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AUDITORY PROCESSING DEFICITS IN BIPOLAR DISORDER WITH AND

WITHOUT A HISTORY OF PSYCHOTIC FEATURES

by

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Bachelor of Arts in Psychology

Indiana University of Pennsylvania

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A thesis submitted in partial fulfillment of

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ABSTRACT

Auditory Processing Deficits in Bipolar Disorder with and without a history of

Psychotic Features

by

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Auditory perception deficits have been identified in schizophrenia and linked to dysfunction in primary auditory cortex. There is also evidence that primary auditory cortex abnormalities are associated with positive symptoms, particularly auditory hallucinations. Given the evidence that individuals with bipolar disorder frequently experience auditory hallucinations, it may be that individuals with bipolar disorder who also exhibit psychotic symptoms demonstrate similar impairment in auditory perception tasks. Additionally, these deficits may contribute to impaired social interactions, as they are likely to interfere with accurate perception of emotion from spoken words. The current study examined this matter by comparing performance of 50 individuals with schizophrenia (SZ), 30 individuals with bipolar disorder with a history of psychotic features (BD+), 28 individuals with bipolar disorder with no history of psychotic features (BD-), and 29 normal controls (NC) on a tone discrimination task likely to activate the auditory cortex. Groups were also compared on a task designed to assess auditory affect recognition, visual affect recognition, and auditory-visual affect recognition. Results indicated that individuals with SZ showed the most impairment on the tone discrimination task. On the difficult condition of the tone discrimination task, individuals

with BD+ performed worse compared to individuals with BD- and NCs, who did not differ from each other. Individuals with SZ also performed the worst on all conditions of the affect recognition task, while individuals with BD+ performed worse than those with BD- and NC only on the auditory affect recognition condition. It was also found that performance on the more difficult condition of the tone discrimination task predicted performance on all three conditions of the affect recognition task. Additionally, no differences were found between those in BD+ who had a lifetime history of auditory hallucinations and those who did not. Findings replicate previous research indicating that individuals with SZ are impaired on basic auditory processing tasks and emotion recognition tasks. Findings also indicate that individuals with BD+ perform at a level that is intermediate between BD- and SZ on a basic auditory processing task and an auditory emotion recognition task, suggesting that those with a history of psychosis may have similar underlying mechanisms and neurocognitive abilities as those seen in SZ. Additionally, poor ability to discriminate between tones appears to be related to social cognitive deficits in both disorders. Results did not support the idea that a history of auditory hallucinations is related to poorer performance on either task. Future research should examine the relationship between severity of auditory hallucinations and impairment in basic auditory processing and auditory emotion recognition across the disorders.

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CHAPTER 1

INTRODUCTION

In 1899, Emil Kraepelin proposed that dementia praecox and manic-depressive psychosis were two distinct disorders, which later became known as schizophrenia (SZ) and bipolar disorder (BD) (Greene, 2007). This dichotomization is still present and utilized by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR; APA, 2000) which has distinct diagnoses for BD and SZ. Recently there has been growing evidence of shared features in BD and SZ, including overlaps in symptoms (Boksa, 2009; Suppes et al., 2001), neurocognitive deficits (Allen et al., 2010; Sponheim et al., 2010), genetic susceptibility (Goes, Sanders, & Potash, 2008; Green et al., 2005), and neuroimaging abnormalities (Ellison-Wright & Bullmore, 2010). These shared features have led some to believe that SZ and BD may not in fact be distinct disorders. Rather, they may occur on a psychosis continuum with overlapping features (Ivelva et al., 2010).

One such overlap between SZ and BD is the co-occurrence of psychotic and affective symptoms. A lifetime history of psychosis has been reported in as much as 67% of individuals with BD (Suppes et al., 2001), while symptoms of depression occur so commonly in SZ that there is a specific post-psychotic depressive disorder diagnosis in the DSM-IV-TR (APA, 2000). There is also the diagnostic category of schizoaffective disorders, where psychotic symptoms are primary but there is substantial affective overlay. More specifically and particularly relevant to this study, auditory hallucinations occur in both patients with BD and SZ (Baethge, Baldessarini, Freudenthal, Steeruwitz, & Baurer, 2005), although it appears that individuals with BD with psychotic features

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(BD+) do not experience them as often as patients with SZ (Shinn et al., 2012). It should also be noted that psychotic symptoms in BD are related to poorer course and prognosis compared with BD without psychotic features (BD-) (Gonzalez-Pinto et al., 1998; Özyildririm, Çakir, & Yazici, 2010).

The mechanisms underlying the symptoms of SZ and BD are not completely elucidated, although there are suspected relationships between brain regions and symptomatology. Auditory hallucinations have been found to be associated with volume decrease (for a review see Sun, Maller, Guo, & Fitzgerald, 2009) and activation in the superior temporal gyrus (for a review see Allen, Larøi, McGuire, & Aleman, 2008), which contains the primary auditory cortex. Although other non-speech related areas have been found to be related to auditory hallucinations, gray matter volume abnormalities in the superior temporal gyrus appear to be the most replicated finding (Allen et al., 2012). Neuroimaging studies examining individuals with BD typically have not compared those with and without psychotic features or have found inconsistent results, with some finding more STG gray mater volume abnormalities in those with psychosis (Tost et al., 2010) and others not replicating this finding (Kasai et al., 2003). It is also thought that there is a relationship between dysfunction at the auditory cortex level and deficits in basic auditory processing (Rabinowicz, Silipo, Goldman, & Javitt, 2009). Individuals with SZ are consistently found to be impaired on tone discrimination ability, which is considered a measure of pre-attentive auditory sensory processing (Javitt, 2009). Similarly, electrophysiological measures of pre-attentive auditory processing indicate impairment in SZ (Olincy et al., 2010; Umbricht & Krljes, 2005). While electrophysiological measures also provide some evidence of pre-attentive auditory

processing impairment in individuals with BD (Jahshan et al., 2012; Lijffijt et al., 2009; Takei et al., 2010), others have suggested that basic auditory processing deficits are specific to SZ (O'Donnell, Vohs, Hetrick, Carroll, & Shekhar, 2004; Salisbury, Kasai, Kuroki, Shenton & McCarley, 2007; Umbricht et al., 2003). However, it may be that psychotic features in BD are related to these deficits, as there is evidence of a potential relationship between basic auditory processing deficits and psychosis (Olincy & Martin, 2005; Schulze et al., 2007; Shaikh et al., 2012). Basic auditory processing has also been found to be related to social cognitive abilities, such as the ability to infer emotion from vocal features, in SZ (Gold et al., 2012; Lietman et al., 2005; Lietman et al., 2010) and BD (Bozikas et al., 2007; Van Rheenen & Rossell, 2013). This has also been found to be associated with auditory hallucinations, regardless of diagnostic group (Rossell et al., 2013). Social cognition is necessary in order to successfully interact with others, and thus has been related to functional outcome in both SZ (reviewed in Couture, Penn, & Roberts, 2006) and BD (Lahera et al., 2012).

Thus, there is ample evidence that individuals with BD experience psychotic symptoms in addition to the affective symptoms that are the core features of the diagnosis, and that these psychotic symptoms may have an impact on characteristics of the illness. The presence of these psychotic symptoms in BD raises the question as to whether individuals who experience these symptoms are differentiated from those who do not experience psychotic symptoms and may share similar cortical abnormalities and outcomes present in individuals with SZ. The current study investigated these matters by comparing performance of a group of individuals with SZ, a group of individuals with BD+, a group of individuals with BD-, and a healthy control group on a tone

discrimination task that likely activates the auditory cortex. Groups were also compared

on a task of visual and auditory affect recognition in order to examine the potential role

of sensory processing on this task. As a secondary analysis, the relationship between

auditory hallucinations and performance on these tasks was examined in the BD+ group.

It was hypothesized that the NC and BD- group would not differ in performance from

each other, and would perform significantly better than the BD+ group on both tasks. The

SZ group was hypothesized to have the poorest performance on all tasks. Additionally, it

was hypothesized that tone discrimination performance in all groups would predict

performance on the auditory affect and auditory-visual affect recognition task, but would

not predict performance on the visual affect recognition task.

CHAPTER 2

LITERATURE REVIEW

<u>Kraepelin Dichotomy</u>

The dichotomization of BD and SZ was first proposed by Emil Kraepelin in 1899. Emil Kraepelin's (1902) view was that diseases could be classified according to their symptoms, which were a reflection of disease etiology. He attributed the etiology of dementia praecox (known today as SZ) to a mostly permanent disease process in the brain, while attributing manic-depressive psychosis (known today as BD) to heredity. He also described the course and prognosis for manic-depressive psychosis as better than for dementia praecox (Greene, 2007). The dichotomization between the disorders is still present and utilized by the DSM-IV-TR, which classifies SZ as a psychotic disorder and BD as a mood disorder (APA, 2000).

Individuals are diagnosed with SZ when they experience two or more characteristic symptoms for at least 1 month duration, with some signs of the disorder persisting for at least 6 months. These symptoms include positive symptoms (i.e., hallucinations, delusions), disorganization symptoms (i.e., disorganized speech, grossly disorganized or catatonic behavior), and negative symptoms (i.e., blunted affect, alogia, avolition). These symptoms must cause marked social or occupational dysfunction. Additionally, while at least two characteristic symptoms are required for the diagnosis, only one symptom is required if the individual experiences delusions that are bizarre, or if hallucinations include voices commenting on behavior or thoughts or two or more voices conversing with each other (APA, 2000). Lifetime prevalence of SZ has been estimated at .87% (Perala et al., 2007).

The lifetime prevalence rate of Bipolar Disorder I (BD I) is estimated at 1.0%, while the lifetime prevalence rate of Bipolar Disorder II (BD II) is estimated at 1.1% (Merikangas et al., 2007). BD is a severe mental illness which typically has its onset in the late teens and early 20's, causing significant disability for many of those who are affected by the disorder. Lifetime costs for treatment are also high, estimated to range from $11,720 for those suffering from a single manic episode to $626,785 for those suffering from chronic episodes (Begley et al., 2001). As a result, BD is viewed as a major health concern and is the focus of much research.

According to the DSM-IV-TR, BD I is a mood disorder characterized by the occurrence of one or more manic or mixed episodes, although individuals with BD also typically experience major depressive episodes. A manic episode is defined as a distinct period of abnormally and persistently elevated, expansive, or irritable mood that lasts at least 1 week, (or any duration if hospitalization is necessary) and includes symptoms of inflated self-esteem or grandiosity, decreased need for sleep, pressured speech, flight of ideas, distractibility, an increase in goal-directed activity, and excessive involvement in pleasurable activities that have a high potential for painful consequences. These symptoms must cause marked impairment in functioning or a need for hospitalization, or must be accompanied by psychotic features. A major depressive episode is defined as a period during which there is either depressed mood or the loss of interest or pleasure in activities. Major depressive episodes include symptoms such as depressed mood or anhedonia, as well as changes in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, diminished ability to think or concentrate or indecisiveness, and recurrent

thoughts of death or a suicide plan or attempt. These symptoms must persist for a minimum of two weeks, unless hospitalization is required. A mixed episode occurs when criteria are met both for a manic episode and for a major depressive episode during the same 1-week period (APA, 2000).

BD is further divided into Bipolar I (BD I) and Bipolar II disorder (BD II). As indicated before, a diagnosis of BD I is given when criteria have been met for one or more manic or mixed episodes. A diagnosis of BD II is given when criteria have been met for one or more major depressive episodes, accompanied by at least one hypomanic episode. A hypomanic episode is similar to a manic episode, but symptoms only need to be present for four days. Additionally, while the symptoms associated with a hypomanic episode still cause a change in functioning that is observable by others, they are not severe enough to cause marked impairment in functioning or a need for hospitalization, and there are no psychotic features (APA, 2000). Despite the continued dichotomous classification of BD and SZ, there has been recent debate about the possibility of a continuum between BD and SZ due to overlapping features between the illnesses. These overlaps include psychotic and affective features, neurocognitive deficits, and genetic susceptibility.

<div align="center">Shared Features of Bipolar Disorder and Schizophrenia</div>

Psychotic and Affective Features

An area of significant overlap between SZ and BD concerns the presence of affective and psychotic symptoms, which occur with a high degree of frequency across both disorders. For example, in addition to the mood episode criteria in BD, there are a number of specifiers for each type of episode (APA, 2000). One that is particularly

<div align="center">7</div>

relevant to the current study is the presence or absence of psychotic features during a manic, depressed, or mixed mood episode. It is well known that individuals with BD may experience psychotic symptoms. In fact, the Stanley Foundation Bipolar Treatment Outcome Network found that 67% of patients with BD I had a history of psychotic symptoms (Suppes et al., 2001). Similarly, Goodwin and Jamison (1990) reported that approximately 58% of patients with BD had a lifetime history of at least one psychotic symptom, usually when manic. Another study found that 90% of a sample of patients with BD reported a history of psychosis based on a self-questionnaire (Dunayevich & Keck, 2000).

Psychotic features that accompany BD vary, and include hallucinations, delusions, formal thought disorder, and psychomotor disturbance (Emilien, Septien, Brisard, Corruble, & Bourin, 2007). BD with psychotic features can often be misdiagnosed as SZ or another psychotic illness. Gonzelez-Pinto and colleagues (1998) found that 31% of the BD patients in their sample had previously been diagnosed with SZ or another psychotic disorder at the onset of illness. Similarly, several studies have found that Schneider's First Rank Symptoms, originally considered specific to SZ, occur more frequently in SZ but they are not specific in that they also occur in BD (Rosen, Grossman, Harrow, Bonner-Jackson, & Faull, 2011; Shinn et al., 2012). There is also evidence that the presence of psychotic features in BD is related to course and prognosis, as psychotic symptoms are related to increased severity of illness and increased number of hospitalizations (Özyildririm, Çakir, & Yazici, 2010).

Similar to the high prevalence of psychotic features in those with BD, individuals with SZ also experience a high incidence of affective symptoms. For example, the

lifetime prevalence rate of experiencing depressed mood at first hospitalization in individuals with SZ is 83% (Häfner et al., 2005). In addition, individuals with SZ often experience depression following a psychotic episode (APA, 2000). In fact, depressive symptoms occur so commonly following active phase psychotic symptoms in SZ that the DSM-IV-TR includes a specific depressive disorder not otherwise specified (NOS) diagnosis pertaining to this phenomenon, referred to as postpsychotic depressive disorder (APA, 2000). It is important to distinguish between SZ with mood symptoms and schizoaffective disorder. If mood symptoms occur in SZ, they have a brief duration compared to the total duration of the illness, only occur during prodromal or residual phases, or do not meet full criteria for a mood episode. In contrast, schizoaffective disorder is diagnosed when a mood episode occurs at the same time as active-phase symptoms of SZ, and is present for a substantial duration of the illness. Additionally, delusions or hallucinations must also be present a minimum of 2 weeks when mood symptoms are absent (APA, 2000). The prevalence of schizoaffective disorder is estimated to be between 0.5-0.8% (Malhi, Green, Fagiolini, Peselow, & Kumari, 2008), and many consider it to be a variant of SZ (Lake & Hurwitz, 2006; Malhi et al., 2008). Thus, in addition to the high percentage of individuals with SZ who experience affective disturbances, there is yet another category of patients who demonstrate substantial psychotic affective comorbidity.

Hallucinations are among the psychotic features that may occur in both SZ and BD. Hallucinations are considered a diagnostic feature of SZ and occur frequently in those who are diagnosed. They can occur in any sensory modality, although auditory hallucinations are the most common (Boksa, 2009). In fact, 60-80% of individuals with

SZ experience auditory hallucinations (Andreasen & Flaum, 1991). There is evidence that hallucinations also occur in BD, although they may not occur as often as in SZ. A study examining hallucinations among patients diagnosed with BD compared to those diagnosed with major depression or SZ found that 11.8% of their BD sample reported one or more hallucination at hospital admission. However, the prevalence of hallucinations was approximately 5 times greater in individuals diagnosed with SZ. The most frequent type of hallucination in both BD and SZ were auditory hallucinations. When individuals who were experiencing hallucinations were matched for sex and age to those with SZ who were also experiencing hallucinations, 56.9% of the BD sample experienced auditory hallucinations that included hearing voices, while 10.8% experienced other auditory hallucinations not including hearing voices. In contrast, 74.6% of the SZ sample experienced auditory hallucinations that included hearing voices, while 23.8% experienced other auditory hallucinations (Baethge et al., 2005). More recently, Shinn et al. (2012) examined auditory hallucinations among a large sample of individuals diagnosed with SZ, schizoaffective disorder, and BD I with psychotic features. They found that 34% of individuals with BD I with psychotic features had a lifetime history of auditory hallucinations, although the rate was much higher in the SZ group. Thus, it appears that while BD patients experience hallucinations, they experience them less often and they are not as severe as for patients with SZ.

Despite extensive research, the mechanisms underlying auditory hallucinations are not clear. Given the role of the auditory cortex in perception and language, several studies using neuroimaging techniques have investigated the association between auditory cortex and auditory hallucinations. The auditory cortex can be divided into

several subdivisions, including the superior temporal gyrus (STG), middle and inferior temporal gyri, and medial temporal lobe structures (McCarley et al., 1999). The STG is involved in speech, language, and communication (Rajaretheinam, DeQuardo, Nalepa, & Tandon, 2000). The STG includes the planum temporal (PT), a language-related area that coincides with Wernicke's area (Shapleske, Rossell, Woodruff, & David, 1999), and Heschl's gyrus (HG), which contains the primary auditory cortex (PAC). Although it is evident that the PAC plays an important role in how sound is recognized and interpreted, its exact role is still debated. Some evidence suggests that the PAC extracts basic acoustic features of sound, while other research has found that acoustic features are processed in subcortical levels. There is also some evidence that the function of PAC can change depending on the contextual properties (King & Schnupp, 2007). Additionally, the left PAC is thought to be specialized for temporal processing, while the right PAC is thought to be specialized for spectral processing (Zatorre & Belin, 2001).

Structural magnetic resonance imaging (MRI) studies have frequently found an association between auditory hallucinations and volume reduction of gray matter in the STG, PAC, and MTG (reviewed in Allen et al., 2008). Reductions in left STG gray matter volume have been found in both first-episode (Tang et al., 2012) and chronic SZ (reviewed in Sun et al., 2009), and have been found to be associated with severity of auditory hallucinations (Barta, Pearlson, Powers, Richards, & Tune,1990; Flaum et al., 1995). Additionally, two recent meta-analyses found significant correlations between left and right STG and severity of auditory hallucinations in SZ (Modinos et al., 2013; Palaniyappan, Balain, Radua, & Liddle, 2012). Furthermore, a recent meta-analysis of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI)

studies that examined individuals with SZ who were actively hallucinating found

increased activity during hallucinations in several language and speech areas including

Broca's area, insula, precentral gyrus, frontal operculum, left MTG and STG (Jardri,

Pouchet, Pins, & Thomas, 2011). Neuroimaging studies examining auditory cortex in

BD have been less common and less consistent. Some studies have found reduced gray

matter of left STG volume in individuals with BD (Rimol et al., 2010; Takahashi et al.,

2010). Others have found reduced gray matter volume in the right STG (Cui et al., 2011),

increased volume of gray matter in the right STG (Adler et al., 2007), or no STG grey

matter abnormalities (Brambilla et al., 2003; Yüksel et al., 2012). A study examining

adolescents with BD (BD I, BD II, BD NOS) and NC found reduced total volume of STG

in BD, which was due to reduced bilateral white matter volumes (Chen et al., 2004)

Inconsistent findings could be due to the heterogeneous nature of symptoms in BD. Tost

et al. (2010) examined a sample of individuals diagnosed with BD, and also examined a

subgroup of those patients who had a lifetime history of psychosis and a subgroup who

had a lifetime history of mood-incongruent psychotic features. They found that those

with mood-incongruent psychotic features showed the most grey matter volume

reduction, including reduction of the STG. Other studies examining psychosis have found

no differences in grey matter volume in BD+ (Yüksel et al., 2012), and progressive loss

of left STG grey matter volume in first episode SZ patients but not in first-episode

affective psychosis (Kasai et al., 2003). Inconsistent findings may also be due to the

effect of medication, as it has been found that lithium treatment can reverse or prevent

grey matter abnormalities in BD (Bearden et al., 2007; Kempton, Geddes, Ettinger,

Williams, & Grasby, 2008; Moore, Bebchuk, Wilds, Chen, & Manji, 2000). For example,

Nugent et al. (2006) found that individuals with BD who had not received medication during the four months prior to testing had smaller left STG gray matter compared to healthy controls, while this was not true for individuals who were currently or recently medicated.

There have been fewer neuroimaging studies specifically examining the HG and included PAC in these disorders. In a recent review, Abdul-Kareem and Sluming (2008) suggest that there may be few structural neuroimaging studies that have concentrated on the HG and included PAC because of the complexity of this region. For example, there are variations in the number of HG found in individuals. It is most often found that individuals have a single gyrus per hemisphere, but there have been reports of up to 5 gyri per hemisphere. Additionally, there are findings of double gyri in both hemispheres. Furthermore, most studies report larger left HG volume compared to right, but there have also been studies that have found no asymmetries or asymmetry favoring the right HG. However, because multiple gyri are more commonly found in the right hemisphere, this could account for a finding of increased right HG volume (Abdul-Kareem & Sluming, 2008). Findings thus far have associated left HG volume reduction with severity of auditory hallucinations (Gaser, Nenadic, Volz, Büchel, & Sauer, 2004; Nenadic, Smesny, Schlösser, Sauer, & Gaser, 2010), found PAC activity during auditory hallucinations (Bentaleb et al., 2002; Dierks et al., 1999; Lennox et al., 2000; van de Ven et al., 2005), or found no activity increases (Shergill, Brammer, Williams, Murray, & McGuire, 2000). There have been even fewer studies examining PAC in BD, but a recent study found no HG gray matter abnormalities in first-episode individuals with affective psychosis (bipolar and major depression) (Takahashi et al., 2009). However, using resting state

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fMRI, Shinn, Baker, Cohen, & Ongur (2013) found abnormal connectivity between the left HG and regions involved in language and memory in individuals with SZ who experience auditory hallucinations. This has not been examined in BD. Although a full review of structural and functional abnormalities associated with auditory hallucinations is beyond the scope of this paper, it should be pointed out that studies have also found associations between auditory hallucinations and non-speech related areas, including the insula, anterior and posterior cingulate, inferior frontal gyrus, thalamus, cerebellum, precuneus, postcentral gyrus, parahippocampal gyrus, and amygdala. However, gray matter volume reduction in auditory cortex appears to be the finding replicated the most often (reviewed in Allen et al., 2012).

Taken together, these findings indicate significant symptom overlap between BD and SZ, such that many patients with SZ will experience affective symptoms and many patients with BD will experience psychotic features, including auditory hallucinations. Additionally, psychotic symptoms in BD appear to negatively affect illness course and outcome (Dunayevich & Kech, 2000; Goodwin & Jamison, 1990; Özyildririm, Çakir, & Yazici, 2010; Suppes et al., 2011). Speech-related areas, including the STG and included PAC, have been found to be associated with auditory hallucinations in SZ, although the underlying mechanisms are still unclear (Gaser et al., 2004; Jardri et al., 2011; Modinos et al., 2013; Nenadic et al., 2010; Palaniyappan et al., 2012). Studies examining the STG and PAC in BD+ have resulted in mixed findings (Takahashi et al., 2010; Tost et al., 2010; Yüksel et al., 2012).

Neurocognitive deficits

It is well known that individuals with SZ show impairment in several cognitive domains. Some of the neuropsychological deficits that are present are deficits in IQ, attention (Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005), executive functioning, verbal and visual memory and learning (Bilder et al., 2000; Fioravanti et al., 2005, Sponheim et al., 2010), working memory, processing speed (Sponheim et al., 2010), and motor dysfunctions (Bilder et al., 2000; Sponheim et al., 2010). While increased symptoms are associated with worsening in some areas of cognition, deficits persist in times of clinical stability (Sponheim et al., 2010) and have also been identified in individuals who are at increased risk for SZ (Snitz, MacDonald, & Carter, 2006), as well as those who are experiencing their first episode of the disorder and not yet medicated (Mohamed, Paulsen, O'Leary, Arndt, & Andreasen, 1999). Thus, symptom exacerbation does not appear to account for most of the variance in neurocognitive deficits present in these individuals. Similarly, medications used to treat SZ have been hypothesized to have deleterious effects on cognition, because of blockade of specific neurotransmitters that underlie cognitive processes (Murray, Lapin, & Di Forti, 2008). An example here would be the hypothesized negative effects of dopamine blockade on executive functions (Floresco & Magyar, 2006). However, most research does not support a substantial negative impact of medication on cognition in SZ, and some suggest that medications improve cognitive abilities (Harvey & Bowie, 2003). Thus, neurocognitive deficits have been viewed as a core feature of SZ that are not accounted for by secondary factors that commonly occur in individuals with the disorder.

There is also evidence that individuals with BD show neurocognitive impairments across all phases of the illness, including in euthymic states when no significant mood features are present (Quraishi & Frangou, 2002). Deficits in executive functioning, verbal learning and memory (Basso, Lowery, Neel, Purdie, & Bornstein, 2002; Martinez-Arán et al., 2004; Quraishi & Frangou, 2002), attention, (Martinez-Arán et al., 2004; Quraishi & Frangou, 2002), and speed of information processing (Basso et al., 2002) have been seen in symptomatic patients with BD. Additionally, deficits in executive functioning (Bora, Yucel, & Pantelis, 2009; Kurtz & Gerraty, 2009; Martinez-Arán et al., 2004; Robinson et al., 2006), verbal learning and memory (Bora et al., 2009, Martinez-Arán et al., 2004; Robinson et al., 2006; Quraishi & Frangou, 2002), sustained and selective attention (Bora et al., 2009; Kurtz & Gerraty, 2009; Martinez-Arán et al., 2004; Robinson et al., 2006; Quraishi & Frangou, 2002), psychomotor speed (Kurtz & Gerraty, 2009; Robinson et al., 2006), response inhibition (Robinson et al., 2006; Bora et al., 2009), and visual working memory (Allen et al., 2010) have been found in euthymic patients. Similar to SZ, neurocognitive deficits have also been identified in individuals who are at increased risk for BD (Frantom, Allen, & Cross, 2008), and in those who are medication free (Pavuluri et al., 2006), suggesting that like SZ these deficits are core features of the illness. However, patients with SZ typically have more severe (Krabbendam, Arts, van Os, & Aleman, 2005) and more stable cognitive impairments compared to BD (Burdick, Goldberg, Harrow, Faull, & Malhotra, 2006).

While there is ample evidence that patients with BD show neurocognitive deficits compared to healthy controls, there have been inconsistent findings regarding the relation of the presence of psychotic symptoms in patients with BD and cognitive impairment.

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There has been some evidence that BD patients with a history of psychosis perform worse on measures of executive functioning compared to BD patients without a history of psychosis (Allen et al., 2010; Bora et al., 2007; Glahn et al., 2007), while other studies have found that measures of executive functioning do not distinguish these two groups (Selva et al., 2007). Similarly, studies have found that BD I patients with a history of psychosis perform worse than BD I patients without a history of psychosis on measures of verbal memory (Bora et al., 2007) and spatial working memory (Glahn et al., 2007), and others have found that there is no difference between the groups on measures of verbal fluency (Bora et al., 2007), speed of processing, declarative memory (Glahn et al., 2007), psychomotor speed and sustained attention (Bora et al., 2007; Glahn et al., 2007). As part of a more recent meta-analytic study, Bora et al. found that BD patients with a history of psychosis were more impaired on verbal memory and executive functioning tasks compared with BD patients with no history of psychosis. However, there were no differences between the groups on measures of attention and nonverbal memory (Bora, Yucel, & Pantelis, 2010).

In summary, it appears that there is overlap in neurocognitive deficits found in SZ and BD, including deficits in executive functioning, verbal memory, and working memory (Allen et al., 2010; Basso et al., 2002; Bilder et al., 2000; Fioravanti et al., 2005; Martinez-Arán et al., 2004; Quraishi & Frangou, 2002; Sponheim et al., 2010). Additionally, although there is heterogeneity in the findings, there is some suggestion that the presence of psychotic features in BD is associated with greater cognitive impairment (Allen et al., 2010; Bora et al., 2007; Bora et al., 2010; Glahn et al., 2007).

Genetic Susceptibility

There is strong evidence that suggests contribution of a genetic component to the etiology of both BD and SZ. Family studies have found that both SZ and BD aggregate in families. First-degree biological relatives of SZ probands have an 8- to 12-fold increased risk of developing the disorder (Ivelva et al., 2010). Similarly, first-degree biological relatives of BD probands have a 10-fold increased risk of developing the disorder (Smoller & Finn, 2003). Additionally, there is evidence of higher concordance of SZ in monozygotic twins compared to dizygotic twins (Farmer, McGuffin, & Gottesman, 1987). This has also been found in BD (Smoller & Finn, 2003), which further suggests a genetic component to both illnesses. Furthermore, in a study examining families with at least two members diagnosed with SZ or schizoaffective disorder, it was found that 57% of the families had other relatives with affective disorders (Henn, Bass, Shields, Crow, & DeLisi, 1995). It has also been found that first-degree relatives of BD have an increased risk for SZ (Vallès et al., 2000). There is also some indication that psychosis in general has a genetic component. For example, Kendler et al. (1993) found that relatives of SZ probands who were diagnosed with an affective disorder were more likely to have psychotic features, compared with relatives of healthy controls who were diagnosed with an affective disorder. Similarly, psychotic affective disorder probands had an increased rate of relatives with SZ compared to healthy controls. Finally, Potash et al. (2001) found that more families of BD I psychotic probands had a relative with an affective disorder accompanied by psychotic symptoms compared to families of BD I nonpsychotic probands.

Genetic studies have also been conducted in order to attempt to identify susceptibility genes and their chromosomal locations in SZ and BD. Several risk genes have been implicated in SZ including NRG1 (neuregulin 1) on chromosome 8p12, dysbindin (distrobrevin-binding proterin 1) on chromosome 6p22.3, DAOA (D-amino acid oxidase activator) on chromosome 13q33, COMT (catechol-O-methyltransferase) on chromosome 22q11, RGS4 (regulator of G protein signaling 4) on chromosome 1q23, DISC1 (disrupted in schizophrenia 1) on chromosome 1q42, and BDNF (brain deprived neurotrophic factor). Risk genes associated with BD also include BDNF, NRG1, and DAOA (see Ivelva et al., 2010 for review). Other genes implicated in BD include CACNA1C (calcium channel, voltage-dependent, L type, alpha 1C subunit) at chromosome 12p13.3, ANK3 (Ankryin 3) at chromosome 10q21 (see de Medeiros Alves, Silva, de Melo Neto, de Andrade, & Nardi, 2011 for a review), and NCAN (neurocan) on chromosome 19p13.11 (Mühleisen et al., 2012). Studies have also found that some of the candidate genes which are associated with both SZ and BD may be associated with certain symptoms in the disorders. For example, there is evidence suggesting NRG1 may be associated with psychotic symptoms in BD (Goes et al., 2008) and mood symptoms in SZ (Green et al., 2005).

In sum, evidence from family and twin studies, genetic linkage studies, and candidate risk studies indicate that both SZ and BD have a genetic component to their etiology. However, evidence from these studies also indicates that there may be some overlap in genetic abnormalities that could contribute to both disorders, and that there may be a genetic component to psychosis that could contribute to the etiology of both diseases.

Structural abnormalities

Beyond brain regions described above that may be implicated in auditory hallucinations across disorders, there is also evidence of other structural abnormalities in SZ and BD. In SZ, evidence of increased lateral ventricle volume has been consistently found. Additionally, MRI studies have consistently found reductions in grey matter in the medial temporal and prefrontal areas (for a review see Karlsgodt, Sun, & Cannon, 2010), as well as reductions in whole brain volume (Wright et al., 2000). Further, there is also evidence that individuals with SZ have white matter deficits in the prefrontal, temporal, and parietal lobes (McDonald et al., 2005). There have also been several MRI studies assessing brain structure in BD, although the findings of these studies have been inconsistent. A meta-analysis of such studies by McDonald et al. (2004) found that BD is associated with increased right lateral ventricle volume, but found no volume abnormalities in whole brain volume, or whole brain grey or white matter (McDonald et al., 2004). It has also been found that individuals with BD have increased amygdala volume (Altshuler et al., 2000; Strakowski et al., 1999), and deficits in white matter in the brainstem, prefrontal, temporal, and parietal lobes (McDonald et al., 2005). A more recent meta-analysis by Ellison-Wright and Bullmore (2010) examined structural abnormalities in BD and SZ and found gray matter volume reductions in both disorders, although volume reductions in BD were not as extensive as in SZ. They found gray matter volume reductions in the bilateral insula, thalamus, anterior cingulate, medial frontal gyrus, and posterior cingulate in SZ, while only finding gray matter reduction in the anterior cingulate and bilateral insula in BD. Thus, while gray matter volume reductions were not as extensive in BD, these findings do provide some evidence of

overlapping structural brain abnormalities in the two disorders (Ellison-Wright & Bullmore, 2010).

Some of these discrepant findings may be due to the presence or absence or psychotic symptoms in BD, as it appears that psychosis in BD may be associated with neuroanatomical differences. For example, a recent study found that BD patients with psychotic features have increased lateral ventricle volume, while BD patients without psychotic features do not show this increase (Edmiston et al., 2011). Similarly, another study found that BD patients with a history of psychosis had enlarged third and lateral ventricles compared to those with no history of psychosis and healthy controls (Strasser et al., 2005). In contrast, a recent study by Yüksel et al. (2012) found gray matter volume abnormalities of multiple regions in SZ compared to healthy controls, while BD patients with psychotic features had no gray matter volume abnormalities. Overall, these findings indicate that there are structural abnormalities in both SZ and BD, and that there are some overlaps between the two disorders. Inconsistent findings in structural abnormalities in BD may be related to the presence or absence of psychotic features in the disorder, however this is currently unclear.

In sum, SZ and BD have historically been conceptualized as two distinct illnesses, and this view continues to predominate current thinking. However, there is growing evidence challenging this perspective as it is commonly observed that there are some overlapping features in both disorders. This includes evidence that both individuals diagnosed with SZ and BD may have similar clinical features, specifically the presence of psychotic and affective symptoms (Bottlender et al., 2000; Dunayevich & Keck, 2000; Goodwin & Jamison, 1990; Suppes et al., 2001). Similarly, individuals with BD and SZ

have overlapping neurocognitive deficits and structural and functional brain abnormalities, and there is some evidence that suggests a history of psychotic symptoms is related to increased cognitive deficits and neuroanatomical differences (Bora et al., 2010; Edmiston et al., 2011; Yüksel et al., 2012). Finally, there is overlap in the genetic contributions of each illness, suggesting that some genetic abnormalities may be related to both illnesses (as reviewed in Ivelva et al., 2012). One key finding from this emerging literature is that psychotic symptoms shared by both disorders may provide a link between the two. For example, individuals with both disorders experience auditory hallucinations (Shinn et al., 2012), which could point to similar underlying mechanisms being present in both disorders. Approaches directed at further understanding the overlap between disorders may then best be directed at comparisons between individuals diagnosed with SZ, individuals diagnosed with BD who experience psychotic symptomatology similar to SZ, individuals diagnosed with BD who do not have psychotic features, and a control population. Such an approach would further benefit from examining robust findings from the literature on SZ, where behavioral abnormalities have been noted to be consistent across studies and are thought to be related to the unique neuropathology underlying symptoms. One such behavioral abnormality is in the area of auditory processing, which consistently differentiates individuals with SZ from controls (Javitt, 2009). This deficit is of particular interest because of the consistency with which associated neural structures are also found to be abnormal in SZ, namely primary auditory cortex (Brenner et al., 2009). The current study takes this approach to understanding the role of psychotic symptoms and the potential overlap between SZ and BD by examining auditory processing in patients with SZ, BD+, BD-, and normal

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controls. As described above, there is evidence that auditory hallucinations, which occur frequently in SZ (Boksa et al., 2009) and BD+ (Baethege et al., 2005), are linked to abnormalities in the STG and its subdivisions, including the primary auditory cortex in the HG (Berta et al., 1990; Sumich et al., 2005). Given that the HG is thought to play a large role in auditory processing and language (Langers, Backes, & Van Dijk, 2007), extensive research has been done on auditory sensory processing in SZ. The following sections provide a review of the literature relevant to auditory processing and associated neural structures.

<div align="center">Auditory Processing</div>

Auditory Pathway

In order to process sound, sound waves must be converted into a neural impulse. This process begins as sound waves travel through the ear and cause the tympanic membrane to vibrate. Vibration of the tympanic membrane sets the ossicles of the ear into motion, which transfer the vibrations to the cochlea in the inner ear (Pickles, 1988). The cochlea is a fluid-filled tube that is divided by the organ of Corti and the basilar membrane (for a review see Munkong & Juang, 2008). An important feature of the cochlea is its tonotopic organization, meaning that higher frequencies vibrate the basilar membrane closer to the apex and lower frequencies vibrate the basilar membrane closer to the base (von Beksy, 1960). Transduction begins as rows of hair cells move on the cochlea (Pickles, 1988). As the hair cells move, stereocilia move and open transduction channels. Action potentials are then created in the auditory nerve and signals are sent to the cochlear nucleus of the brainstem (for a review see Munkong & Juang, 2008).

The cochlear nucleus is divided into three subnuclei but the majority of output is sent to the superior olivary complex, which is the structure responsible for integrating auditory information from both ears. The superior olivary complex is also divided into several subnuclei, including the lateral nucleus and medial nucleus, which are involved in encoding. Output from subnuclei of the cochlea and superior olivary complex are then sent to the inferior colliculus (for a review see Munkong & Juang, 2008). The inferior colliculus can also be divided into three subnuclei (the central nucleus, the dorsal cortex, and the paracentral nuclei) and projects output to the medial geniculate body of the thalamus. Finally, the auditory cortex in the temporal lobe receives input from the medial geniculate body of the thalamus.

The auditory cortex is also tonotopically organized, and can be divided into primary and secondary auditory cortex (for a review see Munkong & Juang, 2008). The primary and secondary auditory cortices receive input from different parts of the thalamus. Neurons in the primary auditory cortex respond to sound, while neurons in the secondary auditory cortex respond to several sensory modalities. From the auditory cortex, auditory information is sent to association cortices and is integrated with other information from the central nervous system (for a review see Moller, 2006).

Auditory Processing Deficits in Schizophrenia

Auditory processing deficits are well documented in SZ. Individuals with SZ show impairments even in basic sensory processes that are considered pre-attentive. In general, early auditory processes are those that occur approximately 100-200ms after presentation of an auditory stimulus and are thought to occur in primary and secondary auditory cortex (Javitt, 2009). Event-related potentials (ERPs) provide one way of

examining auditory processing. Several auditory ERPs have been found to be abnormal in SZ and BD.

The P50 is an early- to middle-latency response that is thought to be reflective of sensory gating (for a review see Patterson et al., 2008). In order to assess sensory gating, participants are typically presented with two identical auditory stimuli (clicks), and the P50 ERP is measured following each click. If sensory gating is occurring, the P50 ERP in response to the second click should be smaller than the response to the first click, indicating that the sound is now considered irrelevant and filtered out (Adler et al., 1982). It has been repeatedly found that individuals with SZ do not show this normal sensory gating response (Baker et al., 1987; Freedman et al., 1996; Jin et al., 1997). Additionally, there is evidence of abnormal P50 suppression in first-degree relatives of individuals with SZ (Siegal, Waldo, Mizner, Adler, & Freedman, 1984; Louchart-de la Chapelle et al., 2005). However, some studies have found normal sensory gating in individuals with SZ who were unmedicated (Arnfred, Chen, Glenthøj, & Hemmingsen, 2003). Even so, abnormalities in P50 sensory gating are considered a familial neurobiological risk factor for SZ (Olincy et al., 2010). The N100 ERP is a late-latency response that occurs in the early stages of information processing. The N100 also occurs regardless of attention, but is found to be more sensitive to the effects of attention (Rosburg, Boutros, & Ford, 2008). Several studies have shown abnormalities in N100 in SZ (Laurent et al., 1999; Ford, Mathalon, Kalba, Marsh, & Pfefferbaum, 2001).

Individuals with SZ also show abnormalities in the mismatch-negativity (MMN) component, which is another measure of pre-attentive information processing. It is a response that occurs when an individual hears a stimulus that is deviant from a standard

stimulus that has been presented repeatedly. MMN is thought to measure echoic memory, which is the development of a brief memory trace of stimulus features (Cowan, Winkler, Teder, & Näätänen, 1993; see Näätänen, 2000 for a review).A meta-analysis concluded that patients with SZ show MMN deficits, although also concluded that MMN may be unimpaired in first-episode SZ (Salisbury, Shenton, Griggs, Bonner-Jackson, McCarley, 2002; Umbricht & Krljes, 2005). However, Kaur and colleagues (2012) found reduced MMN amplitude in response to duration deviant stimuli in a group of individuals experiencing first and second-episode psychosis (schizophrenia, schizoaffective disorder, schizophreniform disorder). Others have found that MMN response following stimuli that deviate in duration is reduced in unaffected family members (Michie, Innes-Brown, Todd, & Jablensky, 2002), as well as MMN response following stimuli that deviate in frequency (Jessen et al., 2001). However, others have found that MMN was not reduced in first-degree biological relatives (Magno et al., 2008). A study examining MMN amplitude to deviations in duration, frequency, and intensity in individuals who had been diagnosed with SZ within 5 years prior to the study and those who had their illness for a longer duration found that MMN to duration and intensity deviations were reduced in those recently diagnosed, while frequency MMN was reduced in those who had a longer duration of illness (Todd et. al., 2008). It appears that MMN is generated in both the temporal and frontal lobe. Generators in the temporal lobe are associated with detecting the change in the deviant and standard stimuli, while generators in the frontal lobe are associated with switching attention (for a review see Näätänen, Paavilainen, Rinne, & Alho, 2007). Studies suggest that abnormal MMN response from temporal generators may be associated with positive symptoms in SZ, while abnormal MMN response from

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frontal generators may be associated with negative symptoms (for a review, see Näätänen & Kähkönen, 2009). MMN has also been found to be associated with reduction in HG volume in SZ. Similarly, further reductions in MMN are associated with progressive left HG volume loss in SZ (Salisbury et al., 2007).

Behavioral measures have also been used to assess well-documented auditory processing deficits in SZ. One such basic sensory process that is impaired in SZ is tone discrimination. Tone discrimination tasks require individuals to listen to pairs of tones that are separated by a short delay, known as an interstimulus interval (ISI). The two tones are either identical or are of different pitches, and participants are asked to indicate if they are the same or different. Individuals with SZ require the pitch separation to be easier (i.e., larger) than that of healthy controls in order to perform at the same level. This is seen as a deficit in echoic memory, or the ability to maintain recollections of the acoustic qualities of a sound (Javitt, Strous, Grochowski, & Ritter, 1997; Strous, Cowan, Ritter, & Javitt, 1995). The auditory cortex must first compare the two tones in order to determine if they are the same or different. Not only must this occur, but the information must also be sent to higher processing areas in order for a response to be selected. It is thought that tone discrimination deficits in SZ are a result of impaired encoding, rather than retaining the representation of the tone, as individuals with SZ also perform comparatively worse than normal controls when there is no delay between the tones (i.e., no ISI) (Javitt et al., 1997). Javitt and colleagues (1997) also concluded that this deficit is not due to attention, because both groups of participants (SZ, healthy controls) in their study had similar decreases in performance from distraction. Similarly, the deficit is not due to hearing ability and not due to a more generalized deficit in SZ (Javitt et al., 1997).

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Similar to generators of MMN, structures in the temporal lobe and frontal lobe are thought to underlie the ability to discriminate between two tones. For example, it has been found that individuals with bilateral lesions to the PAC require a greater difference in frequency between tones in order to discriminate them (Tramo, Shah, & Braida, 2002). However, individuals with lesions in the prefrontal cortex only require a greater difference in frequency between the tones for discrimination in the presence of auditory distracters (Chao & Knight, 1995). Rabinowicz et al. (2000) measured tone discrimination in SZ in the presence and absence of auditory distracters, and found that although SZ participants required a greater frequency difference to be able to correctly discriminate the tones, they were not more susceptible to distracters compared to controls. This provides further evidence that deficits in tone discrimination are a result of abnormalities in the temporal lobe, rather than abnormalities in the frontal lobe (Rabinowicz et al., 2000).

Given that tone discrimination and MMN are both impaired in SZ and are thought to assess pre-attentive sensory memory, Javitt and colleagues examined MMN and tone matching performance in SZ and healthy control groups. They found a correlation between the two measures in both groups, suggesting that tone discrimination deficits are a result of auditory cortex dysfunction during the pre-attentive phase of sensory processing (Javitt, Shelley, & Ritter, 2000). Therefore, it appears that MMN and behavioral tone discrimination tasks may both be measuring change detection in early sensory memory. However, it may also be the case that that MMN and behavioral tone discrimination are not assessing the same underlying impairment. At the most basic level, tone discrimination tasks only require participants to discriminate between two sequential

tones (Javitt et al., 1997; Strous et al, 1995), while MMN is elicited following a deviant

stimulus from a series of standard stimuli (Cowan et al., 1993). Further, it has been found

that MMN can also reflect anticipatory representations of future stimuli and stimulus

generalization (for a review see Näätänen, et al., 2007). Finally, a recent study examining

the relationship between auditory hallucinations and MMN reductions (Fisher, Labelle, &

Knott, 2008) and a recent study examining the relationship between auditory

hallucinations and tone discrimination performance (McLachlan, Phillips, Rossell, &

Wilson, 2013) suggest different conclusions. Fisher et al. (2008) examined SZ groups

with and without a history of auditory hallucinations and found that frequency MMN

reductions were present in both groups and did not differ between those with and without

a history of hallucinations. However, McLachlan et al. (2013) found that individuals with

SZ with a history of auditory hallucinations performed worse than those without auditory

hallucinations on a pure tone discrimination task. It is not clear if these different findings

are due to task differences or differences in the underlying mechanisms being assessed.

Auditory Processing Deficits in Bipolar Disorder

There have also been studies, although smaller in number, that have examined

P50 and N100 in BD. A study by Olincy and Martin (2005) found evidence of P50

suppression abnormalities in BD+, schizoaffective-bipolar type, and SZ groups.

However, the BD- group had no abnormalities in P50 suppression compared to controls.

Similarly, Sánchez-Morla et al. (2008) found that euthymic individuals with BD- did not

differ from controls with respect to P50 gating, while BD+ and SZ showed abnormal P50

gating. Additionally, studies have found P50 suppression abnormalities in unaffected

relatives of those with BD+ compared to controls (Schulze et al., 2007). With regards to

N100, several studies have found no abnormalities in BD (Muir, St. Clair, & Blackwood, 1991; O'Donnell et al., 2004). However, a study by Lijffijt et al. (2009) found N100 abnormalities in BD, but found that there was no association between these abnormalities and history of psychosis in the disorder. However they did find that a history of psychosis was related to a larger P50 gating ratio, suggesting that a psychosis may be related to pre-attentive information processing deficits (Lijffijt et al., 2009). Taken together, these findings suggest that P50 deficits may be related to a common feature of BD+ and SZ.

MMN has also been studied in BD, but not to the extent of SZ. Some studies have found no differences between BD and healthy controls with regard to duration MMN (Catts et al., 1995; Umbricht et al 2003) or frequency MMN (Umbricht et al., 2003). However, these studies either did not examine psychotic symptoms in the disorder (Catts et al., 1995) or included a mixed sample of individuals with BD I and BD II (Umbricht et al., 2003). Hall and colleagues found that relatives of BD+ also show normal duration MMN (Hall et al., 2009). However, Jahshan and colleagues (2012) found duration MMN amplitudes that were decreased compared to healthy controls and intermediate between healthy controls and individuals with SZ. They also pointed out the limited number of studies conducted so far. Further, studies that examined MMN in bipolar disorder typically had small sample sizes (<25), failed to study heterogenous samples of BD, and did not examine the effect of medication (Jahshan et al., 2012). Similarly, other studies have found increased MMN latency in BD II (Andersson, Barder, Hellvin, Løvdahl, & Malt, 2008) and in a sample of individuals with BD who were in active mood episodes and had no history of psychotic symptoms (Takei et al., 2010). Finally, Shaikh and colleagues (2012) found that individuals who were at risk for

psychosis, assessed using the CAARMS measure, had reduced MMN amplitude compared to healthy controls. Additionally, those who went on to develop psychosis also had reduced MMN amplitude compared to those who did not. This suggests that MMN may be specifically related to psychosis (Shaikh et al., 2012). To our knowledge, only one study has examined behavioral tone discrimination ability in BD. This study found that deficits were restricted to pitch and amplitude discrimination, finding no deficits in frequency discrimination (Van Rheenan & Rossell, 2013).

Thus it appears that along with neurocognitive deficits, individuals with SZ also show impairments in basic auditory sensory processes that are thought to originate from dysfunction at the level of the auditory cortex (Javitt, 2009; Rabinowicz et. al., 2000). As described earlier, the STG which contains the PAC, is consistently identified as abnormal in SZ and related to auditory hallucinations (McCarley et al., 1999; Sun et al., 2009; Kim et al., 2003). While individuals with SZ are consistently found to be impaired on behavioral frequency discrimination tasks (Javitt, 2009), findings assessing frequency discrimination ability using MMN are not as consistent (Umbricht & Krljes, 2005). Additionally, findings from a studies assessing discrimination ability in individuals with SZ with auditory hallucinations using MMN (Fisher et al., 2008) have differed from those using behavioral tone discrimination (McLachlan et al., 2013). Given that auditory hallucinations also occur frequently in BD+ (Baethege et al., 2005), it may be that these patients will demonstrate impairment in simple auditory perception tasks. If such a deficit were present, it may suggest underlying neuropathophysiology in PAC or in networks involving the PAC in these individuals. Compared to SZ, there have been fewer investigations of auditory perception in BD+. However, evidence from

electrophysiological studies suggests that there may also be deficits in the auditory sensory system in BD, although there are many inconsistent findings and samples of BD patients have typically not been well characterized. Studies examining frequency discrimination with MMN have not found deficits in BD (Umbricht et al., 2003). Similarly, the single study that examined behavioral frequency discrimination also did not find deficits in BD (Van Rheenan & Rossell, 2013). Clearly, there is a need for clarification regarding frequency discrimination in BD and its potential relationship to psychotic features, including auditory hallucinations. The examination of sensory information processing is important because it may provide insight into the underlying abnormalities in brain structure and function in the disorders. This may lead to more research regarding the underlying mechanisms related to cognitive impairment in the disorders, and provide evidence for a continuous rather than discrete conceptualization of the disorders. Additionally, it could be a target of novel therapeutic treatments.

It is also important to study auditory sensory processing deficits because they may be related to functional outcome in the disorders. For instance, these deficits may contribute to impaired social interactions, as they are likely to interfere with accurate perception and understanding of spoken words (Wynn, Sugar, Horan, Kern, & Green, 2010). Cognitive deficits in SZ are the best predictor of functional outcome, and there has been relatively little treatment success in regards to cognitive symptoms (Green, 2006). Additionally, deficits in social cognition are considered a core feature of SZ and linked to functional outcome in the illness (Brekke, Kay, Lee, & Green, 2005; Green & Horan, 2010). In fact, there is evidence that social processing and emotional processing may serve as mediators between neurocognition and functional outcome in SZ (for a review

see Couture et al., 2006). A recent study that split a group of euthymic BD patients into low functioning and high functioning groups found that the low functioning group had a significant deficit in social cognition compared to the high functioning group, suggesting that social cognition may play a role in the functional outcome of BD (Lahera et al., 2012). Given the potential link between auditory processing and social cognition, and the importance of social cognition and functional outcome in SZ and BD, a brief review of social cognition is provided below.

Social Cognition

Social cognition is considered a different construct than neurocognition, although they are related (Green & Horan, 2010). Social cognition refers to several abilities that involve cognitive processes that are used to communicate with others and guide behavior in the social world (Ostrom, 1984). Social cognitive tasks often involve cognitive processes such as working memory and perception, but ultimately differ from nonsocial cognitive tasks. For example, the stimuli in social cognitive tasks are typically personally relevant while the stimuli in nonsocial cognitive tasks involve stimuli that are not affectively laden. Additionally, the relationship between the participant and stimuli differs because in social cognitive tasks this relationship can be interactive, while this is typically not the case in nonsocial cognitive tasks. Finally, responses to nonsocial cognitive tasks are typically scored as correct or incorrect, while in social cognitive tasks there may not always be a clear correct answer (Penn, Corrigan, Bentall, Racenstein, & Newman, 1997). Additionally, an fMRI meta-analysis by Van Overwalle (2009) suggests that social cognitive tasks are processed in different brain regions compared to other cognitive tasks.

Emotion Processing

       Social cognition is a multi-factorial construct that includes many abilities. The domains of social cognition that are most frequently studied in SZ are emotion processing, social perception, attributional bias, and theory of mind (Green & Horan, 2010). The domain most relevant to the current study is emotional processing. Emotion processing refers to identifying and using emotions from others' facial expression or voice to guide behavior (Green & Horan, 2010). Thus, emotion processing involves receiving information from both visual and auditory modalities. There is some evidence that individuals with SZ have difficulty integrating facial and vocal information (de Jong, Hodiamont, Van den Stock, & de Gelder, 2009), although the majority of studies focus on the two modalities separately. In the visual modality, emotion information can be communicated by identifying facial affect of another. Several studies have found that individuals with SZ have difficulty recognizing affect from facial expression (Edwards, Pattison, Jackson, & Wales, 2001; Feinberg, Rifkin, Schaffer, & Walker, 1986). There is some debate as to whether deficits in this area are general or specific. For example, some studies have found that individuals with SZ perform worse than healthy controls on tasks requiring them to match faces based on emotional expressions, but not on tasks where they were required to match faces based on identity (Kosmidis et al., 2007). Conversely, other studies have found that deficits in facial emotion recognition are predicted by deficits in facial identification, suggesting a more general deficit (Norton, McBain, Holt, Onqur, & Chen, 2009). A recent meta-analysis by Chan, Li, Cheung, and Gong (2010) found that individuals with SZ are impaired on facial emotion tasks and general facial processing tasks, suggesting a more generalized deficit. With regard to BD, studies

examining facial affect recognition have been inconsistent. Some studies have found no facial affect recognition deficits in BD (Armstrong, 2010; Venn et al., 2004; Vaskinn et al., 2007), while others have found that deficits are present in BD I but not BD II (Derntl, Seidel, Kryspin-Exner, Hasmann, & Dobmeier, 2009), or deficits that are not as severe as in SZ (Addington & Addington, 1998).

Emotion can also be identified in the auditory modality. Several studies have found that individuals with SZ have difficulty recognizing affect from voice (Edwards et al., 2001; Kucharska-Pietura, David, Masiak, & Phillips, 2005). Prosody is the term used for non linguistic aspects of speech that can aid in identifying emotion (van Rijn et al., 2005). Beyond semantics of what is being said, acoustic features such fundamental frequency (pitch), voice intensity (loudness), voice quality (timbre), and temporal aspects of speech (speech rate, number of pauses), are used in order to identify emotional state. For example, acoustic cues to denote happiness and anger include high fundamental frequency and large fundamental frequency variability, high voice intensity and large voice intensity variability, and fast velocity. Fear is also denoted by high fundamental frequency, large voice intensity variability, and fast velocity of speech but small fundamental frequency variability. Finally, acoustic cues to denote sadness include low fundamental frequency, small fundamental frequency variability, low voice intensity, small voice intensity variability (Juslin & Laukka, 2003). A meta-analysis confirmed that those with SZ are impaired in both perceiving and expressing emotional prosody, and perform more than one standard deviation below controls (Hoekert, Kahn, Pijnenborg, & Aleman, 2007). There are also few studies regarding auditory affect recognition in BD, although studies have found that adolescents with BD showed impairment in voice affect

recognition (Foster, Shear, & DelBello, 2007), while another study found that euthymic BD I individuals were impaired on affective prosody tasks, but that this was only true in female participants (Bozikas et al., 2007). However, it is not clear from these studies whether deficits on prosody tasks are at least partially accounted for by more basic deficits in auditory perception, including tone discrimination.

Given that differences in pitch are used to communicate emotions and that individuals with SZ have difficulty discriminating between tones of different pitches, one might expect that there is link between deficits in simple auditory processing and deficits in more complex social cognitive processes. Leitman and colleagues (2005) assessed the relationship between auditory emotion identification and a tone discrimination task similar to the one used in the present study. They found that performance on the tone discrimination task was positively correlated with performance on the auditory emotion perception tasks in individuals with SZ and schizoaffective disorder (Leitman et al., 2005). The same authors later used diffusion tensor imaging (fractional anisotropy) and found that structural impairments in primary and secondary auditory pathways are related to voice affect identification deficits, providing further evidence that basic sensory processing may be related to social cognition function (Leitman et al., 2007). Leitman et al. (2010) also examined the relationship between acoustic cues, tone discrimination, and emotion identification from prosody in a sample of individuals with SZ or schizoaffective and healthy controls. Participants were presented with audio recordings of actors portraying various emotions at varying levels of emotion intensity and were asked to identify the emotion expression and to rate its intensity. They were also given two tests of basic auditory perception, including a task similar to the tone discrimination task used in

the current study. When controls were presented with audio recordings with high pitch variability, their ability to identify emotion was better than when they were presented with audio recordings of low pitch variability. Individuals with SZ also improved when presented with recordings of high pitch variability, but not to the extent that normal controls did. This suggests that individuals with SZ are impaired at utilizing pitch-based cues of emotion. To further support this, impairments in emotion identification from prosody were correlated with basic auditory perception measures, including tone discrimination, and measures of functional outcome. Additionally, individuals with SZ were able to utilize intensity-based cues to aid in emotion recognition (Leitman et al., 2010). Similarly, Gold and colleagues (2012) found that a sample of individuals with SZ and schizoaffective disorder performed significantly worse than healthy controls on detecting emotions based on pitch, rather than on intensity. They also found a positive correlation between tone matching performance and accuracy in identifying pitch-based stimuli. Further, tone-matching did not correlate with visual affect identification. Finally, auditory emotion recognition deficits were related to a measure of functional capacity (Gold et al., 2012). These studies suggests that difficulties in detecting differences in pitch in voice may underlie auditory emotion recognition deficits, which may be in turn be related to deficits in functional outcome for individuals with SZ.

A recent study examined basic auditory perception, linguistic prosody, and emotional prosody in a sample of BD patients, which included those in active mood states and those with BD I and BD II, compared to controls. The tone discrimination tasks used in this study included 3 conditions, including judging between tones that differed in amplitude, duration, and pitch. The linguistic prosody task required

participants to determine if a nonsense phrase was inquisitive or declarative, while the emotional prosody task required participants to determine what emotion was being portrayed in nonsense sentences. They found that the BD group performed significantly worse on the duration tone discrimination task, but not the frequency discrimination task. In addition, there was a trend for the BD group to perform poorer on the emotional prosody task. They also found that the recognition of happiness was correlated with pitch and amplitude discrimination ability, but only in the female group. Thus, in opposition to Bozikas et al. (2007), the study concluded that there was a female advantage to identifying emotional prosody in BD. (Van Rheenen & Rossell, 2013). Finally, a recent study compared individuals with SZ, schizoaffective, and BD I (in depressive episode or euthymic) on a battery of affective prosody tasks (Comprehensive Affective Testing System). Individuals with schizoaffective disorder did not significantly differ from controls, individuals with BD and SZ did significantly worse an emotional recognition task compared to controls, and SZ additionally did significantly worse on a task where they were instructed to ignore the emotional meaning of a sentence and identify the emotion based on voice. Particularly important to this study, regardless of diagnosis, accuracy on the emotional recognition task, ignore emotional meaning task, and a task where they were to ignore emotional expression and focus on emotional meaning were significantly correlated with current auditory hallucinations (Rossell et al., 2013).

In summary, individuals with SZ and BD exhibit deficits in social cognition, which have been found to be correlated with negative functional outcome (Couture et al., 2006; Lahera et al., 2012). Most relevant to the current study, there is evidence that individuals with SZ and BD have difficulty recognizing and discriminating emotion from

facial expression (Derntl et al., 2009; Edwards et al., 2001) and from prosody of speech (Bozikas et al., 2007; Kucharska-Pietura et al., 2005). Additionally it has been found that deficits in basic sensory processing, such as tone discrimination, are related to deficits emotion recognition from prosody (Leitman et al., 2005), and individuals with auditory hallucinations may be impaired relative to those without auditory hallucinations (Rossell et al., 2013). Given the evidence that individuals with BD+ may also experience deficits in basic auditory sensory processing, it may also be that they will exhibit deficits in the ability to recognize emotions from the tone of voice of others, and there may be differences between those with and without auditory hallucinations.

<div align="center">Conclusion</div>

While there is a current distinction between BD and SZ, it is clear from the literature that there are multiple overlaps among the disorders. One such overlap that may be particularly important is the presence of psychotic symptoms in both disorders (Boksa, 2009; Suppes et al., 2001). It may be important to examine the role of psychotic symptoms in BD, as the literature indicates that BD+ may be a different subtype of the disorder with poorer course and prognosis (Özyildririm, Çakir, & Yazici, 2010), greater neurocognitive deficits (Bora, Yucel, & Pantelis, 2010), specific neuroanatomical abnormalities (Edmiston et al., 2011) and genetic components (Goes et al., 2008) than BD-.

It may also be the case that psychotic symptoms in BD are markers for impairment in neural systems and neurocognitive abilities that are typically associated with a diagnosis of SZ. If this is the case, then it would lend evidence to the argument that BD and SZ may be better conceptualized as occurring on a continuum. In SZ, there is

ample evidence that suggests auditory hallucinations are related to abnormalities in the superior temporal gyrus, which contains the primary auditory cortex (Kim et al., 2003). Abnormalities of the primary auditory cortex are also related to early auditory information processing deficits in SZ, such as the ability to discriminate between two tones of different pitches (Rabinowicz et al., 2000). Recent studies have found that basic tone discrimination ability is related to the ability to infer emotions from auditory cues in the disorder (Lietman et al., 2005; Lietman et al., 2010; Gold et al., 2012). Given the consistency with which auditory perception and auditory cortex abnormalities are identified in SZ, and links between auditory hallucinations and abnormalities in primary auditory cortex, it may be that patients with BD who also exhibit psychotic symptoms will demonstrate impairment in simple auditory perception tasks that may result from abnormal auditory cortex. This is further supported by evidence suggesting that individuals with BD may also have structural and functional abnormalities in auditory cortex (Adler et al., 2007; Chen et al., 2004; Cui et al., 2011; Rimol et al., 2010; Takahashi et al., 2010; Tost et al., 2010), basic auditory processing deficits (Jahshan et al., 2012; Lijffijt et al., 2009; Olincy & Martin, 2005; Takei et al., 2010), and difficulties identifying emotion from voice (Bozikas et al., 2007; Foster et al., 2007; Van Rheenen & Rossell, 2013), although there is paucity in research examining these in individuals with BD+ and BD-. If auditory perception is impaired in BD+ and linked to greater social cognitive deficits, this would be consistent with more severe functional impairment found in those with psychosis. Recent preliminary evidence indicates that patients with BD+ may exhibit impairments in auditory emotion recognition and that this may be associated with auditory hallucination severity (Rossell et al., 2013). However, there are no studies

examining the relationship between tone discrimination and multi-modal affect recognition in BD+.

<div align="center">Research Aims and Hypotheses</div>

Given the significant overlapping features between SZ and BD, including the presence of auditory hallucinations, it may be that individuals with BD+ are impaired on tasks of basic auditory processing and emotion recognition that have been frequently found to be impaired in individuals with SZ. Thus, the aim of the present study is to examine basic auditory processing, affect recognition, and the relationship between the two in SZ, BD+, BD-, and NC. Based on a review of the literature, we propose the following hypotheses:

1. An overall pattern of performance will be found such that participants in the SZ group will demonstrate the greatest impairment on a behavioral tone discrimination task, followed by the BD+, BD-, and NC groups (SZ < BD+ < BD- < NC).

2. An overall pattern of performance will be found such that participants in the SZ group will demonstrate the greatest impairment on an affect identification task followed by the BD+, BD-, and NC groups (SZ < BD+ < BD-< NC)

3. Performance on the tone discrimination task will predict performance on the auditory and auditory-visual conditions of the affect recognition task in all groups, but not on the visual condition.

CHAPTER 3

METHODOLOGY

Participants

This study assessed 50 individuals with schizophrenia 30 individuals with bipolar

I disorder with a history of psychosis (BD+), 28 individuals with bipolar I disorder

without a history of psychosis (BD-), and 29 normal controls (NC). Participants were

recruited from the general community via flyers, community mental health centers,

support groups, and the University of Nevada, Las Vegas (UNLV) Psychology subject

pool. All participants were between the ages of 18-65 and able to provide informed

consent.

The Structured Clinical Interview for the DSM-IV (SCID-IV; First, Spitzer,

Williams, & Gibbons, 2002) was used to identify a diagnoses. BD patients were put into

the BD+ group if they were identified as having a history of psychotic symptoms,

including hallucinations or delusions in manic or depressed mood states. BD patients

were put into the BD- group if they were identified as having no history of psychotic

symptoms associated with manic or depressed mood states. Additionally, all BD

participants were not currently experiencing a depressive, manic, or mixed episode. The

exclusion criteria for participants were as follows:

a) English is not a primary language

b) A significant impairment in hearing (>40 dB HL from 250-4000 Hz)

c) Corrected vision worse than 20/50

d) History of a medical condition known to significantly affect the central

nervous system

e) Current or history of a neurological condition

f) Current or history of traumatic brain injury

g) Current or recent (within the past 6 months) diagnosis of substance abuse or dependence

h) Currently (within the past week) taking medication that may produce significant cognitive effects, with the exception of medication that is specified for treatment of BD

i) A diagnosis of mental retardation

j) A diagnosis of a mood episode within the last month

Additional exclusion criteria for NC's are as follows:

a) Any current Axis I or Axis II DSM-IV-TR diagnosis

b) History of an Axis I mood disorder

c) A diagnosis of BD or SZ in any first or second degree relative

Measures

Participants were given a battery of assessment measures that were included as part of a larger neuropsychological battery and fell into one of five categories: 1) screening and diagnostic measures, 2) symptom measures, 3) intellectual functioning measures, 4) sensory perception measure, and 5) social cognition measure. Each are described below.

Screening and diagnostic measures

1) *Demographic Questionnaire*

2) *Family History-Research Diagnostic Criteria (FHDC):* The FHDC

(Andreasen, Endicott, Spitzer, & Winoku, 1977) is a semi-structured used to collect and

record relevant family mental health history. Patients are asked about any psychiatric

illness that may be present in their first-degree relatives. The FHDC includes specific

criteria in order to make a diagnosis of schizophrenia, schizoaffective disorder, major

depressive disorder, bipolar disorder, substance abuse, and antisocial personality

disorder. The FHDC is considered a reliable and valid method for assessing family

psychiatric history (Andreasen et al., 1977). It has also been found that the FHDC had a

high sensitivity and specificity for identifying SZ (Li et al., 1997).

3) *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-IV):* The

SCID-IV (First, Spitzer, Williams, & Gibbons, 2002) is a semi-structured interview used

to gather and record information in order to aid in diagnosing Axis I disorders on the

DSM-IV. It can be used to assess current psychiatric patients, medical patients,

community samples, and college students, among other samples. In this study, the SCID-

IV was used in order to verify diagnosis in the bipolar groups, as well as to confirm that

individuals in the control group have no Axis I diagnosis. The inpatient version of the

SCID-IV was used for this study, and administered by researchers who had been trained

in the DSM-IV-TR diagnostic system. This version is organized into 12 modules that

cover different diagnoses, and contain interview questions, criteria, as well as rating

scales for the questions. The rating scale ranges from 1-3, where a rating of 1 is given if

the symptom is absent, 2 is given if it is questionable whether the symptom is present,

and 3 is given when the symptom is present. Once each module is scored, an Axis I

diagnosis may be made. The SCID-IV has been found to have excellent reliability

(Ventura, Liberman, Green, Shaner, & Mintz, 1998). It has also been found that the SCID

has adequate to excellent reliability in diagnosing lifetime and current BD among patient samples (Williams et al., 1992). Additionally, Fennig, Craig, Lavelle, Kovasznay, & Bromet (1994) found that the SCID is a reliable method for diagnosing schizophrenia and bipolar disorder with psychotic features.

4) *Hollingshead Index*: The Hollingshead Index of Social Position (Hollingshead, 1971) was used to estimate the social class of participants using rating scales of education and occupation. The rating scales range from 1-7, and are then combined ([7 x Occupation Level] + [4 x Education Level]) so that individuals can be classified into one of five social classes. Class I is considered upper class, Class II and III are considered middle class, Class IV is considered working class, and Class V is considered poor.

5) *Visual Acuity Check:* The Visual Acuity check is a method to measure the acuity of eyesight. Participants stood 4 feet away from an eye chart on the wall and were asked to read from the chart. This was done to ensure that participants have adequate eyesight to complete all tasks.

6) *Pure-Tone Audiometer Test:* The hearing check was used to measure acuity of hearing. Participants wore audiometry headphones and were first administered a tone of 250 Hz at 30 dB HL in the right ear. They were instructed to raise their hand if they heard a tone. The intensity of the sound was then lowered by increments of 10 decibels until the participant no longer indicated that they could hear a sound. The intensity of the sound was then increased by increments of 10 decibels until the participant indicated that they could again hear a tone. Therefore, the participants responded twice to their lowest audible intensity. This process was then repeated for a

number of different frequencies (500 Hz, 750 Hz, 1000 Hz, 1500 Hz, 2000 Hz, 3000 Hz,

4000 Hz, 6000 Hz, 8000 Hz) and in the left ear. This was done to ensure that each

participant has adequate hearing ability to complete the tone discrimination task.

Symptom Measures

　　1) *Hamilton Depression Rating Scale (HDRS):* The HDRS (Hamilton, 1960) is a

depression rating scale that includes 17 items. It evaluates depressed and anhedonic

mood, cognitive symptoms that accompany depression, and comorbid anxiety symptoms.

Either a 0-2 or 0-4 scale is used for each variable, with increasing scores indicating more

severe symptoms, to quantify the results of the interview. The raw total score is then used

as an estimate of current depressive symptoms. The HDRS has been found to be a

reliable measure of depression (Trajković et al., 2011).

　　2) *Young Mania Rating Scale (YMRS):* The YMRS (Young, Biggs, Ziegler, &

Meyer, 1978) is used to assess manic symptoms. It includes 11 items that correspond to

the core symptoms of mania. Information is based on subjective report of the patient and

clinical observations. Four of the items are rated according to a scale of 0-8, while the

seven of the items are rated according to a 0-4 scale and are given twice the weight of the

other items. The YMRS is considered an adequate and reliable measure of mania (Young

et al., 1978).

　　3) *Scale for the Assessment of Positive Symptoms (SAPS):* The SAPS (Andreason,

1984) is used to assess positive psychotic symptoms. It includes 34 items that that

assesses current (i.e. in the previous week) hallucinations, delusions, bizarre behavior,

and positive formal thought disorder. Items are rated according to a scale of 0-5 and a

total score can be derived from the summation of all items. Four additional total scores can also be calculated pertaining to each of the symptom categories described above.

4) *Scale for the Assessment of Negative Symptoms (SANS:* The SANS (Andreason, 1983) is used to assess negative psychotic symptoms. It includes 30 items that assess current (i.e. in the previous week) affective flattening, alogia, avolition, anhedonia, and attentional impairment. Items are rated according to a scale of 0-5 and a total score can be derived from the summation of all items. Four additional total scores can also be calculated pertaining to each of the symptom categories described above.

Intellectual Functioning Measures

A short form of the Weschsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997) was administered to assess current intellectual functioning. The Vocabulary and Block Design tests were given and used to calculate full scale IQ based on a regression equation (Ringe, Saine, Lacritz, Hynan, & Cullum, 2002).

1) *WAIS-III Vocabulary Subtest:* The Vocabulary subtest of the WAIS-III (Wechsler, 1997) contains 33 items. Participants were asked to provide definitions of words that increase in difficulty, and responses are rated as either a 0,1, or 2-point answer. A score of zero is given if the response is incorrect or very vague, or if no response is given. A score of one is given if the response is vague or not elaborated, and a score of two is given if the response indicates that the participant clearly understands the word. Once a participant gives four consecutive responses that are given a score of zero, administration of the test is discontinued.

2) *WAIS-III Block Design Subtest:* The Block Design subtest of the WAIS-III

(Wechsler, 1997) contains 14 items. Participants were asked to use a number of blocks to recreate designs, which increase in difficulty and complexity, in a specified time limit. The total number of possible points that can be awarded, as well as the time limit given to participants to recreate the design, varies according to the difficulty of the item. Participants are awarded points based on accuracy, and are given a score of zero on an item if they recreate the design incorrectly or go over the specified time limit. Additionally, bonus points may be awarded if participants accurately recreate the design very quickly. Once a participant receives a zero on three consecutive items, administration of the test is discontinued.

3) *WAIS-III Information Subtest:* The Information subtest of the WAIS-III (Wechsler, 1997) contains 28 items. Participants were asked to answer questions that are designed to measure general knowledge of current and historical facts/events. Responses are given a score of zero if they are incorrect and a score of one if they correct. Once a participant gives six consecutive responses that are given a score of zero, administration of the test is discontinued.

Sensory Perception Measure

1) *Tone Discrimination Task:* The Tone Discrimination task was used to assess the ability of participants to discriminate between two tones of different frequencies. It was developed using e-prime software and is a modification of the paradigm used in Javitt, Strous, Grochowski, Ritter, and Cowan, 1997. Participants sat in a dark room and listened to 120 trials of tone pairs that differed in frequency by 0, 5, or 20%. For each trial, two tones were presented sequentially and the participants were prompted to indicate whether the tones were the same or different by pressing a button. Each tone was

presented for 100 milliseconds, with an interstimulus interval of 1 second. The first tone of each pair had a frequency of 500, 1000, or 2000 Hz, and the second tone in the pair was either identical (0% frequency difference), of higher frequency (5% or 20% higher), or of lower frequency (5% of 20% lower). Of the total 120 trials, 60 tone pairs were of the same frequency, 30 tone pairs differed by 5% frequency, and 30 tone pairs differed by 20% frequency. The order of the three conditions was randomized, and each participant was administered the task in the same randomized order. Additionally, participants completed 10 practice stimuli prior to testing.

Social Cognition Measure

1) *Bell-Lysaker Emotion Recognition Test (BLERT)*: The BLERT (Bell, Bryson, & Lysaker, 1997) is an audio-visual affect recognition task that is used to assess an individual's ability to discriminate affects. It contains 10 second vignettes in which an actor portrays one of seven affects (happy, sad, anger, fear, disgust, surprise, and no emotion). Additionally, each affect is portrayed in three different monologues, which results in a total of 21 vignettes. After seeing each vignette, the tape is paused and participants are prompted to indicate which affect the actor was portraying by pointing to it on a response card. Responses are given a score of 0 or 1 depending on accuracy. Scores on items are then summed for a total score, which can be used to indicate affect recognition impairment. Ranges of total scores can be used to indicate normal performance (19-21), mild impairment (15-18), moderate impairment (11-14), moderately severe impairment (7-10), or severe impairment (0-6). Additionally, scores can be obtained for positive affect recognition (happiness and surprise) and negative affect recognition (sadness, anger, disgust, and fear). The authors found that individuals

with SZ typically exhibit moderate, moderately severe, or severe impairment, while normal controls exhibit normal performance or mild impairment (Bell et al., 1997).

The BLERT was also administered in a modified form so that visual affect, auditory affect, and auditory-visual affect recognition could be assessed separately. In order to assess visual affect recognition, the BLERT stimuli were spliced so that participants only see a moving image of the actor talking, but do not hear any information. In order to assess auditory affect recognition, the BLERT stimuli were spliced so that participants hear sound clips of the actor talking, but do not see any video. In total, participants were presented with 21 visual affect recognition clips, 21 auditory affect recognition clips, and 21 clips of the original BLERT stimuli, which yields a total of 63 clips. The clips were intermixed and then presented to participants in one of three pre-determined randomized orders. The original BLERT stimuli have good reliability and have been found to differentiate between schizophrenia, substance abuse, and normal controls groups (Bell et al., 1997).

<div align="center">Procedure</div>

All participants interested in the study contacted researchers by phone. After verbal consent was given, participants were administered a brief phone screen to determine if the participant met initial eligibility criteria. If initial criteria were met, participants were scheduled to complete an in-person interview and assessment to further evaluate inclusionary/exclusionary criteria. The researcher obtained informed consent from the participant, during which two consent forms were signed. The participant was given one copy of the consent form, while the other copy was stored in a locked filing cabinet in the Neuropsychology Research Lab at UNLV. The participant had the

opportunity to ask questions, and provided the name of the principle investigator, Daniel N. Allen, PhD.

After obtaining informed consent, participants were asked to complete a demographic questionnaire and were interviewed using the SCID-IV to further assess eligibility. If a participant was found to be eligible at this point, they were administered several symptoms ratings measures (HDRS, YMRS, SAPS, and SANS) in order to assess current symptomatology. These measures, along with the SCID-IV, were used to determine if a participant met criteria for the BD+, BD-, or HC group. If the participant was determined to meet all eligibility criteria with the exception of having a mood episode in the past month, that participant was asked to return once they have met this criteria. This portion of the study took approximately two to three hours to complete.

After the first portion of the study, the participant was asked to complete an assessment session. The assessment session included the three WAIS-III subtests, the tone discrimination task, and the BLERT, as part of a larger neuropsychological battery that took approximately three to four hours to complete.

Data Analysis

Data Entry and Screening

All screening and diagnostic measures were scored by two individuals who had been trained on the measure and standardized procedure of scoring. Data were double entered and inspected to ensure that underlying statistical assumptions were met. Outliers were defined as having a score $\pm$ 3.0 standard deviations above or below the mean and initial screening of the data indicated that no outliers were present. Frequency distributions of the data indicated skewness and kurtosis were within accepted limits

(skewness < +/-1, kurtosis < +/-1.5). Therefore, parametric analyses were used to test the main hypotheses.

Preliminary Analyses

Prior to the main analysis, a sensitivity index (d-prime) was calculated and used as a primary outcome measure assessing performance on the tone discrimination task. d-prime (d′) is used as an index of sensitivity after controlling for response bias (i.e. having a strict or lax approach to the task) False alarm rates and hit rates were calculated for each participant. A constant of .01 was then added to the calculated false alarm and hit rates in order to correct for rates equal to 0 or 1. A z-transformation of the calculated false alarm and hit rate was then done. Finally, d′ is was calculated by subtracting the z-transformed false alarm rate from the z-transformed hit rate ($d′ = z(H) - z(F)$). An ideal subject would maximize hit rate and minimize false alarm rate, meaning that greater values of d′ correspond with greater sensitivity. On our task, the highest possible value of d′ was 4.65. Descriptive statistics were also calculated for demographic and clinical characteristics for each group. Demographic differences were assessed by comparing groups on age, years of education, IQ, gender, and ethnicity. Clinical characteristics were assessed by comparing groups on number of hospitalizations, medication status, history of auditory hallucinations, SAPS total and symptom category scores, SANS total score, HDRS total score, and YMRS total score. Correlational analyses were used to examine the relationship between the various demographic and clinical characteristics and performance on the tone discrimination task. If significant correlations were found, an analysis of covariance (ANCOVA) was used to determine the potential impact of these characteristics.

Main Analyses

A one-way mixed-model ANCOVA was used to evaluate the main hypothesis of the study. Group served as the between subjects variable, while d′ scores for the 5% and 20% frequency difference conditions on the tone discrimination task served as the within subjects variables. Age was added as a covariate to the analysis. Following a significant result, follow-up univariate ANCOVAs and planned comparisons were used to test the predictions made by each hypothesis. For planned comparisons, the following patterns were hypothesized:

Hypothesis 1 (5% frequency difference): SZ < BD+ < BD- = NC

Hypothesis 2 (20% frequency difference): SZ < BD+ < BD- = NC

Additionally, a one-way mixed-model ANCOVA was used to compare the three groups on BLERT performance. Group membership served as a between subjects variable, while raw total scores for performance on visual affect recognition, auditory affect recognition, and auditory-visual affect recognition conditions served as the within subjects variables. Age was added as a covariate to the analysis. Following a significant result, follow up univariate ANCOVA's and planned comparisons were used to test the predictions made by the hypothesis. For planned comparisons, the following patterns were hypothesized:

Hypothesis 1 (Auditory affect): SZ < BD+ < BD-= NC

Hypothesis 2 (Visual affect): SZ < BD+ < BD- = NC

Hypothesis 3: (Auditory-Visual affect): SZ < BD+ < BD- = NC

Finally, simple regression analyses were used to examine if tone discrimination performance predicted performance on the BLERT. d′ scores on the 5% condition was

used as predictors for total scores on auditory affect recognition, visual affective recognition, and auditory-visual affect recognition of the BLERT. As a follow up analysis, group membership was added to the analysis to determine if group serves as a moderator of the relationship between tone discrimination performance and BLERT performance. Additionally, the BD+ group was separated into those with a history of auditory hallucinations and those without history of auditory hallucinations. Tone discrimination and BLERT performance were compared between the two groups. We hypothesized that those with a history of auditory hallucinations would demonstrate greater impairment on both tasks compared to those without a history of auditory hallucinations.

CHAPTER 4

RESULTS

Preliminary Analyses

Demographic Differences

Demographic variables for the study groups are presented in Table 1. Age, years of education, and estimated full scale IQ (FSIQ) were compared among groups using a one-way ANOVA (Table 1). Significant differences were found among groups for age, F (3, 133) = 6.2, p = .001, education, F (3, 133) = 16.9, p < .001, and estimated FSIQ, F (3, 133) = 31.6, p < .001. Post hoc analysis of age differences using Tukey-b procedure indicated that the SZ group was significantly older than both of the BD groups, while post hoc analyses of education and estimated FSIQ differences indicated that the SZ group had completed significantly fewer years of education and had a significantly lower IQ than all other groups. Gender, and ethnicity were compared among groups, and no significant gender, X^2 (3) = 5.9, p = .12, or ethnicity, X^2 (9) = 13.0, p = .16, differences were found (Table 1). Based on these analyses, age was used as a covariate in the main analyses, given age associated changes in auditory perception. However, we did not control for differences in IQ or years of education, because cognitive deficits are core features of schizophrenia and so diminished IQ and years of education are expected. To control for these variables would essentially be controlling for our independent variable of interest (i.e., diagnosis).

Symptom Differences

Groups were compared on demographic variables related to clinical course and current symptom ratings using a one-way ANOVA and Tukey-b procedure for post hoc

comparisons (Table 2). Significant differences were found among groups for number of hospitalizations, F(3,133) = 14.7, $p < .001$, and post hoc comparisons indicated that the SZ group had a significantly higher amount of hospitalizations compared to all other groups, who did not differ from each other. Significant differences were also found among groups for ratings on the Hamilton Depression rating scale (HDRS), F (3, 133) = 15.6, $p < .001$, and post hoc comparisons indicated that all three clinical groups had significantly higher total scores than the NC group, but did not differ from each other. Significant differences were also found among groups for ratings on the Young Mania rating scale (YMS), F (3, 133) = 33.9, $p < .001$, with post hoc comparisons indicating that the SZ group had significantly higher total scores than all other groups and both BD groups had significantly higher scores than the NC group. These results indicate that all clinical groups were experiencing some depressive and manic symptoms relative to the NC's, even though individuals with BD were excluded if they were current experiencing a depressive, manic, or mixed episode as defined by the DSM-IV-TR. Based on the mean scores, these symptoms were in the very mild range. Significant group differences were also found on ratings of negative symptoms, F (3, 133) = 16.9, $p < .001$, which was assessed using the Scale for the Assessment of Negative Symptoms (SANS). Post hoc analysis revealed that the SZ and BD+ groups were experiencing significantly greater negative symptoms compared to the BD- group, who were experiencing significantly greater negative symptoms compared to the NC group. Again, based on the mean scores these symptoms were in the normal to borderline range.

Positive symptoms were assessed among groups using both the Scale for the Assessment of Positive Symptoms (SAPS). Significant group differences were found, F

(3, 133) = 50.5, $p < .001$, with the SZ group having significantly greater positive symptoms than all other groups, who did not differ from each other. In order to better characterize positive symptoms in our sample, we examined group differences on four factors previously identified within the SAPS. Significant group differences were found on the four factors of the SAPS, which include Hallucinations, F (3, 133) = 37.3, $p <$ .001, Delusions F (3, 133) = 18.9, $p < .001$, Bizarre Behavior F (3, 133) = 3.9, $p = .01$, and Formal Thought Disorder F (3, 133) = 19.4, $p < .001$. Post hoc analyses revealed higher ratings of hallucinations, delusions, and thought disorder in the SZ group compared to all other groups, who did not differ from each other. The only significant differences in bizarre behavior ratings were between the SZ and NC groups, with the SZ groups being rated higher.

Medication Differences

Medication status, type of medication, and number of prescribed drug classes were compared among the clinical groups using chi-square (Table 3). Information regarding medication was not available for one participant in the BD+ group and six participants in the SZ group. Significant group differences were found with regard to medication status, X^2 (2) = 12.8, $p = .002$, with a higher percentage of the BD- group being unmedicated compared to the SZ group. However, no significant correlations were found between medication status and tone discrimination or BLERT performance in any of the clinical groups. Significant differences were also found between groups on the percentage prescribed any type of antipsychotic (typical or atypical), X^2 (2) = 31.3, p <.001, as well as the percentage prescribed typical antipsychotics, X^2 (2) = 11.1, $p <$ .001, and atypical antipsychotics, X^2 (2) = 22.3, $p < .001$, with a higher percentage of the

SZ group being prescribed an antipsychotic of either type compared to both BD groups. No significant correlations were found between antipsychotic use and tone discrimination or BLERT performance in the BD+ or BD- groups. However, there was a significant correlation between atypical antipsychotic use and performance on the 20% frequency difference condition of the tone discrimination task in the SZ group, with those taking atypical antipsychotics performing worse than those not taking atypical antipsychotics, r_{pb} = -.31, n = 44, p = .04However, atypical antipsychotic use was not added as a covariate in the subsequent analyses as only 16 of the BD+ group and 11 of the BD- group were prescribed atypical antipsychotics, while no one in the NC was taking antipsychotic medication. No significant group differences were found on the percentage prescribed antidepressants, X^2 (2) = .41, p = .82, benzodiazapines, X^2 (2) = 4.1, p = .13, mood stabilizers, X^2 (2) = 2.3, p = .31, or lithium, X^2 (2) = .91, p = .63. Groups were also compared on the number of drug classes they were currently prescribed based on antidepressants, benzodiazapines, mood stabilizers, and antipsychotics. Results indicated no significant group differences on the percentage receiving one drug class, X^2 (2) = .93, p = .63, or two drug classes, X^2 (2) = .44, p = .80. However, significant group differences were found on the percentage of receiving three or more drug classes, X^2 (2) = 9.5, p = .008, with a higher percentage in the SZ group compared to the BD groups. Again, there were no significant correlations between being prescribed three or more drug classes and tone discrimination or BLERT performance in any of the clinical groups.

Table 1.

Demographic Information by Group.

Variables	NC ($n = 29$)		BD- ($n = 28$)		BD+ ($n = 30$)		SZ ($n = 50$)		F	p	*post hoc*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Age (years)	38.9	13.8	34.6	11.9	37.1	14.2	46.0	10.9	6.2	.001	BD-, BD+<SZ
Education (years)	14.0	2.2	14.4	1.8	13.5	2.2	11.4	2.0	16.9	< .001	SZ<BD-, BD+, NC
Estimated FSIQ	103.7	12.2	104.1	11.6	99.4	13.0	81.3	12.4	31.6	< .001	SZ<BD-, BD+, NC
									X^2	p	
Sex (% male)	44.8		39.3		26.7		54.0		5.9	.12	
Ethnicity (%)									13.0	.16	
Caucasian	62.1		82.1		73.3		58.0				
African American	13.8		3.6		10.0		26.0				
Hispanic/Latino	6.9		0.0		10.0		6.0				
Other	17.2		14.3		6.7		10.0				

Note. NC = normal control. BD- = bipolar disorder without psychotic features. BD+ = bipolar disorder with psychotic features. SZ = schizophrenia. FSIQ = Full Scale IQ. X^2= Pearson Chi-Square.

Table 2.

Clinical Characteristics by group.

Variable	NC (*n=29*)		BD- (*n=28*)		BD+ (*n=30*)		SZ (*n=50*)		*F*	*p*	*Post hoc*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Hospitalizations	0.0	3.8	1.3	1.6	2.8	3.8	8.4	9.9	14.7	< .001	SZ < BD-, BD+, NC
Current Symptoms											
HDRS	2.5	3.4	9.3	5.9	10.6	6.6	9.9	4.8	15.6	< .001	NC < BD-, BD+, SZ
YMS	1.5	2.7	5.0	5.5	5.0	5.0	12.0	5.2	33.9	< .001	NC < BD+, BD- <SZ
SANS	3.7	7.6	13.3	13.1	21.2	15.9	24.5	14.0	33.9	<.001	NC < BD- < BP+,SZ
SAPS	1.0	3.9	4.3	6.0	6.5	8.2	26.1	14.8	50.5	<.001	NC, BD-, BD+ < SZ
Hallucinations	0.0	0.0	.04	.19	.87	2.1	24.5	14.0	37.3	<.001	NC, BD-, BD+ < SZ
Delusions	0.1	.56	1.2	2.5	1.9	2.8	7.2	7.1	18.9	<.001	NC, BD-, BD+ < SZ
Bizarre Behavior	.24	1.3	1.4	2.2	1.3	2.3	1.9	2.3	3.9	.01	NC < SZ
Thought Disorder	.66	3.9	1.6	2.8	2.3	3.8	6.5	4.7	19.4	<.001	NC, BD-, BD+ < SZ

Note. NC = normal control. BD- = bipolar disorder without psychotic features. BD+ = bipolar disorder with psychotic features. SZ = schizophrenia. HDRS = Hamilton Depression Rating Scale. YMS = Young Mania Scale. SANS = Schedule for the Assessment of Negative Symptoms. SAPS = Schedule for the Assessment of Positive Symptoms.

Table 3.

Medication Information by Group.

Variables	BD- (*n=28*)	BD+ (*n=29*)	SZ (*n=44*)	X^2	P	*post hoc*
Current Medication (%)						
Antidepressant	35.7	41.4	43.2	.41	.82	
Benzodiazapine	17.9	10.3	29.5	4.1	.13	
Mood Stabilizer	39.3	55.2	56.8	2.3	.31	
Antipsychotic	39.3	55.2	97.7	31.3	<.001	BD-, BD+ < SZ
Typical	0.0	0.0	18.2	11.1	<.001	BD-, BD+ < SZ
Atypical	39.3	57.1	90.9	22.3	<.001	BD-, BD+ < SZ
Lithium	7.1	17.2	4.5	3.6	.16	
Unmedicated	32.1	13.8	2.3	12.8	.002	SZ < BD-
Prescribed						
1 Drug Class	14.3	24.1	18.2	.93	.63	
2 Drug Classes	39.3	41.4	34.1	.44	.80	
3+ Drug Classes	14.3	20.7	45.5	9.5	.008	BD-, BD+ < SZ

Note. BD- = bipolar disorder without psychotic features. BD+ = bipolar disorder with psychotic features. SZ = schizophrenia. X^2 = Pearson Chi-Square

<center>Primary Analyses</center>

Hypothesis 1: Overall group differences on tone discrimination performance

Hypothesis 1 predicted that the SZ and BD+ group would perform significantly worse on both frequency difference conditions (5% and 20%) of the tone discrimination task compared to the BD- and NC groups. As described earlier, a sensitivity index (d′) was calculated to be used as the primary outcome measure assessing performance on the tone discrimination task. The hypothesis was tests using a one-way mixed-model ANCOVA (see Table 4) with diagnosis was the between subjects variable, and tone frequency as the within subjects variable. Given that our preliminary results revealed significant age differences among groups, we examined the relationship between age and tone discrimination and found a significant correlation in both the 5%, $r = -.39$, $n = 137$, $p < .001$, and 20%, $r = -.31$, $n = 137$, $p < .001$, frequency difference conditions. As a result, age was included as a covariate in the analysis. Results of the analysis indicated a significant main effect of frequency difference, $F(3, 132) = 5.1$, $p = .03$, and group, $F(3, 132) = 32.1$, $p < .001$). There was also a significant age by frequency difference interaction effect, $F(3, 132) = 5.6$, $p = .02$. Two follow-up univariate ANCOVA's with age as a covariate indicated significant group differences on the 5% frequency difference condition, $F(3, 132) = 26.3$, $p < .001$, and 20% frequency difference condition, $F(3, 132) = 30.6$, $p < .001$. Planned comparisons indicated that on the 5% frequency difference condition, the SZ group performed worse than the BD+ group, $p < .001$, who in turn performed worse than the BD-, $p = .01$. The BD- and NC groups did not differ from each other, $p = .89$. On the 20% frequency difference condition, the SZ group again performed worse than the BD+ group, $p < .001$.

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Table 4.

One-way ANCOVAs of Tone Discrimination Performance by Group.

Frequency Difference	NC(n = 29)		BD- (n = 28)		BD+ (n = 30)		SZ (n = 50)		*F*	*p*	*Partial η2*	*Planned comparisons*
	Mean	SE	Mean	SE	Mean	SE	Mean	SE				
5%	3.0	.21	3.0	.21	2.2	.20	1.0	.16	26.3	<.001	.37	SZ < BD+ < BD-, NC
20%	4.1	.20	3.7	.20	3.3	.19	2.0	.15	30.6	<.001	.41	SZ < BD+, BD-, NC;

Note. NC = controls. BD- = bipolar disorder without psychosis. BD+ = bipolar disorder with psychosis. SZ = schizophrenia. [a] Mean refers to estimated marginal mean after controlling for age

There were no differences between the BD+ and BD- groups, $p = .08$, or between the BD- and NC groups, $p = .20$. Examination of the estimated marginal means indicates that as expected, the 5% frequency difference condition was more difficult than the 20% frequency condition for all groups (see Figure 1).

Figure 1.

Performance on the Tone Discrimination task by Group.
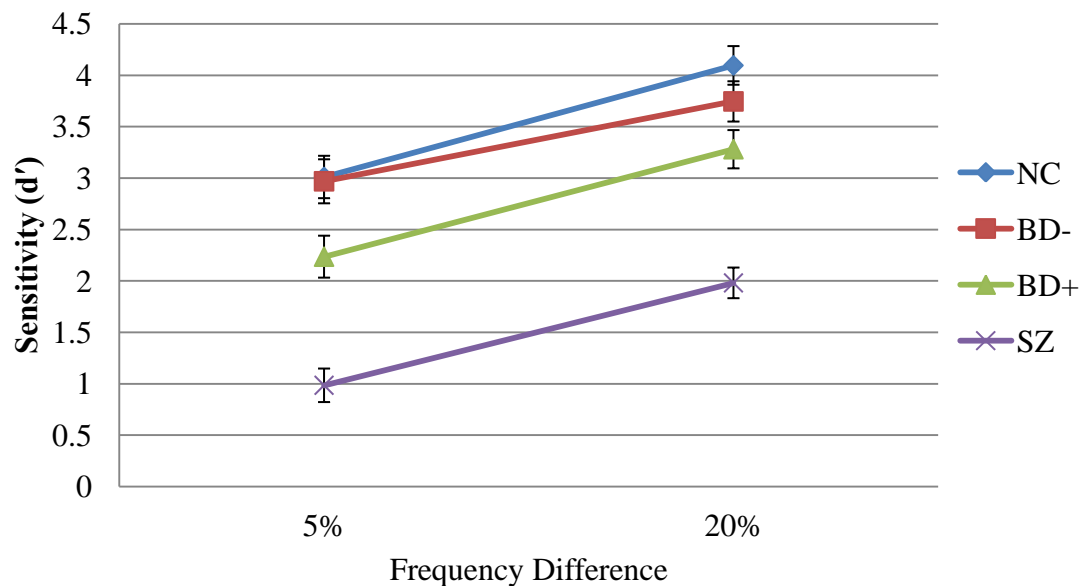
Note. NC = controls. BD- = bipolar disorder without psychosis. BD+ = bipolar disorder with psychosis. SZ = schizophrenia.

Hypothesis 2: Overall group differences on BLERT performance

Approximately 88% of our sample was also administered the BLERT. Hypothesis 2 predicted that the SZ and BD+ group would perform significantly worse (raw scores) on all conditions of the BLERT task compared to the BD- and NC groups. A one-way mixed-model ANCOVA (see Table 5) was used to test this hypothesis. Given that our

preliminary results revealed significant age differences among groups we examined the relationship between and BLERT performance and found a significant correlation in the auditory affect recognition ($r = -.45$, $n = 117$, $p < .001$), visual affect recognition ($r = -.52$, $n = 117$, $p < .001$), and auditory-visual affect recognition ($r = -.48$, $n = 117$, $p < .001$) conditions. As a result, age was included as a covariate in the analysis. Results of the analysis (see table 5) indicate a main effect of BLERT condition, $F (3, 112) = 31.5$, $p < .001$, and of group, $F (3, 112) = 36.3$, $p < .001$, but no significant condition by group or condition by age interactions. Three follow-up univariate ANCOVA's with age as a covariate indicated significant group differences on the auditory affect recognition condition, $F (3, 112) = 23.1$, $p < .001$, visual affect recognition condition, $F (3, 112) = 20.1$, $p < .001$, and auditory-visual affect recognition condition, $F (3, 112) = 20.3$, $p < .001$. Planned comparisons indicated that on the auditory affect recognition condition, the SZ group performed worse than the BD+ group, $p < .001$, who in turn performed worse than the BD- group, $p = .03$. The BD- and NC groups did not differ from each other, $p = .51$. On the visual affect recognition condition, the SZ group performed worse than the BD+ group, $p < .001$. There were no differences between the BD+ and BD- groups, $p = .52$, or between the BD- and NC groups, $p = .16$. Results for the combined audio-visual affect recognition condition indicated that again the SZ group's performance was significantly worse compared to the BD+ group, $p < .001$. Similar to the visual-affect recognition condition, performance of the BD+ and BD- groups were not significantly different, $p = .24$, nor were the performances between the BD- and NC groups, $p = .31$.

Table 5.

One-way ANCOVAs of BLERT Performance by Group.

BLERT Condition	NC (n = 29)		BD- (n = 28)		BD+ (n = 30)		SZ (n = 50)		*F*	*p*	*Partial η2*	*Planned Comparisons*
	Mean	SE	Mean	SE	Mean	SE	Mean	SE				
Auditory	11.8	.46	11.3	.47	9.9	.48	7.4	.34	23.1	<.001	.38	SZ < BD+ < BD-, NC
Visual	16.6	.52	15.5	.56	15.0	.54	11.9	.39	20.1	<.001	.35	SZ < BD+, BD-, NC
Auditory-Visual	17.0	.55	16.1	.55	15.1	.57	12.1	.41	20.3	<.001	.35	SZ < BD+, BD-, NC

Note. NC = controls. BD- = bipolar disorder without psychosis. BD+ = bipolar disorder with psychosis. SZ = schizophrenia. a Mean refers to estimated marginal mean after controlling for age

Examination of the data (Figure 2) indicated that although not statistically significant, the

BD- group performed worse on the auditory affect, visual affect, and combined auditory-

visual affect recognition conditions relative to controls.

Figure 2.

Performance on BLERT task by Group.
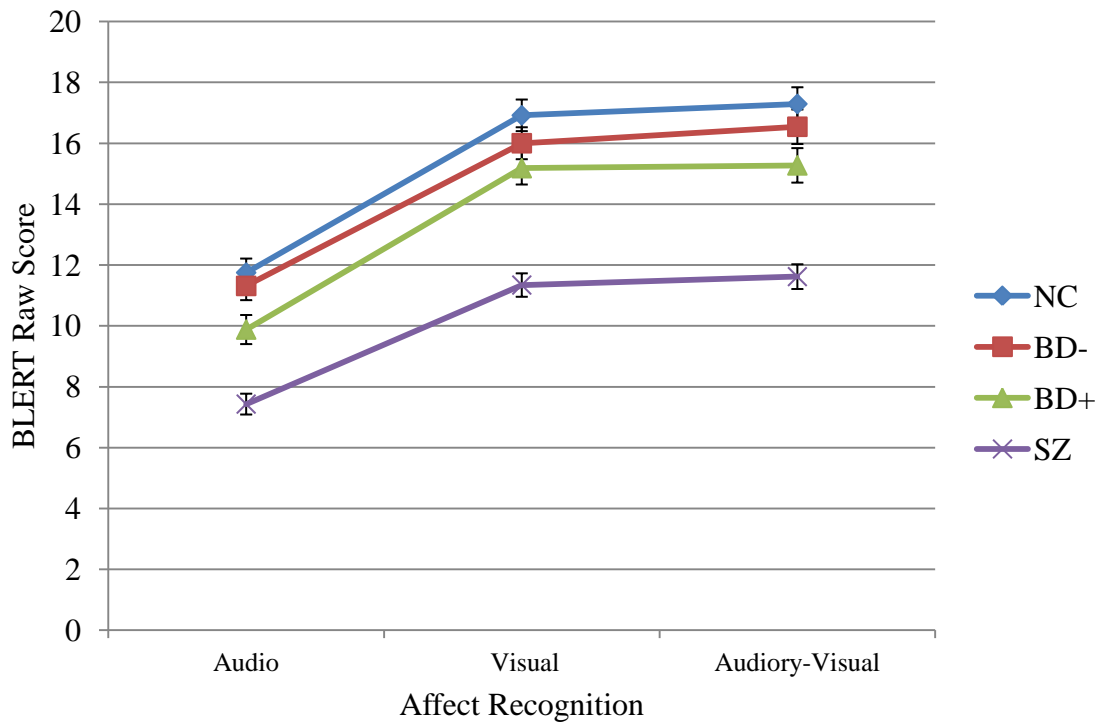
Note. NC = controls. BD- = bipolar disorder without psychosis. BD+ = bipolar disorder
with psychosis. SZ = schizophrenia. Auditory = auditory affect condition. Visual = visual
affect condition. Auditory-visual = auditory-visual affect condition. [a] Estimated marginal
mean after controlling for age.

Hypothesis 3: Relationship between tone discrimination and BLERT performance

Hypothesis 3 predicted that performance on the tone discrimination task would

predict performance on the auditory affect recognition and auditory-visual affect

recognition conditions of the BLERT, but would not predict performance on the visual

affect recognition condition. Before testing this hypothesis, we examined the relationship between d′ scores on the 5% frequency difference condition and d′ scores on the 20% frequency condition and found that they were significantly correlated ($r = .86$, $n = 117$, $p < .01$). Due to this violation of multicollinearity, we decided to run three simple regressions (see Table 6) with d′ score on the 5% frequency difference condition as a predictor variable. This condition was chosen as the predictor due to the fact that it was the harder task and it is where we saw group differences between the BD+ and BD- groups. Consistent with our hypothesis, results indicate that tone discrimination performance significantly predicted BLERT auditory affect recognition, $R^2 = .46$, $F(1,115) = 96.3$, $p < .001$, and BLERT auditory-visual affect recognition scores, $R^2 = .40$, $F(1,115) = 77.2$, $p < .001$. However, we also found that tone discrimination performance significantly predicted BLERT visual affect recognition, $R^2 = .33$, $F(1,115) = 55.5$, $p < .001$.

Table 6.

Regression of Tone Discrimination performance on BLERT performance

Condition	B	SE	B	F	P	R^2
Auditory	1.4	.14	.68	96.4	<.001	.46
Visual	1.4	.18	.57	55.5	<.001	.33
Auditory-Visual	1.5	.18	.63	77.2	<.001	.40

Note. Auditory = auditory affect condition. Visual = visual affect condition. Auditory-visual = auditory-visual affect condition.

Three moderated regressions (see Table 7) with diagnosis as a dichotomous moderator

(BD+, BD-) and tone discrimination as a predictor of BLERT auditory affect recognition,

visual affect recognition, and auditory-visual affect recognition were next examined.

Group membership (BD+, BD-) was not a significant moderator of the relationship

between tone discrimination performance and performance on the auditory affect

recognition (ΔR^2 = .002, b = .13, $t(42)$ = .31, p = .76), visual affect recognition (ΔR^2 =

.01, b = -.319, $t(42)$ = -.58, p = .56), or auditory-visual affect recognition (ΔR^2 = .10, b = -

.2.7, $t(42)$ = -.51, p = .61) conditions of the BLERT.

Table 7.

Moderated Regression of Tone Discrimination performance on BLERT performance

Model	Predictor	Auditory				Visual				Auditory-Visual			
		B	SE B	B	ΔR^2	B	SE	β	ΔR^2	B	SE	B	ΔR^2
1	d′	.48	.20	.33	.26	.12	.27	.07	.03	.54	.26	.31	.15
	Group	1.2	.56	.30		.72	.76	.15		.81	.73	.16	
2	d′	.42	.29	.29	002	.28	.39	.16	.01	.67	.37	.38	.01
	Group	.12	.27	.07		.91	.84	.20		.98	.80	.20	
	d′ x Group	.13	.41	.07		-.32	.55	-.14		-.27	.53	-.12	

Note Auditory = auditory affect condition. Visual = visual affect condition. Auditory-visual = auditory-visual affect condition.

A secondary analysis was conducted to examine the potential relationship

between auditory hallucinations in BD+ and performance on the tone discrimination task

and the BLERT. First, individuals with auditory hallucinations were identified from

SCID item B16 ("Did you ever hear things that other people couldn't, such as noises, or

the voices of people whispering or talking?"). Based on this rating, individuals with BD+

who had experienced an auditory hallucination at any time in their life (n=17) were

compared to individuals with BD+ who had never experienced an auditory hallucination

(n=13). Age, years of education, and estimated FISQ were compared between groups

using independent samples t-tests. No significant differences were found between groups

for age, t (28) = -.27, p = .79, education, t (28) = -.58, p = .57, or estimated FSIQ, t (28)

= -1.16, p = .26. Gender and ethnicity were compared between groups and no significant

ethnicity, X^2 (3) = 5.8, p = .12, differences were found. However, significant gender

differences were found, X^2 (1) = 4.5, p = .04, with 88% of the auditory hallucinations

group consisting of females and 54% of the no auditory hallucinations group consisting

of females. We examined the relationship between gender and tone discrimination and

found that the correlation was not significant in the 5% frequency difference condition,

r_{pb} = -.16, n = 30, p = .39 or in the 20% frequency difference condition, r_{pb} = -.33, n = 30,

p = .08. Independent Groups were compared on demographic variables related to clinical

course and current symptom ratings using an independent samples t-test. No significant

differences were found between groups for ratings on the HDRS, t (28) = 1.6, p = .12,

YMS, t (28) = .07, p = .94, SANS, t (28) = .15, p = .89, or SAPS, t (28) = .38, p = .71.

Additionally, no significant differences were found on the four factors of the SAP, which

include Hallucinations, $t(28) = 1.6$, $p = .12$, Delusions, $t(28) = .47$, $p = .65$, Bizarre

Behavior, $t(28) = -.05$, $p = .96$, and Thought Disorder, $t(28) = -.05$, $p = .96$. With

regards to medication, the only significant group difference was found on the percentage

prescribed benzodiazapines, $X^2(1) = 4.1$, $p = .04$, with no individuals in the auditory

hallucination group taking benzodiazepines and 23% of those in the no auditory

hallucination group taking benzodiazepines. We examined the relationship between

benzodiazepine use and tone discrimination and found that the correlation was not

significant in the 5% frequency difference condition, $r_{pb} = -.24$, $n = 29$, $p = .22$, or in the

20% frequency difference condition, $r_{pb} = -.24$, $n = 29$, $p = .22$. Independent samples t-

test indicated no differences between groups on the 5% frequency difference condition, t

$(28) = 1.7$, $p = .10$, or the 20% frequency difference condition, $t(28) = 1.3$, $p = .20$.

Contrary to our hypothesis, examination of the data indicated that those with auditory

hallucinations were doing better than those without auditory hallucinations, although this

difference was not significant. Approximately 73% of the BD+ group was administered

the BLERT. Examination of the relationship between gender and BLERT performance

found no significant correlations on the auditory affect recognition, $r_{pb} = .23$, $n = 22$, $p =$

.30, visual affect recognition, $r_{pb} = .18$, $n = 22$, $p = .44$, or audio-visual affect recognition,

$r_{pb} = .08$, $n = 22$, $p = .74$, conditions. Examination of the relationship between

benzodiazepine use and BLERT performance also revealed no significant correlations on

the auditory affect recognition, $r_{pb} = -.12$, $n = 22$, $p = .60$, visual affect recognition, $r_{pb} = -$

.36, $n = 22$, $p = .10$, or audio-visual affect recognition, $r_{pb} = -.41$, $n = 22$, $p = .06$,

conditions. Independent samples t-test indicated significant group differences on the

auditory affect recognition condition, $t(20) = 2.8$, $p = .01$. Again contrary to our

hypothesis, individuals with auditory hallucinations performed better than those without

auditory hallucinations. We did not find any significant group differences on the visual

affect recognition, $t(20) = .17$, $p = .87$, or auditory-visual affect recognition, $t(20) = 1.4$,

$p = .19$, conditions.

CHAPTER 5

DISCUSSION

The current study examined tone discrimination performance and performance on

an emotion recognition task (BLERT) in SZ, BD+, BD-, and NCs in order to extend

findings on auditory processing and social cognition in BD and to investigate the

potential role of psychosis in these areas. In the tone discrimination task, where

participants were asked to discriminate between tones that were 5% and 20% apart in

frequency, individuals with SZ performed worse than all other groups. The BD+ group

performed worse compared to the BD- and NC group on the more difficult frequency

condition (5% frequency difference), while there was no difference between the BD+ and

BD- groups on the easier condition (20% frequency difference). With regard to emotion

recognition, again individuals with SZ showed the most impairment on the auditory,

visual, and auditory-visual tasks. Individuals with BD+ only performed worse relative to

those with BD- on the auditory affect recognition, while this difference was not present

on the visual affect or auditory visual recognition tasks. Examination of the association

between basic auditory processing and affect recognition indicated that performance on

the more difficult condition of the tone discrimination task predicted performance on all

three conditions of the BLERT. A secondary analysis examining the relationship between

auditory hallucinations, basic auditory processing, and affect recognition indicated no

differences between those with and without a lifetime history of auditory hallucinations.

Our findings regarding tone discrimination performance replicate and provide

additional support for deficits in tone discrimination ability in SZ, indicating a deficit in

sensory memory in the disorder (Javitt et al., 1997; Javitt et al., 2009; Rabinowicz et al.,

2000; Strous et al., 1995) and suggesting abnormalities in the auditory cortex (Chao & Knight, 1995; Rabinowicz et al., 2000; Tramo, Shah, & Braida, 2002). The findings also suggest that individuals with BD who have a lifetime history of psychosis show a significant impairment in making fine discriminations between frequencies relative to those without a lifetime history of psychosis, who may have intact frequency discrimination ability. Prior research has typically examined frequency discrimination ability in BD using indirect electrophysiological measures, rather than behavioral measures (Umbricht et al., 2003). To our knowledge, there has only been one study that examined behavioral tone discrimination ability in BD, indicating that individuals with BD are impaired in their ability to discriminate tones of differing amplitudes and durations, but not in their ability to discriminate tones of differing frequencies (Van Rheenhan & Rossell, 2013). Findings of the current study are not in agreement. However, the BD sample used in the study by Van Rheenhan and colleagues (2013) was quite heterogeneous, as it included individuals with BD I and BD II who were euthymic or in hypomanic, depressed, or mixed mood states. Similar to the current study, they did not include individuals who were actively psychotic, but they also did not report on how many individuals in their sample had a lifetime history of psychosis. Interestingly, combining our BD+ and BD- groups into one BD group for analysis results in significantly better performance compared to the SZ group, with no differences between the BD and NC groups. Thus, this underscores the importance of examining the relationship between psychosis and basic auditory processing deficits in BD, as those with a history of psychosis appear to be differentiated from those without a history of psychosis and may more closely resemble performance of individuals with SZ.

Previous research indicates that impaired tone discrimination ability in SZ is associated with dysfunction at the level of the auditory cortex (Javitt et al., 2000; Rabinowicz et al., 2000; Tramo et al., 2002). Therefore, it may be that individuals with BD who have psychotic features also have dysfunction at the level of the auditory cortex. Of course, we cannot rule out the fact that individuals with BD+ may do worse than those with BD- for reasons different than dysfunction of the auditory cortex. For instance, those with BD+ have been found to have abnormalities in non-speech related areas relative to those without psychosis (Anticevic et al., 2013; Sarrazin et al., 2014) and typically have greater levels of neurocognitive impairment (Bora et al., 2010). However, there were no differences between estimated FSIQ between the two groups in our study. It may still be that a higher-order cognitive deficit is present in those with BD+ that is similar to those with SZ, but not shared with those with BD-, which may impact tone discrimination performance.

Our findings of impaired performance on the emotion recognition task is consistent with previous findings of deficits in emotion recognition in individuals with SZ (Kohler, Walker, Martin, Healey, & Moberg, 2010; Savla, Armstrong, Penn, & Twamley, 2013). Although average scores in the current study for the SZ group on all three conditions of the BLERT appear markedly low, it should be noted that performance in this group on all three conditions was still above chance level. Group differences on the auditory affect recognition task also replicated previous findings of impaired emotion recognition in the auditory domain in SZ (Leitman et al., 2005; Leitman et al., 2010; Gold et al., 2012) and extend these findings to those with BD+. There is little prior research on emotional prosody processing in BD, but our study adds to the findings that

individuals with BD do have difficulty recognizing emotion from speech (Bozikas et al., 2007; Rossell et al., 2013). Given that the ability to infer emotion from voice is important in everyday communication and has been associated with poor functional outcome in SZ (Lietman et al., 2010), our findings provide support for investigating this relationship in BD. Prior research has also indicated that severity of hallucinations in BD and SZ is related to deficient ability to recognize emotion from voice (Rossell et al., 2013). While we did not replicate this finding (discussed below), the finding that individuals with BD+ are more impaired than those without psychosis even when they are not actively psychotic indicates that underlying mechanisms may be present in those with SZ and with BD+.

With regards to visual affect recognition, we again replicated findings that individuals with SZ have decreased ability to recognize emotion from facial expression (Chan et al., 2010; Kohler, Walker, Martin, Healey & Mobert, 2010). Contrary to our hypothesis, while individuals with BD+ performed worse than NCs, the differences between BD+ and BD- were no longer significant. However, it should be pointed out that overall pattern of performance still held. Interestingly, lack of differences between the BD+ and BD- group appear to be due to the BD- group performing worse than NCs on the visual affect recognition condition compared to their performance on the auditory affect recognition condition. Studies investigating early visual processing in BD (Butler et al., 2009) and SZ (Maekawa et al., 2013) and have found that these individuals show impairments in processing basic visual features of the face, which may make it difficult for them to identify emotion from facial expressions. Based on findings of impaired basic auditory processing in SZ along with the findings of impaired basic visual processing in

SZ in their study, Butler et al. (2009) hypothesized that the combination of impaired visual and auditory information may be associated with social cognitive deficits in the disorder. If this account is correct, perhaps a similar relationship is present in BD+.

Again, individuals with SZ demonstrated the greatest impairment on the auditory-visual affect condition. We found a similar deficit in BD relative to controls, but did not see differences between the BD+ and BD- groups. Compared to research on emotion recognition in the auditory and visual domains separately, there has been much less research regarding auditory-visual integration of emotional information in BD and SZ. A prior study indicated that individuals with SZ have impairments in their ability to integrate emotion from voice and emotion from face (de Gelder, Croomen, Annen, Masthof, & Hodiamont, 2003), while another study found that individuals with SZ are better able to integrate auditory and visual information than healthy controls (Stone et al., 2011). To our knowledge, there are no studies examining integration of auditory and visual affect recognition in BD.

Regarding the associations between basic auditory processing and emotion recognition, we hypothesized the presence of a relationship between tone discrimination performance and the two conditions involving auditory affect recognition (auditory and auditory-visual), but we did not anticipate the presence of a relationship between tone discrimination performance and visual-affect recognition. It may be that individuals who have impaired basic auditory perception abilities also have impaired basic visual perception abilities. Leitman et al. (2005) also found evidence of impaired facial affect recognition in SZ, although these deficits were not related to auditory affect recognition ability. However, similar to the current study, they did not include a measure of basic

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visual processing ability (Leitman et al., 2005). Given that we did not administer a task of basic visual processing ability, we were also not able to investigate visual perception or its impact on visual affect recognition across the disorders. However, the relationship between frequency discrimination ability and auditory emotion recognition has been found previously in SZ (Leitman et al., 2005; Lietman et al., 2010; Gold et al., 2012), and the current study extends these findings to individuals with BD. However, we did not find any differences in this relationship between those with and without psychotic features, suggesting that this relationship may be present independent of psychosis.

Findings from our secondary analysis indicated no differences on tone discrimination performance between those with and without a history of auditory hallucinations in our BD+ group. However, we did find that those with auditory hallucinations showed better performance on auditory emotion recognition performance. These findings could be due to various reasons. . The novel finding in our study was that individuals with BD+ are more impaired on tone discrimination and recognition of auditory emotion compared to BD-. While the auditory cortex is thought to be implicated in auditory hallucinations, it may be that we see differences in BD+ compared to BD- due to deficits outside the auditory cortex. A study examining performance of individuals with BD+ and BD- on a wide neurocognitive battery found that the two groups were differentiated based on tasks that required frontally mediated executive processing, suggesting that psychosis may be related to prefrontal abnormalities (Glahn et al., 2007). Therefore, it is possible that the BD+ groups poorer performance is not associated with auditory hallucinations, but instead associated with impaired fronto-temporal processing, given that tone discrimination and MMN are also both thought to have frontal generators

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(Molholm, Martinez, Ritter, Javitt, & Fox, 2005; Baldeweg, Klugman, Gruzelier, & Hirsch, 2002). Our auditory hallucination group also largely consisted of females, while the non-hallucination group had approximately an equal number of males and females. Although the correlations between gender, tone discrimination, and emotion recognition were not significant in our sample, it is unclear how gender differences may have influenced our results. This is especially relevant given that recent studies present contradictory findings regarding gender, frequency discrimination, and auditory affect recognition, with some indicating a female disadvantage (Bozikas et al., 2007) and others indicating a female advantage (Van Rheenen & Rossell, 2013). Finally, given that this was a secondary analysis, we separated our groups according to their answer to item B16 on the SCID ("Did you ever hear things that other people couldn't, such as noises, or the voices of people whispering or talking?"). Therefore, individuals were placed into the auditory hallucination group if they had ever experienced an auditory hallucination during the course of their illness, independent of severity. Prior studies examining individuals with SZ with and without hallucinations have found that superior temporal gyrus volume is associated with severity of auditory hallucinations, with no differences between those who have a lifetime history of hallucinations versus those who do not (Modinos et al., 2013). Therefore, it may be that those who have more persistent or severe auditory hallucinations have greater dysfunction at the level of the auditory cortex, which could be related with impaired tone discrimination ability, although this remains to be seen. A study examining affective prosody in BD and SZ found that regardless of diagnosis, severity of auditory hallucinations was related to poorer performance (Rossell

et al., 2013). These findings indicate that future research examining the relationship between severity of auditory hallucinations across BD and SZ should be investigated.

There are a number of limitations to the current study. First, individuals in the SZ group were administered the tone discrimination task while wearing headphones, while individuals in the BD group did not wear headphones. Presumably this would have led to an advantage in the SZ group over the BD group. Given that we still found that individuals with SZ performed worse than those with BD on the tone discrimination task, we do not believe that this influenced our results. Our tone discrimination task was also limited to discriminating between tones of differing pitches, as we did not ask participants to discriminate between tones that varied according to other acoustic cues (e.g., duration, amplitude, intensity) which may have lead to a better characterization of auditory processing deficits in our sample. Additionally, the task appears to have been relatively easy for the NC and BD- groups, who may have been performing near ceiling levels. A more challenging task where individuals must discriminate between two tones that differ by even smaller frequency amounts may have led to better characterization of auditory processing deficits in our sample. We also did not include a measure of basic visual processing and therefore were unable to ascertain whether a deficit in basic visual processing may have been related to decreased performance on the visual-affect recognition condition or visual-auditory affect recognition condition in our emotion recognition paradigm. Additionally, a larger number of subjects in our BD+ with auditory hallucinations and BD+ without auditory hallucinations may have revealed significant differences between these two groups in our study. Due to the small number of individuals with SZ who did not have a history of auditory hallucinations, were also not

able to compare those with and without auditory hallucinations in SZ. Finally, there were age, education, and IQ differences present among groups. While it is expected that individuals with SZ would have lower IQ and fewer years of education, we did not use these as covariates in the analyses. However, this does raise the question as to whether the BD group was higher functioning than those with SZ. Additionally, we cannot rule out the effects of medication on performance, although many medications overlapped between our groups.

In summary, it appears that on tasks of basic auditory processing and auditory affect recognition, individuals with BD who also have psychotic features perform at a level that is intermediate between individuals with BD who do not have psychotic features and SZ. This provides further evidence that psychotic symptoms may provide a link between BD and SZ, pointing towards impairment in common neural systems and neurocognitive abilities across the disorders. Additionally, we found a relationship between frequency discrimination ability and auditory affect recognition, indicating that impairments in basic auditory processing may be associated with impairment in social cognitive functioning. Future research should continue to use behavioral measures of tone discrimination and affect recognition in BD, as current findings in this area are inconsistent. It would be beneficial for future studies to examine these areas in a group of individuals across disorders that can be well characterized according to the presence of psychotic symptoms and their severity. Additionally, further examination of the auditory cortex in BD with and without psychotic features may be warranted.

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CURRICULUM VITAE

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EDUCATION

University of Nevada, Las Vegas   Fall 2011–Present
Las Vegas, NV
Advisor: Daniel N. Allen, Ph.D.
Doctoral Student in APA-Accredited Clinical Psychology Program

Indiana University of Pennsylvania   Fall 2004–Fall 2008
Indiana, PA
Bachelor of Arts
GPA: 4.0
Major: Psychology   Minor: Criminology
    Honors Thesis: "An Examination of Pseudo-stalking in the Absence of Threat"
     Advisor: David LaPorte, Ph.D.

HONORS AND AWARDS

Patricia Sastaunak Scholarship   2013
University of Nevada, Las Vegas
Scholarship awarded for outstanding achievement in graduate school.

Stanley W. Lore Scholarship   2007
Indiana University of Pennsylvania
Scholarship awarded to the highest QPA for junior psychology majors and evidence of
outstanding academic work.

Honors Psychology Track   Fall 2006-Spring 2008
Indiana University of Pennsylvania
Admission to track focusing on independent research working closely with a faculty
member to develop an honors thesis.

Dean's List   Fall 2004-Fall 2008
Indiana University of Pennsylvania

<u>**Clinical Training**</u>

Center for Applied Neuroscience   June 2013-Present
Las Vegas, NV   Supervisor: Thomas F. Kinsora, Ph.D.

Doctoral Practicum Student: Responsible for conducting neuropsychological assessments with individuals ranging in age from 7 to 79 in an outpatient private practice setting. A flexible neuropsychological battery approach is used. Further responsibilities include scoring and interpretation, and partial report writing. Commonly presented patient diagnoses include dementia and cognitive disorders of varying etiologies, affective disorders, pervasive developmental disorders, learning disabilities, and TBI. Weekly individual supervision meetings are held. Also attend weekly practicum seminars on campus, which include didactics, group supervision and case conference components.

Partners for Research, Assessment, Counseling,   August 2012-Present
Therapy, and Innovative Clinical Education (PRACTICE)
University of Nevada, Las Vegas   Supervisor: Noelle Lefforge, Ph.D.

Doctoral Practicum Student: Provided supervised long-term individual therapy to a caseload of approximately 4-7 clients for 4-7 hours per week. Diagnoses seen included affective disorders, adjustment disorders, trauma, and severe mental illness diagnoses such as bipolar disorder and schizophrenia. Primary theoretical approach used was interpersonal. Supervision was comprised of weekly individual and small-group meetings. Also attended weekly practicum seminar on campus, which included didactic and group supervision components, as well as case conferences.

Psychological Assessment and Testing Clinic   August 2012–Present
University of Nevada, Las Vegas   Supervisor: Noelle Lefforge, Ph.D.

Doctoral Practicum Student: Responsible for conducting comprehensive neuropsychological and psychoeducational assessments for adult clients referred from the community and the University Disability Resource Center. A flexible neuropsychological battery approach is used, with commonly administered assessments including WJ-III ACH, WJ-III COG, WAIS-IV, WMS-IV, ASR, PAI, MMPI-2, and MCMI-III. Further responsibilities include scoring, interpretation, integrated report writing, and provision of feedback to clients.

Tests fluent in: Finger Tapping, Grip Strength, Grooved Pegboard, MMPI-2, PAI, MCMI-III, SCID-IV, Search Identification Task, Stroop Task, Trailmaking Test A & B, WAIS-III, WAIS-IV, Wisconsin Card Sorting Test (computer administration), Woodcock-Johnson III Tests of Achievement and Cognitive Abilities, TOVA, WMS-IV, Halstead Category Test.

The Collaborative IRB Training Initiative (CITI) Program   Fall 2012-Present
Certified to work with human participants through The Protection of Human Research Subjects online course, sponsored by The Collaborative IRB Training Initiative (CITI) Program. (http://www.citiprogram.org).

Graduate Research

Neuropsychology Research Program   August 2012–Present
University of Nevada, Las Vegas   Advisor: Daniel N. Allen, Ph.D.

Study: *Standardization of Wechsler Intelligence Scale for Children- Fifth Edition (WISC-V) and WISC-V Integrated (June 2012-present)*
Responsibilities included recruiting, screening, and assessing children with Traumatic Brain Injury, Intellectual Disability, and Attention Deficit Hyperactivity Disorder on a standardization version of the WISC-V and WISC-V Integrated in order to assist Pearson in establishing normative data.

Study: *Standardization of Halstead Category Test Computer Version (Fall 2011-Present)*
Responsibilities included assessment of individuals from UNLV Psychology subject pool in a 2-part neuropsychological battery. Assessments included Halstead Category Test (computer and original version), Stroop Task, Finger Tapping, Grip Strength, Grooved Pegboard, Trailmaking Test A & B, WAIS-III subtests, Wisconsin Card Sorting Test (computer administration), and TOVA.

Study: *Social cognition in individuals with schizophrenia and bipolar disorde*r *(Fall 2012-Present)*
Responsibilities included phone screening of potential participants, scheduling of participants, and training on test scoring and assessment procedures. Assessments included the SCID, quality of life self-report questionnaires, a semi-structured interview regarding and subsequent ratings of current psychiatric symptomatology, measures of verbal and nonverbal learning and memory, executive functioning and processing speed measures, and functional outcome measures.

Undergraduate Research

Clinical Cognitive Neuroscience Lab   December 2008-July 2011
University of Pittsburgh   Advisor: Raymond Cho, M.D., M.Sc.
Research Specialist: Conducted behavior, EEG, and fMRI experiments with healthy control subjects and clinical populations to study the mechanisms of cognitive control and their disturbances in psychiatric illness, including first-break medication naïve schizophrenia and bipolar disorder. Responsibilities included recruitment, phone screening, informed consent procedures, administering the SCID-IV, BPRS, SANS, SAPS, WASI, and MCCB, attending clinical rating rounds, implementing and organizing studies, processing and analyzing behavioral, EEG, and fMRI data, monitoring participants vitals, administering EKG's, centrifuging blood samples, keeping and organizing participant files in compliance with IRB regulation, and training of research assistants

Psychology Practicum   December 2008
Indiana University of Pennsylvania   Advisor: William Meil, Ph.D.
Assisted fellow student on honors thesis project investigating the effect of pre-exposure to cannabinoid agonist HU-210 during adolescence on behavioral sensitization to cocaine in rats. Responsibilities included administering rat injections and watching videotapes of behavior and reporting feedback.

Honors Psychology Thesis Research   Spring 2007-Spring 2008
Indiana University of Pennsylvania   Advisor: David LaPorte, Ph.D.
Responsibilities included attending IRB meetings, recruitment, preparing and administering questionnaires, consent forms, and debriefing forms, administering MMPI-2, conducting post-study interviews, analyzing results using SPSS statistical software, and writing up results to present to faculty.

PRESENTATIONS AND POSTERS

Presentations

Auditory perception deficits are present in patients   2012
with bipolar disorder with psychotic features. Presented at the Annual Conference of the National Academy of Neuropsychology, Nashville, TN, 2012.

An examination of pseudo-talking in the absence of threat.   2008
Presented at the Mid-America Undergraduate Psychology Research Conference (MAUPRC), Crestview Hills, KY, 2008.

An examination of pseudo-stalking in the absence of threat.   2008
Presented at the Undergraduate Scholars Forum, Indiana, PA, 2008.

Posters

Verbiest, R., Ringdahl, E.N., Thaler, N.S., Sutton, G.P., Vogel, S.J., Reyes, A. & Allen, D.N. Basic auditory perception deficits are related to impaired perception of sarcasm. Annual Conference of the National Academy of Neuropsychology, San Diego, CA.

Verbiest, R., Thaler, N., Snyder, J., Kinney, J., & Allen, D.N. (2012). Auditory perception deficits are present in patients with bipolar disorder with psychotic features. Annual Conference of the National Academy of Neuropsychology, Nashville, TN.

Verbiest, R., Thaler, N.S., Ringdahl, E.N., Vertinski, M., & Allen, D.N. (2012). Tone discrimination is uniquely linked to bipolar disorder with psychotic features. Annual Meeting of the American College of Professional Neuropsychology, Las Vegas, NV.

Verbiest, R., Thaler, N.S, Strauss, G.P., Allen, D.N. (2011) Slowed Processing Speed Influences Neurocognitive Impairments In Patients with Deficit Syndrome Schizophrenia. Annual Meeting of National Academy of Neuropsychology, Marco Island, FL.

Cho, R.Y., Walker, C., Verbiest, R., Frankle, W.G., Lewis, D.A. (2010). Effects of Dextro-amphetamine on cortical oscillations in schizophrenia vs. healthy control subjects. Annual Meeting of NCDEU, Boca Raton, FL.

Cho, R.Y., Walker, C., Verbiest, R., Frankle, W.G., Lewis, D.A. (2010). Differential Effects of Dextro-Amphetamine Administration In Schizophrenia Vs. Healthy Control Subjects. Annual Meeting of Society of Biological Psychiatry, New Orleans, LA.

Bangalore, S.S., Ramaswamy, R., Carter, C.S., Cohen, J., Cutler, V., Verbiest, R., Cho, R.Y. (2009). Selective DLPFC Deficits in Cognitive Control Network in Relatives of Individuals with Schizophrenia using a Functional Imaging Paradigm. Annual Meeting of Society of Biological Psychiatry, Vancouver, BC

SERVICE

National Academy of Neuropsychology
Student Volunteer at Annual Conferences   Fall 2011-Fall 2013
   NAN Annual Conference, San Diego, CA   October 2013
   NAN Annual Conference, Nashville, TN   November 2012
   NAN Annual Conference, Marco Island, FL   November 2011
Responsibilities: Aiding in registration procedures for attendees and checking attendees in and out of workshops to ensure continuing education credits.

PROFESSIONAL AFFILIATIONS

National Academy of Neuropsychology, Student Affiliate   Summer 2011-Present
American Psychological Association, Student Affiliate   Fall 2011-Present
Nevada Psychological Association, Student Affiliate   Fall 2012-Present

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OTHER RELEVANT WORK AND TRAINING EXPERIENCE

10-Day Comprehensive Training in Dialectical Behavior   Fall 2012-Summer 2013
Therapy
Las Vegas, NV
Alan Fruzzetti, Ph.D.

TBI, Amnesia, and Competency to Stand Trial   Spring 2012
Las Vegas, NV
Susan Hatters-Friedman, M.D., Renee Sorrentino, M.D., Rich Bissett, Ph.D., Steve
Zuchowski, M.D.

SCID Training Program   Spring 2012-Spring 2013
University of Nevada, Las Vegas   Training Supervisor: Daniel N. Allen, Ph.D.
Completed a training program for administration of the Structured Clinical Interview of
the DSM-IV-TR Axis I Disorders (SCID).   Training was comprised of a series of
workshops for a total of approximately 40 workshop hours. Training culminated in a
final mock interview conducted with an advanced graduate student trained in
administration in order to assess proficiency and endorsement to administer the SCID in
numerous studies being conducted within Dr. Allen's research lab, as well as other labs
within the UNLV Psychology Department.