrias, I., Gabbriellini, M., Lai, V., Muratore, T., Pinuts, E., ... Carta, M. G. (2015). The independence of schizotypy from affective temperaments – A combined confirmatory factor analysis of SPQ and the short TEMPS-A. *Psychiatry Research*, 225, 145-150.
- Psychology Software Tools, Inc. (2012). E-Prime 2.0. Pittsburg, PA.
- Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., & Fusar-Poli, P. (2015). Ventral striatal activation during reward processing in psychosis: A neurofunctional meta-analysis. *JAMA Psychiatry*, 72(12), 1243-1251.
- Raine, A. (2006). Schizotypal personality: Neurodevelopmental and psychosocial trajectories. *Annual Review of Clinical Psychology*, 2, 291-326.
- Schalet, B. D., Durbin, E., & Revelle, W. (2011). Multidimensional structure of the Hypomanic Personality Scale. *Psychological Assessment*, 23(2), 504-522.
- Scherk, H., Pajonk, F. G., & Leucht, S. (2007). Second-generation antipsychotic agents in the treatment of acute mania. *Archives of General Psychiatry*, 64(4), 442-455.
- Schulberg, D. (1990). Schizotypal and hypomanic traits, creativity, and psychological health. *Creativity Research Journal*, 3(3), 218-230.

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

Seeman, P. (2010). Dopamine D2 receptors as treatment targets in schizophrenia.

Clinical Schizophrenia & Related Psychoses, 4(1), 56-73.

Sellbom, M., Anderson, J. L., & Bagby, R. M. (2013). Assessing *DSM-5* Section III

personality traits and disorders with the MMPI-2-RF. *Assessment*, 20(6), 709-722.

Shotbolt, P., Stokes, P. R., Owens, S. F., Touloupoulou, T., Picchioni, M. M., Bose, S. K.,

... Howes, O. D. (2011). Striatal dopamine synthesis capacity in twins discordant for schizophrenia. *Psychological Medicine*, 41(11), 2331-2338.

Slagter, H. A., Georgopoulou, K., & Frank, M. J. (2015). Spontaneous eye blink rate

predicts learning from negative, but not positive, outcomes. *Neuropsychologia*, 71, 126-132.

Walsh, M. A., DeGeorge, D. P., Barrantes-Vidal, N., & Kwapil, T. R. (2015). A 3-year

longitudinal study of risk for bipolar spectrum psychopathology. *Journal of Abnormal Psychology*, 124(3), 486-497.

Watson, D., Stasik, S. M., Ro., E., & Clark, L. A. (2013). Integrating normal and

pathological personality: Relating the *DSM-5* trait-dimensional model to general traits of personality. *Assessment*, 20(3), 312-326.

Woodward, N. D., Cowan, R. L., Park, S., Ansari, M. S., Baldwin, R. M., Li, R., ... Zald,

D. H. (2011). Individual differences in schizotypal personality traits correlate with amphetamine induced dopamine release in striatal and extra-striatal brain regions.

American Journal of Psychiatry, 168(4), 418-426.

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Table 1

Demographics

Sex	
Male	47.2%
Female	52.5%
Age	
Mean (SD)	18.93 (0.99)
Ethnicity	
Caucasian	78.4%
African American	12.3%
Asian American	2.5%
Latino/Latina	1.8%
American Indian/Alaska Native	0.5%
Native Hawaiian/Other Pacific Islander	0.2%
Biracial	2.8%
Other	1.3%
Missing	0.3%

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Table 2

Zero-Order Pearson Correlations Among Questionnaires and Spontaneous Eye Blink Rate

Measure	1	2	3	4	5	6	7	8
<i>Psychosis Scales</i>								
1. PerAb	—							
2. MagicId	.68**	—						
3. CAPS	.65**	.68**	—					
4. PQ-Likert Pos	.53**	.54**	.60**	—				
5. PID-5	.51**	.52**	.62**	.65**	—			
<i>Mania Scales</i>								
6. GBI	.49**	.51**	.51**	.51**	.47**	—		
7. HPS	.35**	.45**	.40**	.36**	.37**	.59**	—	
<i>Other Schizotypy</i>								
8. SocAnh	.34**	.25**	.23**	.22**	.31**	.06	.18**	—
9. PQ-Likert Neg	.45**	.41**	.46**	.75**	.53**	.17**	.43**	.34**
10. PQ-Likert Disorg	.44**	.44**	.50**	.82**	.60**	.29**	.44**	.22**
<i>Manic-Like Episode Measures</i>								
11. CIDI	.34**	.27**	.27**	.34**	.31**	.33**	.34**	.06
12. MDQ No Impairment	.25**	.30**	.33**	.39**	.37**	.41**	.34**	.08*
<i>General Distress & Mood</i>								
13. PQ-Likert Gen	.38**	.34**	.40**	.66**	.45**	.52**	.25**	.19**
14. Mood Pos	-.11**	.00	.03	-.05	.02	-.08	.07	-.14**
15. Mood Neg	.20**	.17**	.20**	.29**	.18**	.34**	.16**	.06
<i>Physiological</i>								
16. sEBR	.02	-.01	-.05	-.01	-.07	.05	.04	.01

(Continued)

PSYCHOSIS AND MANIA RISK WITH STRIATAL DOPAMINE

Table 2

Zero-Order Pearson Correlations Among Questionnaires and Spontaneous Eye Blink Rate (Continued)

Measure	9	10	11	12	13	14	15	16
<i>Other Schizotypy</i>								
9. PQ-Likert Neg	—							
10. PQ-Likert Disorg	.76**	—						
<i>Manic-Like Episode Measures</i>								
11. CIDI	.33**	.36**	—					
12. MDQ No Impairment	.30**	.34**	.28**	—				
<i>General Distress & Mood</i>								
13. PQ-Likert Gen	.80**	.71**	.32**	.35**	—			
14. Mood Pos	-.16**	-.12**	-.07	-.04	-.19**	—		
15. Mood Neg	.37**	.30**	.11**	.15**	.48**	-.19**	—	
<i>Physiological</i>								
16. sEBR	.02	-.02	-.03	-.06	.04	-.02	.06	—

Note. * Correlation is significant at $p < .05$; ** Correlation is significant at $p < .01$; PerAb = Perceptual Aberration Scale; MagicId = Magical Ideation Scale; CAPS = Cardiff Anomalous Perceptions Scale; PQ-Likert Pos = Prodromal Questionnaire-Likert Positive Symptoms Subscale; PID-5 = Personality Inventory for *DSM-5* Psychoticism Domain; HPS = Hypomanic Personality Scale; GBI = General Behavior Inventory; SocAnh = Revised Social Anhedonia Scale; PQ-Likert Neg = Prodromal Questionnaire-Likert Negative Symptoms Subscale; PQ-Likert Disorg = Prodromal Questionnaire-Likert Disorganized Symptoms Subscale; CIDI = WHO CIDI 3.0 Bipolar Screening Scales; MDQ = Mood Disorder Questionnaire; PQ-Likert Gen = Prodromal Questionnaire-Likert General Symptoms Subscale; Mood Pos = Current Positive Mood; Mood Neg = Current Negative Mood; sEBR = Spontaneous Eye Blink Rate

Figure 1. *Model 2: Psychosis Risk and Mania Risk Model*

Note. CAPS = Cardiff Anomalous Perceptions Scale; PerAb = Perceptual Aberration Scale; MagicId = Magical Ideation Scale; PQ Pos = Prodromal Questionnaire-Likert Positive Symptoms Subscale; PID-5 = Personality Inventory for *DSM-5* Psychoticism Domain; GBI = General Behavior Inventory; HPS = Hypomanic Personality Scale

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Table 3

Associations Between Risk Factors and Other Measures

	Psychosis Risk	Mania Risk
<i>Other Schizotypy</i>		
SocAnh	.37**	-.05
PQ-Likert Neg	.68**	.00
PQ-Likert Disorg	.85**	-.11
<i>Manic-Like Episode Measures</i>		
CIDI	.09	.40**
MDQ	.14	.38**
<i>General Distress & Mood</i>		
PQ-Likert Gen	.36**	.29**
Mood Pos	.03	-.07
Mood Neg	.02	.35**
<i>Physiological</i>		
sEBR	-.16*	.17*

Note. Associations with Model 2; * Correlation is significant at $p < .05$; ** Correlation is significant at $p < .01$; SocAnh = Revised Social Anhedonia Scale; PQ-Likert Neg = Prodromal Questionnaire-Likert Negative Symptoms Subscale; PQ-Likert Disorg = Prodromal Questionnaire-Likert Disorganized Symptoms Subscale; CIDI = WHO CIDI 3.0 Bipolar Screening Scales; MDQ = Mood Disorder Questionnaire; PQ-Likert Gen = Prodromal Questionnaire-Likert General Symptoms Subscale; Mood Pos = Current Positive Mood; Mood Neg = Current Negative Mood; sEBR = Spontaneous Eye Blink Rate

Supplemental Methods

Weather Prediction Task (WPT). Participants completed the WPT (as in Karcher, Martin, & Kerns, 2015), as well as two additional versions of the task (i.e., Butterfly, and Mr. Potato Head). These two versions had the same underlying task structure but included different stimuli. In the Weather Prediction version of this task, participants needed to decide if it would rain or shine. They were shown four different cues or shapes, and each shape was associated with a fixed probability of either rain or shine. Participants were then shown combinations of one, two, or three of the possible shapes. Participants chose one of the possible outcomes (i.e., rain or shine) and then were given feedback after each choice. Based on this feedback, participants gradually learned how to respond in order to predict the most rewarded outcome. In the Butterfly version, participants were shown different colored butterflies and needed to predict if the butterfly would land on the purple or pink flower. In the Mr. Potato Head version, participants saw different facial features (i.e, hat, mustache, glasses, and ears) and needed to predict which ice cream (i.e., chocolate or vanilla) Mr. Potato Head would purchase. Participants completed all three versions of this task (i.e., WPT 1, WPT 2, and WPT3), with the order of versions randomized across participants. Each version consisted of 4 quartiles with 30 trials in each.

Analyses. Invalid trials (i.e., trials faster than 200 ms) were removed from analyses. If 25% or more of the trials across the task were invalid or if 25% or more of the trials in the fourth quartile were invalid, then all of the participant's responses for that specific WPT version were removed from analyses. After removing poor performers, data were analyzed for the remaining participants (WPT 1, $n = 596$; WPT 2, $n = 534$;

WPT 3, $n = 456$). For this task, accuracy was calculated by quartile. Additionally to assess learning, I calculated an accuracy difference score between the first and last quartiles for each version.

Supplemental Results

As can be seen in Supplementary Table 1, there was no learning effect across time on any of the WPT tasks. Additionally the WPT is a difficult task, and over time participants' performance became quite poor, as indicated by more poor performers for WPT 2 and WPT 3.

As can be seen in Supplementary Table 2, the difference scores for the WPT were not significantly correlated with any of the psychosis or mania risk scales. Additionally, when accounting for shared variance, these scores were also not associated with either the psychosis risk or mania risk factors. However as performance was quite poor on these tasks, it is unclear if the current data could validly test the relationship between WPT learning with psychosis risk and mania risk.

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Supplemental Table 1

Weather Prediction Task Accuracy By Quartile

	Accuracy				
	<i>N</i>	Quartile 1 Mean (<i>SD</i>)	Quartile 2 Mean (<i>SD</i>)	Quartile 3 Mean (<i>SD</i>)	Quartile 4 Mean (<i>SD</i>)
WPT 1	596	.55 (.13)	.60 (.14)	.61 (.15)	.61 (.15)
WPT 2	534	.54 (.13)	.57 (.14)	.58 (.14)	.58 (.14)
WPT 3	456	.54 (.12)	.57 (.14)	.57 (.14)	.57 (.14)

Note. WPT = Weather Prediction Task

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Supplemental Table 2

Zero-order Pearson Correlations and Associations Between Weather Prediction Task and Psychosis and Mania Risk

	WPT 1 Difference	WPT 2 Difference	WPT 3 Difference
<i>Weather Prediction Task</i>			
1. WPT 1 Difference	—		
2. WPT 2 Difference	.02	—	
3. WPT 3 Difference	.13**	.07	—
<i>Psychosis Scales</i>			
4. PerAb	.01	.01	-.06
5. MagicId	.03	-.02	-.04
6. CAPS	.02	.02	.01
7. PQ-Likert Pos	.01	.01	-.07
8. PID-5	-.03	-.02	-.03
<i>Mania Scales</i>			
9. GBI	-.02	-.03	.01
10. HPS	.02	-.02	.02
<i>Risk Factors</i>			
11. Psychosis Risk	.05	.05	-.10
12. Mania Risk	-.05	-.07	.08

Note. **Correlation is significant at $p < .01$; WPT = Weather Prediction Task; PerAb = Perceptual Aberration Scale; MagicId = Magical Ideation Scale; CAPS = Cardiff Anomalous Perceptions Scale; PQ-Likert Pos = Prodromal Questionnaire-Likert Positive Symptoms Subscale; PID-5 = Personality Inventory for *DSM-5* Psychoticism Domain; HPS = Hypomanic Personality Scale; GBI = General Behavior Inventory