Using Negative Feedback to Guide Behavior: Impairments on the Wisconsin Card Sorting Test Relates to Psychosis

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USING NEGATIVE FEEDBACK TO GUIDE BEHAVIOR: IMPAIRMENTS ON THE
WISCONSON CARD SORTING TEST RELATES TO PSYCHOSIS

By

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Bachelor of Arts in Psychology
University of Nevada, Las Vegas
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May 2012
Abstract

Using Negative Feedback to Guide Behavior: Impairments on the Wisconsin Card Sorting Test Relates to Psychosis

by

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There is increasing controversy regarding the distinction between schizophrenia and bipolar disorder as separate diagnostic categories because these disorders share many features in common. These and other findings suggest that bipolar disorder and schizophrenia may be better conceptualized along a continuum or within more homogeneous subsets of affective, psychotic, and mixed symptomatology.

Dopamine dysregulation has been found in schizophrenia and bipolar disorder, particularly those that experience psychosis during the acute phases of their bipolar illness. Dopamine has been found to play a role in reward and reward learning. Recently, research has found that individuals with schizophrenia experience deficits in reward learning, particularly negative feedback learning.

The current study examined accuracy on the first four cards of the Wisconsin Card Sorting Test as well as the use of negative and positive feedback on these initial trials in controls, bipolar with and without psychosis, and schizophrenia. Results indicate that controls and bipolar disorder without psychosis perform significantly better than the schizophrenia group with regard to ability to utilize feedback and learn the task. However, bipolar disorder with psychosis performed neither significantly better nor
worse than any other group on the first two cards analyzed, but by card 4 performed at the same level as the control and bipolar without psychosis groups, which was significantly better than the schizophrenia group. Analysis of the use of positive feedback found no difference among the groups in their ability to utilize positive feedback. Use of negative feedback, on the other hand, was significantly different among groups on cards 2 and 4. Post hoc analyses demonstrated that the SZ group performed significantly worse than the controls on both cards 2 and 4 and significantly worse than the bipolar without psychosis on card 2. No other significant differences were found among the groups on use of negative feedback. Results replicate those previously found with regard to individuals with schizophrenia’s impaired ability to effectively utilize feedback to learn a task. Contrary to expectations, this deficit was not found in individuals with bipolar disorder with psychosis. Results do not support the idea that those with psychosis experience the most severe deficits in reward learning. The pattern of findings in the bipolar with psychosis group may suggest that, although they are experiencing psychosis, the dopamine dysregulation is less severe thus reward learning is not being affected to the same degree.
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Chapter 1:

Introduction

Bipolar disorder and schizophrenia have many features in common with one another. Included in these shared features are symptom presentation, genetic overlap and neurocognitive deficits. Because they share numerous overlapping features, the categorical diagnoses have been called into question, with some suggesting that dimensional approaches might provide more meaningful conceptualizations of the disorders. In order to further evaluate this issue more research is needed to determine if affective disorders are better conceptualized along a continuum with psychosis or if they are indeed discrete diagnostic categories.

To further investigate these matters, the present study examined temporal difference error (TDE) reinforcement learning in patients with schizophrenia, bipolar disorder with and without psychotic features, and healthy controls. TDE reinforcement learning can be conceptualized as learning driven by the outcomes of actions. Outcomes that produce positive or better than expected outcomes result in positive TDE signals, which increase the probability of repeating the action. Outcomes that produce negative or worse than expected outcomes result in negative TDE signals, which decrease the likelihood of repeating the action. TDE learning is mediated primarily by circuits that are highly dopaminergic, including the mesocorticolimbic pathway. In schizophrenia, dysfunction of the mesolimbic and mesocorticial dopamine circuits are considered key in the neuropathophysiology. Related to this dysfunction are such symptoms as diminished executive function, auditory hallucinations, and the development of delusions. Dysfunction in dopamine circuits may also result in abnormalities in reward contingent
learning. Experimental paradigms designed to assess reward contingent learning have been localized to midbrain dopamine neurons that have also been found to be abnormal in patients with schizophrenia. Given that patients with bipolar disorder who experience hallucinations and/or delusions (BP+) as a part of their disease phenomenology also demonstrate neurocognitive deficits, and to some degree are distinct from those without psychotic symptoms who also have bipolar disorder (BP-), some reason exists to question whether reward learning is also impaired in these BP+ patients. The current investigation examined this issue using the Wisconsin Card Sorting Test, which has been recently applied to investigate reward contingent learning in patients with schizophrenia (Prentice, Gold, & Buchanan, 2008). It was hypothesized that those patients with bipolar disorder who also exhibit psychotic features as part of their symptomatology would also exhibit deficits in reward learning similar to those observed in schizophrenia, and in this way be distinguished from patients with bipolar disorder who do not have psychotic symptoms. Identification of such deficits may provide valuable insights into 1) key neural systems that differentiate BP+ and BP-, 2) help explain why BP+ patients have poorer outcomes than those with BP-, 3) provide information that may help clarify whether schizophrenia and bipolar disorder should be considered distinct or distributed along a continuum, and 4) may serve as endophenotypic marker for psychotic symptoms in bipolar disorder or psychosis in general.
Chapter 2:
Literature Review

Kraepelin Dichotomy

The current distinction between bipolar disorder and schizophrenia can be attributed to Emil Kraepelin (1919). He proposed the existence of two distinct disorders, dementia praecox and manic-depressive psychosis, known today as schizophrenia and bipolar disorder, respectively. Bipolar disorder and schizophrenia exhibit lifetime prevalence rates of roughly 1% each worldwide and both have strong genetic determinants. Bipolar disorder is characterized by periods of elevated, euphoric or irritable mood as well as periods of depression. Schizophrenia is characterized by positive symptoms, such as hallucinations and delusions, as well as disorganization symptoms and negative symptoms, such as blunted affect and anhedonia. While the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (APA, 2000) categorizes the two disorders as distinct, they share numerous overlapping features. Included in these overlapping features are symptoms, neuropsychological functioning, and genetic overlap. Kraeplin recognized some of these shared features but proposed their separation largely because it seemed as though schizophrenia was a more severe, pervasive disorder, while the impairments seen in bipolar disorder were largely episodic with inter-episode recovery of functioning. Further detail on these overlapping features and evidence counter to Kraeplin’s distinction between these disorders is provided below.

Disorder Overlap

Symptoms. Häfner and colleagues (2005) found that 83% of individuals on first admission to a hospital for schizophrenia had experienced a clinically significant
depressive episode. They also found that during their first psychotic episode 23% of individuals diagnosed with schizophrenia experienced a clinically significant depressive episode. Similarly, 20-50% of individuals with bipolar disorder experience psychosis during acute phases of mania and 58% of individuals with bipolar disorder will experience at least one psychotic symptom during a mood episode, more often manic, at some point during the course of their illness (Keck et al., 2003). Taken together, this indicates that the majority of individuals diagnosed with schizophrenia or bipolar disorder will experience episodes of psychosis and affective disturbance rather than only one or the other.

Neuropsychological functioning. Kraeplin’s distinction between bipolar disorder and schizophrenia was based at least in part by his observation that individuals with bipolar disorder did not appear to exhibit cognitive impairment outside of a mood episode (Bearden, 2001; Bora et al., 2008), while individuals with schizophrenia often had pervasive and severe cognitive impairment. However, since that time cognitive impairment has been documented in both the acute states of bipolar illness (Bora et al., 2007; Hoff, Shukla, Aronson, & Cook, 1990; Kurtz & Gerraty, 2009) as well as during euthymic states (Allen et al., 2010; Bora et al., 2007; Kurtz & Gerraty, 2009; Martínez-Arán et al., 2004). Impairments in attention, executive function, verbal and nonverbal learning and memory, and psychomotor speed have been documented during acute phases of illness (Martínez-Arán et al., 2004; Zubieta, Huguelet, O’Neil, & Giordani, 2001). With regard to euthymic states, neurocognitive impairments have also been found in working memory (Allen et al., 2010; Kurtz & Gerraty, 2009), verbal learning (Kurtz & Gerraty, 2009; Martínez-Arán et al., 2004), verbal and nonverbal memory, sustained
visual and auditory attention, response inhibition, and psychomotor speed (Bora, Yucel, & Pantelis, 2009; Kurtz & Gerraty, 2009). The most consistent finding in patients with bipolar disorder, regardless of illness state, has been deficits in executive functioning and verbal learning and memory (Bora, Yucel, & Pantelis, 2009; Kurtz & Gerraty, 2009; Martínez-Arán et al., 2004), and less consistently, attention (Bora et al, 2007).

Kraeplin’s observation that individuals with schizophrenia exhibit a number of neurocognitive impairments has also been established in numerous neurocognitive studies of the disorder, and much evidence also supports the presence of a generalized deficit and corresponding global brain dysfunction (Bilder, 2000; MacDonald & Shulz, 2009). Included in these deficits are verbal and non-verbal learning and memory, working memory, attention, and executive functioning deficits (Allen et al, 2010; Bilder, 2000; MacDonald & Shulz, 2009). Notably, individuals with schizophrenia do not typically demonstrate a declining course, with neurocognitive deficits growing more severe as time passes. Rather, it appears that cognitive decline in most individuals with schizophrenia progresses at a rate comparable to that seen in normal individuals, although those with schizophrenia exhibit poorer cognitive abilities overall (Goldstein, Allen & van Kammen, 1998)

Given the neurocognitive deficit similarities between schizophrenia and bipolar disorder, some research has examined bipolar disorder with psychosis, postulating that the presence of psychosis indicates a shared pathology characterized by both psychotic and affective symptoms. Thus, Kraepelin’s distinction between schizophrenia and bipolar disorder, that individuals with schizophrenia exhibit more severe impairment and course of illness, has also been questioned due to the large amount of symptom and
functional overlap between the two disorders, particularly within those cases where the diagnostic distinction is unclear (i.e. bipolar disorder with psychosis and schizoaffective disorder). Consistent with the idea of shared pathology, patients with bipolar disorder who also experience psychosis have a more severe course of illness, as well as more impaired functional outcome as opposed to those with bipolar disorder who do not exhibit psychotic features (APA, 1994; Bora et al., 2007). Additionally, while similar neurocognitive impairments have been reported in individuals with bipolar disorder with or without psychotic symptoms (Bora et al., 2007; Bora, Yucel, & Pantelis, 2010; Zubieta et al., 2001) these neurocognitive impairments appear to be more severe when psychotic features are present (Bora et al., 2007; Bora, Yucel, & Pantelis, 2010; Glahn et al., 2007; Levy & Weiss, 2009; Zubieta et al., 2001). More severe deficits have been reported in the areas of planning and reasoning, working memory, verbal memory, processing speed (Bora, Yucel, & Pantelis, 2010), verbal learning, executive functioning, and motor coordination (Glahn et al., 2007; Zubieta et al., 2001).

In sum, there is a large amount of overlap in the neurocognitive impairment seen in bipolar disorder and schizophrenia, with a similar but intermediate level of impairment found in those disorders that share multiple symptoms between the two (e.g. bipolar disorder with psychosis).

**Genetics.** Twin and adoption studies have found both schizophrenia and bipolar disorder to be highly heritable disorders (Cardno, 2002; Chen et al., 2009; Potash, 2006), with heritability estimates ranging between 50 and 75% for each disorder (Potash, 2006). In addition to twin and adoption studies, family studies have also suggested high heritability, with increased rates of schizophrenia in families of individuals with
schizophrenia and increased rates of bipolar disorder in families of individuals with bipolar disorder (Bora et al., 2008; Potash, 2006). In addition to increased prevalence of the same disorder and similar symptomatology in families of individuals with these disorders, increased rates of both psychotic and affective disorders and symptomatology have been found in families of both disorders (Bora et al., 2008; Potash, 2006). These results suggest not only a genetic component of schizophrenia and bipolar disorder but also a genetic linkage between the two disorders. Thus, gene variations have been examined in both groups (Bora et al., 2008; Chen et al., 2008; Goghari & Sponheim, 2008; Lin & Mitchell, 2008).

Overall, there is a large amount of evidence suggesting a link between bipolar disorder and schizophrenia, more so than the current categorical diagnostic classification system allows and Kraeplin’s dichotomy suggest. Clarification of this issue is important, as examining more homogeneous subsets of a disorder may help clarify functional, behavioral, and neurological discrepancies within the literature and aid in effective treatment strategies. In addition to neurocognitive deficits and potential shared genetic risk factors, dysfunction in similar brain regions and neurotransmitters have been implicated in the disorders and their symptom presentation. Dopamine dysregulation is a leading theory in the pathophysiology of schizophrenia and this concept has been extended to bipolar disorder, primarily those with psychotic features. This system and their behavioral implications are reviewed next.

**Dopamine and Rule-Guided Behavior**

The first evidence of dopamine’s role in schizophrenia was the realization that antipsychotic medications acted on dopamine systems, a theory confirmed by imaging
studies (Kapur, Mizrahi, & Li, 2005). Dopamine blocking medications, such as antipsychotics and catecholamine synthesis inhibitors, have also been found to be effective in the treatment of mania and psychosis in bipolar disorder (Cousins, 2009).

Four primary dopamine pathways exist in the brain (Hauber, 2010) and three of these are particularly relevant for schizophrenia and rule guided behavior. These pathways are the nigrostriatal, mesolimbic, and mesocortical pathways. All pathways share common features, routes, and interact, thus their anatomical and functional separation is an oversimplification (Hauber, 2010). In fact, the mesolimbic and mesocortical pathways are often referred to as the mesocorticolimbic pathway (Beaulieu & Gainetdinov, 2011). Due to overlap, separation of function of discrete pathways is difficult, but the mesocorticolimbic pathway has been implicated in reward learning based on immediate temporally located reward processing as well as long term reward processing contributing to motivation (Beaulieu & Gainetdinov, 2011; Hauber, 2010). The present study focuses on immediate reward learning driven by temporally located events in the environment and the connection found between dopamine fluctuations in response to these events, although dopamine is not directly measured.

Rewards can be defined as “objects or events that generate approach and consummatory behavior, produce learning of such behavior, represent positive outcomes of economic decisions and engage positive emotions and hedonic feelings” (Schultz, 2010; pg.1). Dopamine’s role in reward and the behavioral response following reward is strongly linked in empirical evidence and theories of substance abuse and dependence, lesioning studies, and psychopharmacological studies (Hauber, 2010; Schultz, 2010). Drugs of abuse have been found to alter the synthesis, release, and reuptake of dopamine.
and this is thought to be a primary mechanism that contributes to the pleasurable effects and continued use of these drugs. Further research into the role of dopamine and reward have implicated it in evaluation of novel reward, comparisons to already established predicted reward information, and learning and motivation in relation to reward prediction and response (Kapur, 2005; Schultz, 2007a, 2007b, 2010).

Temporal difference error reinforcement learning. Temporal difference error (TDE) reinforcement learning is learning driven by the outcomes of actions. When a behavior results in an outcome that is better than the outcome expected a positive TDE occurs, which increases the probability of repeating the action. When a behavior results in an outcome that is worse than expected a negative TDE occurs, which decreases the likelihood of repeating the action. Human and animal studies have found associations between the fluctuations of positive and negative TDEs and increases and decreases in dopamine (DA) cell activity (Schultz, 2002, 2007). This has also been found to be true specifically during learning tasks (Aron et al., 2004; Liu et al., 2007; Monchi et al., 2004, 2001; Ullsperger and von Cramon, 2003; Yacubian et al., 2006). This effect is thought to be occurring during probabilistic learning tasks. On these tasks, response options yield probabilities of being correct rather than any response being 100% correct or incorrect. Thus, someone must learn the responses that yield the highest probability of success through the accumulation of trial and error responses. Both individuals with schizophrenia and bipolar disorder have been found to exhibit impairments in probabilistic learning tasks, such that they appear unable to use trial-by-trial information and the accumulation of that information to guide behavior that will result in greater likelihood of reward (Pizzagalli et al., 2008; Weiler et al., 2009).
The Wisconsin Card Sorting Test is a type of reward measure used in both human and animal studies to evaluate the effective use of reward in order to respond appropriately and learn a task (Buckley, et al., 2009; Prentice et al., 2008). Examining the WCST on a trial-by-trial basis can provide a measure of one’s ability to respond appropriately following feedback thus can be conceptualized in the temporal difference error learning framework (Prentice et al., 2008). The earliest trials of this task in particular are useful for examining this as they are not preceded by any reinforcement and the distinction between the ability to use feedback to guide behavior and the ability to shift away from a previously reinforced response can be made (Prentice et al., 2008). Accuracy on initial trials following the completion of one or more categories requires not only the ability to respond appropriately to feedback but also the ability to shift away from a previously reinforced response (i.e. the previously completed category response set).

**Conclusion**

While the severity of deficits, functional outcome, and disease severity are generally greater in schizophrenia than bipolar disorder, it is clear that individuals with these disorders share many deficits in common. Given these similarities between schizophrenia and bipolar disorder, it may be beneficial to examine differences between these disorders in a new manner. There does not appear to be a clear distinction between the two disorders but examining their differences with regard to psychosis versus no psychosis may decrease the variability and highlight differences among the groups. Given the unique roles that reward learning deficits appear to play in schizophrenia, this neurocognitive domain was selected for examination in the current study. It would be
relevant to extend previous examinations of reward learning performance within schizophrenia to bipolar disorder with and without psychotic features, to determine whether these deficits are found in individuals that experience psychosis during the acute phases of their affective disorder. The Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993) has been used previously to examine reward learning in individuals with schizophrenia (Prentice, et al., 2008). This task requires subjects to discover, follow and switch rules for sorting cards into categories. Schizophrenia patients typically perform poorly on the WCST, completing fewer categories and having higher rates of perseverative errors. With regard to dopamine activity, the earliest trials of the WCST have been conceptualized within the framework of temporal difference error (TDE) reinforcement learning models (Montague et al., 2004; Prentice et al., 2008; Schultz, 2002). On the early trials of the WCST, the ability to learn from positive outcomes would be evident in repetition of a reinforced response, and the ability to learn from negative outcomes would be evident in the abandonment of previously unsuccessful responses in favor of new ones.

Given that psychosis in general is associated with both learning deficits and abnormal dopamine function (Kapur et al., 2005), WCST performance can be examined in relation to the TDE framework. Similar to Prentice, Gold, and Buchanan (2008), a novel approach to investigating WCST performance will be used in the current study by analyzing data from the first four WCST trials to examine whether patients with schizophrenia and bipolar disorder with psychosis have greater deficits than bipolar disorder patients without psychosis and controls in using rapid, trial-by-trial feedback to
guide behavior. Additionally, overall performance on the WCST will be compared across the four groups.

**Research Aims and Study Hypotheses**

Given the extensive overlap between bipolar disorder and schizophrenia, the question arises as to whether each disorder is in fact distinct. Furthermore, given that SZ and BP patients, particularly those with psychotic features, display both learning deficits and abnormal DA function (Kapur et al., 2005), the purpose of the present study is to examine whether WCST performance could be understood within the TDE framework in individuals with bipolar disorder with psychosis, as has been shown in schizophrenia (Prentice, Gold & Buchanan, 2008). If bipolar disorder and schizophrenia are better conceptualized as non distinct it is predicted that:

**Hypothesis 1.** An overall pattern of performance will be found, such that participants in the schizophrenia group will demonstrate the greatest impairment on the overall task as measured by categories completed and percent perseverative errors, followed by the bipolar disorder with psychosis, bipolar disorder without psychosis, and finally normal controls (SZ < BP+ < BP- < NC). Additionally, the same incremental pattern of task performance will be evident in two novel measures of task performance, the number of categories taken to complete categories one and two.

**Hypothesis 2.** On each trial participants in the schizophrenia group will have the lowest correct responses and exhibit the most gradual trial-by-trial correct response gain, suggesting the greatest impairment in learning the task. This effect is also hypothesized to exhibit an incremental performance gain by group, with the schizophrenia group
followed by the bipolar disorder with psychosis, then bipolar disorder without psychosis, and finally the healthy controls (SZ < BP+ < BP- < NC).

**Hypothesis 3.** Patients with psychosis’ poor WCST performance stems from compromised negative error signaling, which may be critical to the ability to shift away from non-rewarded behaviors (i.e., negative feedback) in favor of those more likely to be rewarded. Impairment should be evident on the initial WCST learning trials where errors cannot be due to a failure to abandon a previously rewarded response because subjects have not yet received positive feedback. So, while the traditional view of perseveration hinges on over-valuing positive feedback, we investigated whether the same behavior could reflect under-valuing of negative feedback. These deficits were expected to be greatest in schizophrenia patients and bipolar disorder patients with psychosis given evidence indicating that these patients have diminished dopamine activity and increased executive function impairments.

**Hypothesis 4.** Finally, spearman correlations were used in order to determine if a relationship exists between accuracy on these early trials and overall performance on the task. Prentice and colleagues, 2008 found that accuracy on these initial trials predicted overall task performance in schizophrenia and controls better than group membership. It was therefore expected that all four groups would exhibit significant correlations between initial trial accuracy and the task performance variables categories completed and percent perseverative errors. Additionally, correlations were conducted between the accuracy on the initial trials following the completion of one category and overall task measures to determine if performance on these cards which require a shift from a previously
reinforced response, predict overall task performance differently than accuracy on trials at the beginning of the task, which required initial learning of the task.
Chapter 3:

Method

Participants

Participants included 133 individuals assessed using a comprehensive neuropsychological battery over the past several years, beginning in 2007. Of the 133 participants, 58 individuals were diagnosed with bipolar disorder, of which 23 had a history of psychotic symptoms during manic and/or depressed episodes and 35 had no history of psychotic symptoms. Thirty-five individuals had a diagnosis of schizophrenia, and 40 participants had no Axis I diagnosis and served as psychologically and neurologically normal controls. The participants with schizophrenia and 17 healthy controls were assessed beginning in 2007 using a specific comprehensive neuropsychological battery. The participants with bipolar disorder and 23 healthy controls were assessed beginning in 2008 using a similar but slightly modified comprehensive neuropsychological battery. Thus, all participants in all groups do not have all symptoms ratings forms. Data on the scores of the symptom ratings forms are provided for those participants that had them. Participants ranged in age from 18 to 60 years. Individuals were selected for inclusion in the patient groups if they had been diagnosed with DSM-IV-TR (American Psychiatric Association, 2000) bipolar disorder or schizophrenia as identified by a treating psychiatrist or psychologist. Additionally, these clinical diagnoses were confirmed using the Structured Clinical Interview for DSM-IV-TR (SCID; First et al, 1995). The healthy control group consisted of individuals who had not been diagnosed with an Axis I psychiatric disorder or neurological condition,
which was also confirmed using the SCID. Exclusionary criteria for every group included:

- English as a second language;
- history of traumatic brain injury or any other medical condition or neurological disease/damage that could cause cognitive deficits;
- history of alcohol or substance abuse or dependence within the past six months;
- diagnosis of mental retardation or other cognitive dysfunction;
- current use of prescription or over-the-counter medications that could produce significant cognitive effects, other than those medications used to treat bipolar disorder or schizophrenia.

Participants were recruited from the University of Nevada, Las Vegas, community mental health centers, support groups, and the community at large. Participants recruited from the University of Nevada, Las Vegas were recruited through posted advertisements on campus and through the Psychology Department Subject Pool. Participants recruited from the community at large were also recruited through posted advertisements as well as various support groups within the community, such as the National Alliance for the Mentally Ill (NAMI) and the Depression and Bipolar Support Alliance of Southern Nevada (DBSA). Participants recruited from community mental health centers were recruited from Mojave Adult, Family, and Child Services, an affiliate of the University of Nevada, Reno medical school. Participants were compensated for participation. Subject pool participants received compensation in the form of partial fulfillment of their course requirements or extra credit points, equivalent to one credit hour for each hour of participation. All other participants received monetary compensation at a rate of $5/hour.
and a $30 bonus for completing the study with an approximate total of $60 per participant. Study procedures were approved by the IRB for protection of Human subjects.

**Measures**

Three domains were measured in the current study:

- clinical symptomatology,
- reward learning, and
- estimated premorbid intelligence.

Descriptions of the tests used to measure these domains are provided below. Client demographic and clinical information including medical, developmental, and family history was obtained from a demographic form.

**Clinical Symptom Measures.** The Structured Clinical Interview for DSM-IV-TR (SCID; First, Gibbon, Spitzer, & Williams, 1996) was used to verify DSM-IV-TR Axis-I diagnosis of bipolar disorder and schizophrenia and, in the case of bipolar disorder, to determine presence or absence of psychotic symptoms. The SCID was also used to verify absence of Axis I psychiatric disorders in the healthy control group. In order to measure current clinical symptomatology all participants were administered the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1963). Participants with bipolar disorder were also administered the Young Mania scale (YMS; Young, Biggs, Ziegler, & Meyer, 1978) and the Hamilton Depression Rating Scale (HDRE; Hamilton, 1960, 1967). Participants with schizophrenia were administered the Calgary Depression Scale for Schizophrenia (CDS; Addington, Addington, Maticka-Tyndale, Joyce, 1992), the Scale for the Assessment of Positive Symptoms (SAPS; Andreason, 1984) and the
Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983). The YMS and HDRS are included to assess manic and depressed symptoms, respectively. The SAPS, SANS, and BPRS are included to assess affective, anxiety, and positive and negative symptoms. The CDS is included to assess depression specific to individuals with schizophrenia. The healthy control group was administered the BPRS, YMS, and HDRS, or the BPRS, SANS, and SAPS depending on the study they participated in. Only the schizophrenia group was rated on the CDS.

**Structured Clinical Interview for the DSM-IV-TR.** The Structured Clinical Interview for DSM-IV-TR (SCID; First, et al., 1996) is a semi-structured interview designed to identify clinical symptoms and determine Axis-I psychiatric diagnoses.

As mentioned, the SCID was used to verify a diagnosis of bipolar disorder or schizophrenia, rule out the presence of several other conditions that exhibit similar symptoms, as well as confirm the lack of Axis I disorder in the healthy control group.

**Brief Psychiatric Rating Scale.** The Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1963) is an 18-item clinician administered rating scale designed to assess affective symptoms as well as symptoms of anxiety and positive and negative psychotic symptoms. Each item is rated on a scale from 1 to 7 (absent to extremely severe). The rating of each item is based on the individual’s subjective report over the previous week or behavioral observations made by the clinician during the time of the interview. Total scores are derived by summing the 18 items.

**Young Mania Rating Scale.** The Young Mania Scale (YMS; Young, Biggs, Ziegler, & Meyer, 1978) is an 11-item clinician administered rating scale designed to determine symptoms of mania. Seven of the items are rated on a 0 to 4 scale (absent to
overtly present), while four items receive double weighting and are rated from 0 to 8. The rating of each item is based on the individual’s subjective report over the previous week, as well as on the behavioral observations of the clinician during the time of the interview. A total score was derived by summing all 11 items.

**Hamilton Depression Rating Scale.** The Hamilton Depression Rating Scale (HDRS; Hamilton, 1960, 1967) is a 21-item clinician administered depression rating scale designed to evaluate depressive and comorbid anxiety symptoms. Each item is rated on a scale from either 0 to 4 or 0 to 2 (absent to severe). The rating of each item is based on the individual’s subjective report over the previous week, as well as on the behavioral observations of the clinician during the time of the interview. A total score was derived by summing all 21 items.

**Calgary Depression Scale for Schizophrenia.** The Calgary Depression Scale for Schizophrenia (CDS; Addington, Addington, Maticka-Tyndale, Joyce, 1992) is a nine-item clinician administered rating scale designed to assess symptoms thought to be sensitive to depression in individuals with schizophrenia. Items are rated on scale from 0 to 3 (absent to severe). The rating of each item is based on the individual’s subjective report over the previous week, as well as on the behavioral observations of the clinician during the time of the interview. A total score was derived by summing each of the nine items.

**Scale for the Assessment of Positive Symptoms.** The Scale for the Assessment of Positive Symptoms (SAPS; Andreason, 1984) is a 34-item clinician administered rating scale designed to assess positive psychotic symptoms. Positive symptoms include hallucinations, delusions, bizarre behavior, and positive formal thought disorder. Global
ratings are also evaluated and are used to represent overall severity within each of these four domains. Items are rated on a scale from 0 to 5 (absent to severe). The rating of each item is based on the individual’s subjective report over the previous week, as well as on the behavioral observations of the clinician during the time of the interview. A total score was derived by summing all 34 items.

**Scale for the Assessment of Negative Symptoms.** The Scale for the Assessment of Negative Symptoms (SANS; Andreason, 1983) is a 30-item clinician administered rating scale designed to assess negative psychotic symptoms. Negative symptoms can be conceptualized and are organized in this scale in 5 core domains: affective flattening, alogia, avolition, anhedonia, and attentional impairment. Global ratings are also evaluated and are used to represent overall severity within each of these five domains. Items are rated on a scale from 0 to 5 (absent to severe). The rating of each item is based on the individual’s subjective report over the previous week, as well as on the behavioral observations of the clinician during the time of the interview. A total score was derived by summing all 30 items.

**Reward Learning.** One measure of reward learning, the Wisconsin Card Sorting Test, will be used in the current study in the same manner it was used by Prentice and colleagues (2008) to examine reward learning in individuals with schizophrenia.

**Wisconsin Card Sorting Test.** The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948; Heaton, Chelune, Talley, Kay, & Curtiss, 1993) is traditionally used as a measure of executive functioning. For this measure, participants are asked to categorize a stack of test cards one at a time to one of four stimulus cards placed in front of them. The stimulus cards consist of a red triangle on the first card, two green stars on the
second, three yellow crosses on the third, and four blue circles on the fourth card. The test cards consist of different geometric forms, which have a different shape, number, and color. The subject is asked to sort one card at a time according to an underlying principle, which he or she must infer. The subject is given corrective feedback in the form of “correct” or “incorrect” with each attempt at sorting in order to deduce the sorting principle, but no further directions or prompts are given. The categorization rule shifts without warning after ten successful, consecutive responses, and the subject must then decipher the new sorting principle using examiner feedback. After an additional 10 correct, consecutive sorts, the sorting principle changes again without warning. This sequence continues until six categories are completed or all of the 128 cards are sorted. This test measures abstract concept formation and the ability to shift cognitive sets as feedback is given. It has been shown to be sensitive to dorsolateral prefrontal cortex dysfunction (Sullivan, Mathalon, Zipursky, Kersteen-Tucker, Kight, & Pfeerbaum, 1993). This study will examine the WCST in a novel manner, determining whether the chosen response for each participant was correct or incorrect on the first four trials. In addition, traditional variables of this task, specifically, the number of categories completed and the percent of perseverative errors will be evaluated with respect to the performance on the first four trials to determine if the first four trials relate to overall performance on the WCST. Finally, the number of cards sorted to complete the first category and the number of cards sorted to complete the second category will be examined.
Current Estimated Full Scale Intelligence. Two subtests from the WAIS-III (Wechsler, 1997a), Vocabulary and Block Design, will be used to calculate an estimated current full scale IQ.

WAIS-III Vocabulary Subtest. The Vocabulary subtest from the Wechsler Adult Intelligence Scale III (WAIS-III; Wechsler, 1997) consists of 33 items in which the participant is asked to define words of increasing difficulty. Total raw scores are converted to age-corrected scaled scores.

WAIS-III Block Design Subtest. The Block Design subtest from the WAIS-III (Wechsler, 1997) requires an individual to construct a series of 3-dimensional designs of increasing complexity based on an image in a stimulus book. Total raw scores are converted to age-corrected scaled scores.

Procedure

Individuals interested in participating in the study called a private study line located in the Neuropsychology research laboratory on the UNLV campus. Before answering any questions or providing any identifying information, participants were given a brief description of study procedures, including initial screening questions, and asked to provide verbal consent to be asked the initial telephone screening questions. Once verbal consent was obtained, participants answered questions during an initial telephone screening to determine the presence or absence of exclusionary criteria. Individuals that met initial selection criteria on phone screening were then scheduled to complete additional testing procedures at the UNLV Neuropsychology research laboratory. When participants arrived to the UNLV Neuropsychology research laboratory, written informed consent was obtained before any study procedures were
completed and subjects were given the opportunity to ask questions. Two consent forms were signed, one of which was given to the participant and one of which was kept in a locked filing cabinet in the Neuropsychology research laboratory at UNLV.

Once informed consent was reviewed and obtained, participants completed diagnostic and screening procedures. As part of these procedures, basic demographic information was collected, the SCID was administered to determine the presence or absence of Axis I psychiatric disorders, and current symptomatology was assessed. This took approximately three hours.

After screening procedures were complete and it was determined that a participant was eligible for the study, they were administered a battery of neurocognitive tests in a fixed order. The battery of tests lasted approximately 3 hours and included the WCST which provided the data for the current study. The interviews, questionnaires and neuropsychological tests used in this study were administered as part of a larger battery of tests. All testing was conducted by trained graduate students, and occurred in a quiet setting at the UNLV Neuropsychology research laboratory or at Mojave Mental Health Center. Participants were provided a lunch break when approximately half of the battery was complete or if requested sooner. Additional breaks were given as needed by participant request or when deemed appropriate by the examiner in order to control for fatigue effects.

**Data Analysis**

**Data screening.** Trained individuals scored all tests according to standardized procedures. Data was entered into a Microsoft Access database. Scoring and data entry was checked by visual inspection also by trained individuals. The WCST is computer
scored but values were visual inspected by a second individual to ensure accuracy. In addition to the standard scores typically used for interpretation of the WCST, the performance of each participant on each trial of the WCST were entered for the first four trials, such that a 0 indicates an incorrect response and a 1 indicates a correct response. This method allowed the examination of trial-by-trial performance and the frequency of correct and incorrect responses following negative and positive feedback.

**Preliminary analyses.** In order to determine whether the four groups significantly differ on age, education, and IQ a one-way ANOVA was used. Additionally, in order to determine whether the three clinical groups (bipolar disorder with and without psychosis and schizophrenia) significantly differ on clinical course of illness as measured by years since onset of illness and number of hospitalizations, a one-way ANOVA was conducted. Finally, differences among clinical groups on current symptoms and medications were examined, also using one-way ANOVAs and the lambda statistic, respectively. The lambda statistic is a form of contingency coefficient appropriate for examining the predictability of one item given the state of another item in binomial data. Because medication information is coded in terms of presence or absence, the lambda statistic was chosen to evaluate group differences. In the event of significant ANOVAs, Tukey-b post hoc comparisons were conducted.

**Main analyses.** Analyses of WCST data focused on trial-by-trial accuracy, accuracy following either positive or negative feedback, and the scores that are typically used to interpret performance across the entire WCST (e.g., categories completed and percent perseverative errors). Participant responses on cards 1–4 were coded with a score of 1 or 0 reflecting whether the response was correct or incorrect, respectively. Chi-
Square analyses were used to compare the four groups' accuracy on Cards 2–4, as well as the groups' accuracy on those cards following positive and negative feedback. Tukey's-q (Tukey’s wholly significant difference), was used as the post hoc analysis to examine group differences when overall significance was found. This statistic is a variant of the studentized range statistic such that the value of r, or the number of steps between ordered means is set to the maximum (4 in the case of these analyses) and fixes the familywise error rate of $\alpha$ against all possible null hypotheses (Howell, 2010). Finally, the relationship between accuracy on the first four trials and three of the full task's main outcome variables, specifically categories completed and percent perseverative errors, were investigated in order to determine if accuracy on these first trials is related to overall task performance.

**Hypothesis 1.** A one-way ANOVA will be used to investigate the differences between groups on categories completed and percent perseverative errors. In these analyses, the WCST scores will serve as the dependent variables, while group membership will be the between subjects variable. In the event of an overall significant F value, Tukey-b post hoc analyses will be used to examine group differences on the individual test scores. It is hypothesized that participants in the schizophrenia group will perform the worst, followed by bipolar disorder with psychosis, bipolar disorder without psychosis, and finally normal controls. These analyses extend the findings of Prentice et al. (2008) by including the bipolar groups with and without psychosis, to determine whether the deficits identified by Prentice et al. were associated with the presence of psychosis rather than a diagnosis of schizophrenia.
**Hypothesis 2.** To test hypothesis 2, a chi-square was used to investigate the four groups’ accuracy on WCST cards 2 through 4. In the event of significant findings, post hoc Tukey’s-q tests were used to examine the relationships found to be significant. It was hypothesized that on each trial, participants in the schizophrenia group will have the lowest correct responses and exhibit the most gradual trial-by-trial correct response gain, suggesting the greatest impairment in learning the task. This effect was also hypothesized to exhibit an incremental performance gain by group, with the schizophrenia group followed by the bipolar disorder with psychosis, then bipolar disorder without psychosis, and finally the healthy controls.

**Hypothesis 3.** Chi-squares were also used to examine the groups’ accuracy following negative and positive feedback on the preceding trial in order to further elucidate the occurrence and use of negative and positive feedback. Tukey’s-q post hoc tests were used to examine the relationships found to be significant. It was hypothesized that the schizophrenia group would exhibit the highest frequency of receiving negative feedback (caused by the highest prevalence of incorrect responses). In addition to receiving more negative feedback, they will have the lowest frequency of responding correctly following negative feedback but not exhibit significant impairment in adapting responses following positive feedback. These effects, similar to the previous hypotheses, will exhibit an incremental increase in performance and effective use of negative feedback with the schizophrenia group being followed by the bipolar disorder group with psychosis, then the bipolar disorder group without psychosis, and finally the healthy controls performing the best and most effectively utilizing negative feedback.
Hypothesis 4. Finally, spearman correlations were used in order to determine if a relationship exists between accuracy on these early trials and overall performance on the task. Prentice and colleagues, 2008 found that accuracy on these initial trials predicted overall task performance in schizophrenia and controls better than group membership. It was therefore expected that all four groups would exhibit significant correlations between initial trial accuracy and the task performance variables categories completed and percent perseverative errors. Additionally, correlations were conducted between the accuracy on the initial trials following the completion of one category and overall task measures to determine if performance on these cards which require a shift from a previously reinforced response, predict overall task performance differently than accuracy on trials at the beginning of the task, which required initial learning of the task.
Chapter 4:
Results

Preliminary Analyses

**Demographic Differences.** Preliminary analyses examining group differences on basic demographic variables and demographic variables related to clinical course of illness were conducted using a one-way ANOVA and lambda and can be found in Table 1. No significant differences were found among all groups for age, $F(3, 131) = 2.4, p > .05$, or among clinical groups in illness duration, $F(2, 90) = 2.16, p > .05$. Significant differences were found among all groups in education, $F(3, 131) = 8.3, p < .001$, IQ, $F(3, 131) = 31.0, p < .001$, and among clinical groups in number of hospitalizations, $F(2, 90) = 10.28, p < .01$. Tukey-b post hoc analyses indicated that the control and both bipolar disorder groups significantly differ from the schizophrenia group in years of education and IQ, such that the schizophrenia group had completed a significantly fewer number of years of education and has a significantly lower IQ than all other groups. Similarly, Tukey-b post hoc analyses indicate that both bipolar disorder groups significantly differ from the schizophrenia group in number of hospitalizations, such that the schizophrenia group has a higher number of hospitalizations than both bipolar disorder groups. No significant differences were found between groups in gender, $\lambda = 0.14, p = .05$, or ethnicity, $\lambda = 0.09, p > .05$.

**Current Symptoms.** Preliminary analyses examining group differences on current symptoms were conducted using a one-way ANOVA and can be found in Table 2. Approximately half of the control group was rated on the Hamilton Depression rating scale (HDRS) and the Young Mania rating scale (YMS; $n = 23$) along with both bipolar
disorder groups, while the remaining control participants \((n = 17)\) were rated on the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) along with the schizophrenia group. Thus, comparisons were made between symptom measures for the participants that were rated on them. Analyses indicate that significant differences exist between groups on the HDRS, \(F(2,78) = 13.48, p < .001\), and the YMS, \(F(2,78) = 12.90, p < .001\). Although all bipolar disorder participants were euthymic at the time of testing, Tukey-b post hoc comparisons show that both bipolar disorder groups were significantly different than the control group on both of these symptom measures such that the bipolar disorder groups were currently experiencing greater mania and depressive symptoms than the control group suggesting that even between active mood episodes individuals with bipolar disorder continue to experience some symptoms related to these states. Also, significant differences were present between groups on the SANS, \(F(1, 51) = 46.89, p < .001\), and the SAPS, \(F(1, 51) = 64.55, p < .001\). Inspection of raw data shows that the schizophrenia group had significantly more positive and negative symptoms than the control group. Only the schizophrenia group was rated on the Calgary Depression Scale, as this is a depression scale designed for rating depression specifically in schizophrenia, so these values are simply reported in Table 2 and no comparisons between groups were made. Data indicates minimal depressive symptoms in the schizophrenia group within two weeks of the time of testing.

The Brief Psychiatric Rating Scale (BPRS) was the only symptom measure that all participants in all groups received. Therefore, this is the measure that can provide the most direct comparisons of current symptom severity between clinical groups. One-way
ANOVA indicated that the groups significantly differ on BPRS total score, $F (3, 130) = 127.7, p < .001$. Tukey-b post hoc analyses indicate that the control group had significantly lower total scores than all clinical groups and both bipolar disorder groups had significantly lower total scores than the schizophrenia group. In addition to the total score, four factors previously identified within the BPRS (Mueser, Curran, & McHugo, 1997) were examined in order to evaluate group differences on symptoms in these domains. The four factors include:

- Thought disturbance, composed of items rating grandiosity, suspiciousness, hallucinatory behavior, and unusual thought content, resulting in a minimum score of 4 and a maximum score of 28.

- Anergia, composed of items rating emotional withdrawal, motor retardation, uncooperativeness, and blunted affect, resulting in a minimum score of 4 and a maximum of 28.

- Affect, composed of items rating somatic concern, anxiety, guilt feelings, depressive mood, and hostility, resulting in a minimum score of 5 and a maximum of 35.

- Disorganization, composed of items rating conceptual disorganization, tension, and mannerisms and posturing, resulting in a minimum score of 3 and a maximum of 21.

Significant differences were found among groups on thought disturbance, $F (3, 130) = 57.8, p < .001$, anergia, $F (3, 130) = 40.6, p < .001$, affect, $F (3, 130) = 18.2, p < .001$, and disorganization, $F (3, 130) = 33.4, p < .001$. Tukey-b post hoc analyses indicate that
for the factors thought disturbance, anergia, and disorganization the control and both bipolar disorder groups obtained significantly lower scores than the schizophrenia group, indicating they are experiencing less symptoms in these domains than the schizophrenia group. Tukey-b post hoc analyses indicate that, similar to BPRS total score, the control group has significantly lower affect scores than all clinical groups and both bipolar disorder groups have significantly lower affect scores than the schizophrenia group.

**Medication Differences.** The Lambda statistic was used to examine clinical group differences regarding medication status and type of medication and can be found in Table 3. With regard to medication status, 28.6% of the bipolar disorder without psychosis, 17.4% of the bipolar disorder with psychosis, and 2.9% of the schizophrenia groups were unmedicated at the time of testing. This was not a significant difference, $\lambda = 0.12, p = .24$. Similarly, no significant differences were found between clinical groups on the percentage prescribed antidepressants, $\lambda = 0.01, p = .87$, or mood stabilizers, $\lambda = 0.13, p = .18$. In contrast, significant differences were found between groups on the percentage prescribed any type of antipsychotic (typical or atypical), $\lambda = 0.42, p < .001$, as well as the percentage prescribed atypical, $\lambda = 0.41, p < .001$, and typical, $\lambda = 0.08, p < .05$, with the schizophrenia group being prescribed significantly more antipsychotics of either type than both bipolar disorder groups. In addition to primary drug class comparisons, participants were coded and compared on the number of drug classes they were currently prescribed based on antidepressants, mood stabilizers, and antipsychotics (both atypical and typical). Analyses indicate no significant differences between groups on the percentage receiving just one drug class, $\lambda = 0.06, p = .48$, two drug classes, $\lambda = 0.10, p = .31$, or all three drug classes, $\lambda = 0.07, p = .16$. 
Table 1. Demographic Information by Group.

<table>
<thead>
<tr>
<th>Group</th>
<th>NC (n = 40)</th>
<th>BP- (n = 35)</th>
<th>BP+ (n = 23)</th>
<th>SZ (n = 35)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age</td>
<td>34.1</td>
<td>11.6</td>
<td>32.6</td>
<td>12.9</td>
<td>36.7</td>
<td>13.7</td>
</tr>
<tr>
<td></td>
<td>39.7</td>
<td>10.5</td>
<td>2.4</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>13.8</td>
<td>1.5</td>
<td>14.2</td>
<td>2.3</td>
<td>14.4</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>12.2</td>
<td>1.8</td>
<td>8.3</td>
<td>&lt; .001**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IQ</td>
<td>101.2</td>
<td>13.2</td>
<td>103.7</td>
<td>14.8</td>
<td>106.5</td>
<td>10.3</td>
</tr>
<tr>
<td></td>
<td>79.5</td>
<td>11.4</td>
<td>31.0</td>
<td>&lt; .001**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Course</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>-</td>
<td>-</td>
<td>1.3</td>
<td>1.8</td>
<td>2.9</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6.4</td>
<td>7.1</td>
<td>10.3</td>
<td>&lt; .01**</td>
</tr>
<tr>
<td>Years since Onset</td>
<td>-</td>
<td>-</td>
<td>17.1</td>
<td>12.7</td>
<td>18.5</td>
<td>13.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>23.2</td>
<td>12.2</td>
<td>2.2</td>
<td>0.12</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>32.5</td>
<td>34.3</td>
<td>39.1</td>
<td>65.7</td>
<td>0.14</td>
<td>0.05</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>55</td>
<td>74.3</td>
<td>60.9</td>
<td>48.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.09</td>
<td>0.12</td>
</tr>
<tr>
<td>African American</td>
<td>15</td>
<td>5.7</td>
<td>4.3</td>
<td>34.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>7.5</td>
<td>0</td>
<td>8.7</td>
<td>5.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>22.5</td>
<td>20</td>
<td>26</td>
<td>11.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note. NC = normal control. BP- = bipolar disorder without psychotic features. BP+ = bipolar disorder with psychotic features. SZ = schizophrenia.*
Table 2. Current symptom information by group.

<table>
<thead>
<tr>
<th>Group</th>
<th>NC (n=40)</th>
<th>BP- (n=35)</th>
<th>BP+ (n=23)</th>
<th>SZ (n=35)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Current Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YMS (NC=23)</td>
<td>0.7</td>
<td>1.2</td>
<td>3.8</td>
<td>2.8</td>
<td>3.7</td>
<td>2.8</td>
</tr>
<tr>
<td>HDRS (NC=23)</td>
<td>1.8</td>
<td>2.1</td>
<td>7.0</td>
<td>5.4</td>
<td>8.1</td>
<td>4.6</td>
</tr>
<tr>
<td>CDS</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.3</td>
</tr>
<tr>
<td>SANS (NC=17)</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>50.6</td>
</tr>
<tr>
<td>SAPS (NC=17)</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>28.4</td>
</tr>
<tr>
<td>BPRS Total</td>
<td>19.1</td>
<td>1.8</td>
<td>24.8</td>
<td>4.3</td>
<td>25</td>
<td>3.5</td>
</tr>
<tr>
<td>Thought Disturbance</td>
<td>4.0</td>
<td>0.3</td>
<td>5.0</td>
<td>1.6</td>
<td>5.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Anergia</td>
<td>4.0</td>
<td>0.0</td>
<td>4.4</td>
<td>0.8</td>
<td>4.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Affect</td>
<td>5.9</td>
<td>1.4</td>
<td>9.7</td>
<td>3.1</td>
<td>9.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Disorganization</td>
<td>3.1</td>
<td>0.3</td>
<td>3.4</td>
<td>0.6</td>
<td>3.4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Note. NC = normal control. BP- = bipolar disorder without psychotic features. BP+ = bipolar disorder with psychotic features. SZ = schizophrenia. YMS = Young Mania Scale. HDRS = Hamilton Depression Rating Scale. CDS = Calgary Depression Scale. SANS = Schedule for the Assessment of Negative Symptoms. SAPS = Schedule for the Assessment of Positive Symptoms. BPRS = Brief Psychiatric Rating Scale.
Table 3. Medication information by group.

<table>
<thead>
<tr>
<th>Group</th>
<th>BP- (n=35)</th>
<th>BP+ (n=23)</th>
<th>SZ (n=35)</th>
<th>Lambda</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmedicated %</td>
<td>28.6</td>
<td>17.4</td>
<td>2.9</td>
<td>0.12</td>
<td>0.24</td>
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<tr>
<td>Antidepressants %</td>
<td>48.6</td>
<td>39.1</td>
<td>45.7</td>
<td>0.01</td>
<td>0.87</td>
</tr>
<tr>
<td>Mood Stabilizers %</td>
<td>40.0</td>
<td>78.3</td>
<td>57.1</td>
<td>0.13</td>
<td>0.18</td>
</tr>
<tr>
<td>Antipsychotics %</td>
<td>28.6</td>
<td>65.2</td>
<td>97.1</td>
<td>0.42</td>
<td>&lt; .001**</td>
</tr>
<tr>
<td>Atypical %</td>
<td>28.6</td>
<td>65.2</td>
<td>94.3</td>
<td>0.41</td>
<td>&lt; .001**</td>
</tr>
<tr>
<td>Typical %</td>
<td>0</td>
<td>0</td>
<td>14.3</td>
<td>0.08</td>
<td>&lt; .05*</td>
</tr>
<tr>
<td>Prescribed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Drug Class</td>
<td>34.3</td>
<td>8.7</td>
<td>20.0</td>
<td>0.06</td>
<td>0.48</td>
</tr>
<tr>
<td>2 Drug Classes</td>
<td>25.7</td>
<td>47.8</td>
<td>51.4</td>
<td>0.10</td>
<td>0.31</td>
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<td>3 Drug Classes</td>
<td>11.4</td>
<td>26.1</td>
<td>25.7</td>
<td>0.07</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Note. BP- = bipolar disorder without psychotic features. BP+ = bipolar disorder with psychotic features. SZ = schizophrenia.
Primary Analyses

Hypothesis 1: Overall task performance differences among groups.

Hypothesis 1 predicted that an incremental increase in overall task performance would be seen between groups, such that the schizophrenia group would perform the worst on the overall task as measured by categories completed and percent perseverative errors, followed by the bipolar disorder with psychosis group, bipolar disorder without psychosis, and controls. A one-way ANOVA was conducted in order to examine overall task performance differences on these variables. One-way ANOVAs (see Table 4) indicate significant main effects for percent perseverative errors, $F(3, 132) = 23.1, p < .001$, and categories completed, $F(3, 132) = 21.7, p < .001$. Tukey-b post hoc analyses indicate that the significant difference was between the schizophrenia group and all other groups for both overall task performance variables, such that the schizophrenia group completed fewer categories and had a higher percent of perseverative errors than all other groups. Inspection of raw data shows that the expected trend in performance is present among the groups, with the schizophrenia group performing the worst, followed by the bipolar disorder with psychosis, bipolar disorder without psychosis, and controls, although only significant for the schizophrenia group. Next, the number of cards required to complete the first and second categories were examined using one-way ANOVAs to examine group differences. Results indicated a significant effect among groups on cards to complete the first, $F(3, 132) = 15.2, p < .001$, and second, $F(3, 121) = 3.1, p < .05$, categories. Tukey-b post hoc analyses demonstrate a significant difference between the schizophrenia and all other groups on the number of cards required to complete the first category, such that the schizophrenia group required a larger number of
Table 4. One-way ANOVAs of task performance between each group.

<table>
<thead>
<tr>
<th>Group</th>
<th>NC (n = 40)</th>
<th>BP- (n = 35)</th>
<th>BP+ (n = 23)</th>
<th>SZ (n = 35)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>% Perseverative Errors</td>
<td>10.9</td>
<td>6.9</td>
<td>11.5</td>
<td>6.3</td>
<td>14.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Categories Completed</td>
<td>5.2</td>
<td>1.7</td>
<td>5.6</td>
<td>1.0</td>
<td>4.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Cards to Complete 1st Category</td>
<td>14.6</td>
<td>18.7</td>
<td>13.2</td>
<td>5.9</td>
<td>12.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Cards to Complete 2nd Category</td>
<td>25.5</td>
<td>26.4</td>
<td>23.6</td>
<td>14.4</td>
<td>32.6</td>
<td>34.0</td>
</tr>
</tbody>
</table>

Note. NC = controls. BP- = bipolar disorder without psychosis. BP+ = bipolar disorder with psychosis. SZ = schizophrenia. \textsuperscript{a}SZ n = 25 and NC n = 39 for cards to complete 2\textsuperscript{nd} category analyses, as participants that never completed one category could not be included.
cards to complete the first category than all other groups. While not statistically significant, inspection of raw data demonstrated a pattern opposite to what would be expected on this variable, such that the bipolar disorder with psychosis group required the fewest number of cards to complete the first category, followed by the bipolar disorder without psychosis, controls, and then schizophrenia. In contrast, Tukey-b post hoc analyses and inspection of raw data demonstrate the expected pattern of performance for the number of cards required to complete the second category, such that the schizophrenia group required the largest number of cards to complete this category, followed by the bipolar disorder with psychosis, bipolar disorder without, and then controls. Results suggest that once an initial category has been completed, the groups with psychosis (i.e. schizophrenia and bipolar +) have more trouble shifting responses and relearning the new category than those without psychosis.

**Hypothesis 2: Overall initial trials accuracy within and between groups.**

Hypothesis 2 predicted that the groups would exhibit an incremental pattern of performance on these initial trials, such that the schizophrenia group would have the lowest number correct on each of the initial trials and exhibit the lowest accuracy gain, suggesting the greatest impairment learning the task, followed by the bipolar disorder with psychosis, bipolar disorder without psychosis, and then controls. To test hypothesis 2, a chi-square test of independence was conducted in order to examine each groups’ accuracy on cards 1 through 4. Results indicate that there is a significant change in accuracy on cards 1 through 4 for the control, χ² (3, N = 40) = 66.88, p < .001, bipolar disorder without psychosis, χ² (3, N = 35) = 48.86, p < .001, bipolar disorder with psychosis, χ² (3, N = 23) = 24.58, p < .001, and schizophrenia, χ² (3, N = 35) = 18.67, p <
.001, groups. See Table 5 for these values. Inspection of figures and raw data demonstrates that each groups’ accuracy increases as they progress through the task. See Figure 1 for a graphic presentation of each groups increase in accuracy as they proceed through WCST trials.

A chi-square test of independence was conducted in order to examine the relationship among groups accuracy on cards 2-4. Card 1 was excluded from these analyses, as accuracy on this card reflects a random guess and is not representative of the study aim in examining accuracy following feedback. Results indicate that there is a significant difference among groups on card 2, $\chi^2(3, N = 133) = 11.6, p < .01$, card 3, $\chi^2(3, N = 133) = 16.8, p < .001$, and card 4, $\chi^2(3, N = 133) = 27.1, p < .001$. Tukey’s-q post hoc analyses examining group differences on each card indicated that the control and bipolar disorder without psychosis groups were significantly different than the schizophrenia group ($q$-stat = 3.73, $p < .05$ and 3.68, $p < .05$, respectively) on card 2. See Table 6 for chi-square and Tukey’s-q values for overall accuracy between groups. The bipolar disorder with psychosis group did not significantly differ from any other group. Similarly, on card 3 the control and bipolar disorder without psychosis groups significantly differed from the schizophrenia group ($q$-stat = 4.58, $p < .01$ and 3.94, $p < .05$, respectively) while the bipolar disorder with psychosis group did not significantly differ from any other group. No significant differences were found among the control or bipolar disorder groups. Finally, on card 4 the control, bipolar disorder without psychosis, and bipolar disorder with psychosis groups significantly differed from the schizophrenia group ($q$-stat = 6.42, $p < .001$, 4.40, $p < .02$, and 3.80, $p < .05$, respectively). The control and bipolar disorder with and without psychosis groups did
Figure 1. Accuracy on cards 1-4 by group.

not significantly differ from one another. Figure 1 represents each group’s accuracy on cards 1-4, although card 1 was not analyzed because it is a guess and thus does not represent a variable of interest on use of feedback to guide behavior, it is included in this graph for visualization purposes. As can be seen from Figure 1, each group increased in accuracy as they progressed through trials, suggesting overall learning of the task for each group. However, as depicted in the Figure as well as analyses there was an incremental decrease in overall accuracy and learning among groups. The control and bipolar disorder without psychosis groups performed the best, followed by the bipolar disorder with psychosis group, and finally with the schizophrenia group having achieved the lowest accuracy on cards 2-4. The bipolar disorder with psychosis group fell intermediate to the control and bipolar disorder without psychosis group on one end and the schizophrenia group on the other end for cards 2 and 3 but increased in overall
Table 5. Chi-square of accuracy on first 4 cards within each group.

<table>
<thead>
<tr>
<th>Group</th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>66.9</td>
<td>.001</td>
</tr>
<tr>
<td>BP-</td>
<td>48.9</td>
<td>.001</td>
</tr>
<tr>
<td>BP+</td>
<td>24.6</td>
<td>.001</td>
</tr>
<tr>
<td>SZ</td>
<td>18.7</td>
<td>.001</td>
</tr>
</tbody>
</table>
Table 6. Chi-square and Tukey’s-q of accuracy per trial among groups.

<table>
<thead>
<tr>
<th>Pairwise Comparison</th>
<th>Card 2</th>
<th>Card 3</th>
<th>Card 4</th>
<th>Card</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC vs BP-</td>
<td>0.52</td>
<td>1.24</td>
<td>2.91</td>
<td>2</td>
<td>11.60**</td>
</tr>
<tr>
<td>NC vs BP+</td>
<td>0.86</td>
<td>1.75</td>
<td>2.69</td>
<td>3</td>
<td>16.82**</td>
</tr>
<tr>
<td>NC vs SZ</td>
<td>3.73*</td>
<td>4.58**</td>
<td>6.42**</td>
<td>4</td>
<td>27.09**</td>
</tr>
<tr>
<td>BP- vs BP+</td>
<td>0.39</td>
<td>0.63</td>
<td>0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP- vs SZ</td>
<td>3.68*</td>
<td>3.94*</td>
<td>4.39*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP+ vs SZ</td>
<td>2.90</td>
<td>2.88</td>
<td>3.80*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* denotes significance at p < .05, ** denotes significance at p < .01
accuracy to more closely fit the control and bipolar disorder without psychosis groups than the schizophrenia group by card 4.

**Hypothesis 3: Initial trial accuracy following feedback.** A chi-square test of independence was conducted in order to examine the relationship among group accuracy on cards 2-4 after receiving positive feedback on the preceding trial (card – 1). Again, card 1 was excluded from analyses, as no feedback preceded it and thus cannot be examined with regard to use of feedback. Accuracy on card 1, however, was used in order to determine the proportion of each group having received positive (correct on card 1) and negative (incorrect on card 1) feedback. Those that sorted correctly on card 1 are included in these analyses for card 2. Results indicate no significant difference among groups on cards 2 ($\chi^2 (3, N = 20) = 4.29, p = .23$), 3 ($\chi^2 (3, N = 81) = 2.45, p = .48$), and 4 ($\chi^2 (3, N = 101) = 2.60, p = .46$). Figure 2 represents each groups’ accuracy on each card after having just received positive feedback on the preceding card. As you can see from Figure 2, the overall height of each groups’ bar is increasing as trials progress, demonstrating increased accuracy. This can also be seen from Table 5 demonstrating significance within each group among trials 1-4, as well as Figure 1. Also, as demonstrated by Figure 2, the ratio of accurate to inaccurate responses following positive feedback for each group on each card is large, indicating that each group is utilizing positive feedback effectively and continuing to sort correctly.

A chi-square test of independence was conducted in order to examine the relationship among groups accuracy on cards 2-4 after receiving negative feedback on the preceding trial (card – 1). Again, card 1 was excluded from analyses, as no feedback preceded it and thus cannot be examined with regard to use of feedback. Accuracy on
Figure 2. Accuracy when responding to positive feedback.

Note. Bars represent response accuracy on Card N having just received positive feedback for the response to the previous card. The percentage of participants within each group that received positive feedback on the preceding trial and then sorted correctly on the identified trial is written in each bar.

card 1, however, was used in order to determine the proportion of each group having received positive (correct on card 1) and negative (incorrect on card 1) feedback. Those that sorted incorrectly on card 1 are included in these analyses for card 2. Results indicate significant differences among groups on cards 2 ($\chi^2 (3, N = 113) = 15.5, p < .01$), and 4 ($\chi^2 (3, N = 32) = 9.54, p < .05$). No significant difference was found among groups.
Figure 3. Accuracy when responding to negative feedback.

Note. Bars represent response accuracy on Card N having just received positive feedback for the response to the previous card. The percentage of participants within each group that received negative feedback on the preceding trial and then sorted correctly on the identified trial is written in each bar.

Accuracy following negative feedback for card 3 ($\chi^2 (3, N = 52) = 6.37, p = .09$). Tukey’s-q post hoc analyses indicate that the control and bipolar disorder without psychosis groups both significantly differed from the schizophrenia group on card 2 accuracy following negative feedback (q-stat $= 4.50, p < .01$ and $3.92, p < .05$, respectively). Tukey’s-q also indicated that the control and schizophrenia groups
Table 7. Chi-square of accuracy following positive feedback per trial among groups.

<table>
<thead>
<tr>
<th>Card</th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4.29</td>
<td>0.23</td>
</tr>
<tr>
<td>3</td>
<td>2.45</td>
<td>0.48</td>
</tr>
<tr>
<td>4</td>
<td>2.60</td>
<td>0.46</td>
</tr>
</tbody>
</table>
Table 8. Chi-square and Tukey’s-q of accuracy following negative feedback per trial.

<table>
<thead>
<tr>
<th>Pairwise Comparison</th>
<th>Card 2</th>
<th>Card 4</th>
<th>Card</th>
<th>$\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC vs BP-</td>
<td>1.35</td>
<td>1.79</td>
<td>2</td>
<td>15.50**</td>
</tr>
<tr>
<td>NC vs BP+</td>
<td>1.51</td>
<td>1.99</td>
<td>3</td>
<td>6.37</td>
</tr>
<tr>
<td>NC vs SZ</td>
<td>4.50**</td>
<td>4.56**</td>
<td>4</td>
<td>9.54*</td>
</tr>
<tr>
<td>BP- vs BP+</td>
<td>0.35</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP- vs SZ</td>
<td>3.92*</td>
<td>2.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP+ vs SZ</td>
<td>3.02</td>
<td>1.94</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. * denotes significance at p < .05, ** denotes significance at p < .01
significantly differed from one another on card 4 accuracy following negative feedback. Figure 3 represents each group’s accuracy on each card after having just received negative feedback on the preceding card. As you can see from the Figure, the overall height of each group's bar is decreasing in size as trials progress, signifying that each group is decreasing in the number receiving negative feedback, thus demonstrating increased accuracy. Also, as demonstrated by Figure 3, the ratio of accurate to inaccurate responses following negative feedback for each group on each card is large, suggesting that all groups are utilizing negative feedback less effectively than positive feedback.

**Hypothesis 4: Initial trials accuracy and overall task performance.** Spearman correlations were conducted between accuracy on cards 2-4 and the overall task performance measures of percent perseverative errors and categories completed to determine if performance on these initial trials is related to overall task performance. Results can be found in Table 9. Results indicated that, when all participants are included, initial trial accuracy was significantly correlated with the percent of perseverative errors, $r = -.42, p < .001$, and number of categories completed, $r = .40, p < .001$, suggesting initial performance is related to overall task performance. Next, spearman correlations were conducted between these same variables but the groups were delineated into control and patient groups. Results indicated significant correlations between initial trial accuracy and percent perseverate errors, $r = -.48, p < .001$, and number of categories completed, $r = .43, p < .001$, for the schizophrenia group. Number of categories completed was also significantly correlated with initial trial accuracy, $r = .40, p < .05$, in the bipolar without psychosis group.
In order to determine whether the number of cards to complete the first category was a better predictor of overall task performance, spearman correlations were conducted among this variables and the overall task measures of percent perseverative errors and categories completed for the sample overall as well as the specific groups (see Table 9). Results indicated, similar to initial trial accuracy, number of cards to complete the first category was significantly correlated with percent perseverative errors, \( r = .40, p < .001 \), and categories completed, \( r = -.43, p < .001 \), for the overall sample. Within the groups, number of cards to complete the first category was significantly correlated with both the percent perseverative errors, \( r = .38, p < .05 \), and number of categories completed, \( r = -.70, p < .001 \), for the schizophrenia group. No significance was found between number of cards to complete the first category and overall task performance measures for the control or either bipolar disorder groups.

Finally, number of cards to complete the second category was correlated with overall task performance measures in order to determine if this is a better predictor of overall task performance. Prior research has shown that individuals with schizophrenia struggle shifting away from a previously reinforced response. Thus, this variable may be a better predictor of overall task performance than initial trial or category performance. Results indicate significant correlations between percent perseverative errors and categories completed for the overall sample, controls, and all three clinical groups.
Table 9. Spearman correlations among accuracy on initial trials and overall task measures.

<table>
<thead>
<tr>
<th>Group</th>
<th>% Perseverative Errors</th>
<th>Categories Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Cards 2-4</td>
<td>-.42**</td>
</tr>
<tr>
<td>NC</td>
<td>Cards 2-4</td>
<td>-.14</td>
</tr>
<tr>
<td>BP-</td>
<td>Cards 2-4</td>
<td>-.31</td>
</tr>
<tr>
<td>BP+</td>
<td>Cards 2-4</td>
<td>-.03</td>
</tr>
<tr>
<td>SZ</td>
<td>Cards 2-4</td>
<td>-.48**</td>
</tr>
</tbody>
</table>

*Note.* * denotes significance at \( p < .05 \), ** denotes significance at \( p < .01 \).
Table 10. Spearman correlations among cards to complete the first and second category and overall task measures.

<table>
<thead>
<tr>
<th>Group</th>
<th>% Perseverative Errors</th>
<th>Categories Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>.40**</td>
<td>-.43**</td>
</tr>
<tr>
<td>Category 2</td>
<td>.62**</td>
<td>-.65**</td>
</tr>
<tr>
<td>NC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>.16</td>
<td>-.23</td>
</tr>
<tr>
<td>Category 2</td>
<td>.42**</td>
<td>-.55**</td>
</tr>
<tr>
<td>BP-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>.24</td>
<td>-.32</td>
</tr>
<tr>
<td>Category 2</td>
<td>.57**</td>
<td>-.54**</td>
</tr>
<tr>
<td>BP+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>.06</td>
<td>.16</td>
</tr>
<tr>
<td>Category 2</td>
<td>.68**</td>
<td>-.75**</td>
</tr>
<tr>
<td>SZ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>.38*</td>
<td>-.70**</td>
</tr>
<tr>
<td>Category 2</td>
<td>.55**</td>
<td>-.58**</td>
</tr>
</tbody>
</table>

Note. * denotes significance at p< .05, ** denotes significance at p< .01. a indicates a lower n for these groups in these analyses, as some participants did not complete a category; NC n = 39, SZ n = 25.
Chapter 5:

Discussion

The present study examined accuracy on the first four cards and overall task performance of the Wisconsin Card Sorting Test (WCST) among controls (NC), bipolar disorder with (BP+) and without (BP-) psychosis, and schizophrenia (SZ) in order to extend previous finding with regard to the impact of psychosis on learning in response to positive and negative feedback of individuals with bipolar disorder. With regard to overall task performance, results indicated that the SZ group performed significantly worse than NC, as indicated by an increased number of perseverative errors and a decreased number of categories completed. Prior research has suggested that this deficit in related to structural and functional abnormalities in dorsolateral prefrontal cortex in patients with SZ (e.g., Weinberger et al., 1987), which is one of the key neuroanatomical regions identified in the disorder. Furthermore, examination of two novel variables, cards to complete the first category and cards to complete the second category, was accomplished. Number of cards to complete the second category was used as an indicator of the efficiency with which participants were able to shift away from the initial category to the new category. Again, the only significant difference was identified for the SZ group who took longer to solve both the first and second categories. Results from the first card suggest that concept formation is impaired in SZ and, as will be discussed later, that these patients have greater difficulty using negative feedback to modify responses than the other groups. Poorer performance on the second category also indicate impaired learning and concept formation, but additionally suggests that individuals with SZ have greater difficulty shifting way from the previously established
problem solving strategy in order to develop a new strategy. While not significantly
different from the NC and BP- groups, the BP+ group performed more poorly than these
two groups, but only on the cards to complete the second category. Since significant
differences were not present, firm conclusions cannot be drawn from these data, but it
may be that a larger sample size would have increased power so that differences may
have been significant. In any case, the performance of the BP+ group was consistent
with the hypothesis. These results suggest that psychosis may have a role in ones’ ability
to shift from previously rewarded behaviors in order to learn a new response, more than
ones’ ability to initially learn a task. With regard to differences on ability to complete the
initial trial, research suggests this initial learning is related to negative symptoms of
schizophrenia (Barney, et al., unpublished manuscript), rather than the positive symptoms
more commonly seen in bipolar disorder.

Also consistent with prior studies were the findings of associations between
performance on the first four WCST cards and overall performance on the test. Prentice
and colleagues (2008) found significant correlations between performance on cards 2-4
and overall task performance as indicated by categories completed and percent
perseverative error scores. Similar finding were noted here for the SZ and the BP-
groups, as well as when the total sample was examined, suggesting that performance on
the first four cards was predictive of overall test performance. Theses associations were
not found in our control group, although they were in the Prentice study. The reason for
this is unclear, but comparison of mean scores between study groups suggest that our NC
group performed somewhat better than theirs on cards 2-4, which may have caused
ceiling effects in our sample and attenuated the correlations. For the BP+ group,
correlations were also nonsignificant. Examination of scatter plots suggested that the slope of the regression line was consistent across groups, although the small number of cases in the BP+ groups combined with greater variability in performance as subjects moved from one card to three cards correct may have attenuated the correlations for that group. Similarly, in comparison to the Prentice study, results among the SZ and NC samples were remarkably similar. For example, the SZ groups from both studies score approximately .38 correct on card 2, increasing to approximately .60 correct on card 4. The NC in this study performed somewhat better than those studied by Prentice et al., but demonstrated comparable learning curves. Finally, when comparisons were made between the influence of positive versus negative feedback on the accuracy of responses to cards 2 – 4, like Prentice, the current results suggest that individuals with schizophrenia have more difficulty using negative feedback to modify responses, as the number of correct responses following negative feedback was significantly lower for the schizophrenia group, although no such differences were present in response to positive feedback supporting the concept that they under-value negative feedback. Thus, there is robust evidence suggesting that patients with schizophrenia have difficulty initially establishing a problem solving strategy when faced with a novel task, and that this difficulty may arise to a large extent from difficulties using negative feedback to correct inappropriate responding. The ability to benefit from negative feedback has been associated with dysfunction of the negative temporal difference error signaling system.

In considering the bipolar groups with psychosis (BP+) and without psychosis (BP-), examination of differences among the groups on the number of errors made on cards 2, 3, and 4 indicate that the NC and BP- groups were significantly more accurate on
these three cards than the SZ group. Also, the BP+ group was significantly more accurate than the schizophrenia group on card 4. Results suggest that the NC and BP- groups are performing at similar levels and achieving comparable accuracy on these first trials. While the absence of significant differences between the BP+ and BP- groups do not support the hypothesis, the BP+ group appears to be performing at an intermediate level to the other groups, performing slightly but not significantly worse than the NC and BP- groups and slightly but not significantly better than the SZ group. However, on card 4 the BP+ group becomes significantly more accurate than the SZ group and performs similarly to the NC and BP- groups. These findings suggest that the presence of psychosis in bipolar disorder impacts strategy acquisition at very early stages but do not have as substantive effects on strategy acquisition and problem solving as is seen in schizophrenia. Although there is tentative evidence for a small to moderate effect in this regard, which may indeed become significant with a larger sample size and the associated increase in statistical power.

In addition to overall accuracy on these initial trials, accuracy among bipolar groups following positive and negative feedback was examined in order to determine group differences on use of positive and negative feedback. With regard to accuracy following positive feedback, no significant difference was found among any of the groups, including the bipolar groups, suggesting each group is performing similarly with regard to use of positive feedback. Data and Figure inspection demonstrate that as the task progresses, each group increases in the number receiving positive feedback, representing increased accuracy on the task. This increased accuracy was also examined using chi-square analyses on card 1 through 4 within each group. Each group was found
to have a significant increase in accuracy from trials 1 through 4. Additionally, as represented by Figure 2, the large ratio of correct to incorrect sorts for each group following positive feedback demonstrates that each group is effectively utilizing positive feedback and continuing to sort correctly to the proceeding trial once the correct sorting principle is determined. With regard to accuracy following negative feedback on the initial trials, significant differences were found among groups on cards 2 and 4, but not 3. The control group performed significantly better than the schizophrenia group on both of these cards, while the bipolar without psychosis performed significantly better than the schizophrenia group on card 2. The bipolar with psychosis was not significantly different than any group on these cards. Inspection of raw data (and as demonstrated by Figure 3) the groups are all decreasing in the amount of negative feedback received as trials progress, suggesting increased accuracy. With regard to appropriate use of negative feedback, an incremental pattern of performance is evident with the largest proportion of schizophrenia group continuing to sort incorrectly, followed by the bipolar with psychosis, bipolar without, and controls.

Next, the relationship between the number of cards to complete the first category and overall task performance measures was evaluated. Results indicate that number of cards to complete the first category was related to the number of categories completed for only the schizophrenia group. No other relationship within groups was found between these variables. Finally, the relationship between number of cards to complete the second category and overall task performance was evaluated. Number of cards to complete the second category was predictive of overall task performance in the control and both bipolar groups, but not the schizophrenia group. A contributing factor to lack of
significance for the schizophrenia group may be that participants unable to complete a single category had to be removed from these analyses, resulting in an exclusion of 10 participants from the schizophrenia group and removing those that are performing the poorest on this measure. Those that are unable to complete a single category may be qualitatively different than those that are able to learn the task to at least a small degree. Future research examining differences between those that are able to learn the task and those that are not could provide important information. Failure to maintain set was correlated with cards to complete second category in the overall sample and the bipolar without psychosis group. This was the only variable to show a relationship with failure to maintain set for any group, suggesting it may be a good measure of ones’ ability to shift set and may be predictive of overall task performance.

Given the significant overlap of drug classes prescribed both within and between clinical groups, analyses examining the effect of specific drug classes on WCST performance were unable to be conducted. However, the only significant difference in the percent of a drug class prescribed among groups was for antipsychotics, with the schizophrenia group having the largest percentage of participants taking antipsychotics. Prior research has suggested that antipsychotics would improve performance on reward learning (Kapur, Mizrahi, & Li, 2005), thus the larger percentage of antipsychotics prescribed to the schizophrenia group may not be accounting for the poor performance seen in this study.

There are a number of limitations to this study that may have affected the results. First, while the size of the groups was adequate to detect medium to large effects, the decreased number of subjects in the bipolar with psychosis group may have precluded
detection of significant group differences. Larger sample of bipolar with psychosis would help address this limitation and may reveal the pattern of significant findings hypothesized in this study. Also, there are significant differences between patient groups on an illness severity measure, number of hospitalizations, as well as years of education and IQ. Additionally, many of the bipolar participants were recruited from colleges and universities, as were the control participants, while all schizophrenia participants were recruited from an outpatient treatment facility, suggesting that the bipolar group is higher functioning. While it is expected that individuals with schizophrenia would have lower IQ and fewer years of education than controls or patients with bipolar disorder, these factors nonetheless resulted in clinical groups differing in illness severity and functional impairment, which may have contributed to the small difference found in the bipolar and control groups. Recruiting from additional locations would have been beneficial. Also, by card 4 the control group was performing at 100% accuracy, suggesting a possible ceiling effect for the control group, possibly precluding performance differences between the control and bipolar disorder groups. Finally, while the Wisconsin Card Sorting test has been used in human and animal studies examining reward learning, perhaps examining the relationship among these groups with an additional measure of reward learning would have been beneficial to supplement these results.

In summary, consistent with prior research, the bipolar disorder with psychosis group is performing at an intermediate level between the bipolar disorder without psychosis and schizophrenia groups. Additionally, when the bipolar disorders with and without psychosis groups are separated, the bipolar disorder without psychosis is performing at a similar level to the controls. Much of the data in the present study
demonstrates the expected incremental pattern of performance from controls to bipolar disorder without psychosis, bipolar disorder with psychosis, and schizophrenia, however many of these differences were not significant. Future research using reward measures, higher number of subjects, comparable clinical groups in terms of education, illness severity, and functioning, as well as functional measures of mesolimbic and mesocortical dopamine circuitry would be warranted.
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associated with different neurobiological markers? Acta


A meta-analysis of neuropsychological deficits in euthymic patients and their
doi:10.1016/j.jad.2008.06.009

Bora, E., Yücel, M., & Pantelis, C. (2010). Neurocognitive markers of psychosis in
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Curriculum Vitae

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EDUCATION

University of Nevada, Las Vegas
Las Vegas, NV
Advisor: Daniel N. Allen, Ph.D.
Doctoral Student in APA-Accredited Clinical Psychology Program
Ph.D. Candidate for December 2014 graduation
Dissertation: “Deconstructing Psychosis and Reward: The Differential Role of
Positive versus Negative Symptoms”
Proposal preparation in progress

Master of Arts in Clinical Psychology
Las Vegas, NV
Cards of the Wisconsin Card Sorting Relates to Psychosis”
Passed oral defense December 2011

University of Nevada, Las Vegas
Las Vegas, NV
Bachelor of Arts
Major: Psychology
Honors Thesis: “Neurocognitive Deficits in Bipolar Disorder with Co-Occurring
Borderline Symptomatology”
Advisor: Daniel N. Allen, Ph.D.

HONORS AND AWARDS

Graduate & Professional Student Association travel funding to attend and present at the
National Academy of Neuropsychology annual convention in Marco Island, FL
($500) 2011

Patricia Sastaunak Scholarship, Awarded for Outstanding Achievement in Graduate
School, University of Nevada, Las Vegas ($2500) 2011

Edward Lovinger Psychology Scholarship, Awarded for Outstanding Achievement in
Graduate School, University of Nevada, Las Vegas ($2000) 2010

Department Honors 2009

Student grant through CSUN for Dr. Philip Zimbardo to give a presentation at the
University of Nevada, Las Vegas 2009
Psi Chi Travel Grant to attend the American Psychological Association 116th annual convention in Boston, MA ($1800) 2008

Second Place Poster Award, Psi Chi National Honor Society Annual Conference, Las Vegas, Nevada ($75) 2006

John P. & Mary V. Hughes Valedictorian Scholarship, Awarded to Nevada Valedictorians, University of Nevada, Las Vegas ($10,000) 2004

Provost Scholarship, for Excellence in Scholastic Achievement, Nevada Board of Regents, University of Nevada, Las Vegas ($12,000) 2004

Governor Guinn Millennium Scholarship, for Nevada High School Graduates Demonstrating Excellence in Scholastic Achievement ($10,000) 2004

Dean’s List 2004–2009

GRANTS

National Science Foundation-EPSCoR Undergraduate Research Award 2007-2008
University of Nevada, Las Vegas Research Funding ($4,310)

CLINICAL EXPERIENCE

Center for Applied Neuroscience June 2011–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 and group supervision meetings are held. Also attend weekly practicum seminars on campus, which include didactics, group supervision and case conference components.

Center for Individual, Couple, and Family Counseling (CICFC) Aug 2010–Aug 2011
University of Nevada, Las Vegas Supervisor: Christopher A. Kearney, Ph.D.
Doctoral Practicum Student: Provided long-term individual therapy to a caseload of approximately 7-10 clients for 6-10 hours per week. Diagnoses seen included personality disorders, affective disorders, anxiety disorders and adjustment disorders. Primary theoretical approach used was CBT culminating in three months of a more Interpersonal approach. Supervision consisted of weekly individual and group meetings as well as weekly practicum seminars, which included didactics, group supervision, and case conference components.

Psychological Testing Clinic August 2010–September 2011
University of Nevada, Las Vegas Supervisor: Michelle G. Carro, Ph.D.
Doctoral Practicum Student: Responsible for conducting comprehensive neuropsychological and psychoeducational assessments for adult and child clients referred from the community and the University Disability Resource Center. A flexible
A neuropsychological battery approach was used. Further responsibilities include scoring, interpretation, integrated report writing, and provision of feedback to clients. Supervision included reviewing cases, joint determination of assessment battery, report revisions, and discussion of feedback.

PUBLICATIONS AND PRESENTATIONS

Manuscripts submitted


Refereed Articles Published or In Press


Presentations and Published Abstracts

* Denotes presentation has a corresponding published abstract, reference follows entry.


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**RESEARCH EXPERIENCE**

**Graduate Research**

**Neuropsychology Research Program**

University of Nevada, Las Vegas  
Advisor: Daniel N. Allen, Ph.D.

Study: Deconstructing Psychosis and Reward: The Differential Role of Positive versus Negative Symptoms (*Fall 2011 – Present*)
Responsibilities to date include project development, which involves selection of test battery, proposal preparation, IRB approval preparation, database creation, and organization of such materials as assessment materials, administration instructions and scoring, and subject recruitment resources.

Study: Affect identification and interpersonal skills: An in-depth evaluation of social cognition in schizophrenia (*Summer 2010 – Fall 2011*)
Responsibilities included assessment of individuals with schizophrenia using a 6-hour-long neuropsychological and neuroscience battery. Assessments include the SCID, quality of life self-report questionnaires, a semi-structured interview regarding and subsequent ratings of current psychiatric symptomatology, functional outcome measures, and measures of sensory perception, affect identification, perception and interpretation of complex social situations, and theory of mind.

Study: Longitudinal study of neuropsychological and functional deficits in adults with bipolar disorder (*Summer 2008 – Spring 2010*)
Responsibilities included phone screening of potential participants, scheduling eligible participants for assessments, test scoring, data entry, and training research assistants in test scoring and entry 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.

**Auditory Cognitive Neuroscience Laboratory**

University of Nevada, Las Vegas  
Advisors: Joel S. Snyder, Ph.D., Daniel N. Allen, Ph.D.
Study: Neural mechanisms of perceptual processing in schizophrenia and bipolar disorder
Responsibilities include assessment of individuals with schizophrenia using a 4-hour long neuropsychological and neuroscience battery. In addition, responsibilities include phone screening of potential participants, scheduling eligible participants for assessments, electroencephalograms, and magnetic resonance imaging scans as well as accompanying participants to Nevada Imaging Center for magnetic resonance imaging scans, scoring, data entry, and training research assistants in scoring and entry protocols of participant assessments, which include the SCID, ratings of current psychiatric symptomatology, and selected WAIS-III subtests (i.e., Block Design, Digit Symbol-Coding, Letter-Number Sequencing, and Vocabulary).

Achievement Center Fall 2009–Present
University of Nevada, Las Vegas Advisor: Bradley Donohue, Ph.D.

Study: Concurrent drug abuse treatment and HIV prevention in child neglecting mothers, NIDA funded RO1 grant (DA020548-01A1)
Responsibilities include evaluating substance abusing mothers who had been identified by Child Protective Services to participate in a therapeutic program as well as organizing efforts to regain contact with out of contact participants. Assessments were administered in the clients’ homes and included the SCID, urine analysis, home safety ratings, and verbally administered self-report measures of child abuse potential, family interaction styles, and life satisfaction.

Undergraduate Research

University Of Nevada, Las Vegas Advisor: Daniel N. Allen, Ph.D.

Honors Thesis Title: Neurocognitive Deficits in Bipolar Disorder with Co Occurring Borderline Symptomatology. Advisor: Daniel N. Allen, Ph.D.

Projects:
• Emotion processing in adults with bipolar disorder
• Development and Validation of the Facial Affect Learning and Memory Test – Second Edition (FALMT-II).
• Positive Emotion Processing Deficits in Schizophrenia.
• Search Identification Task Project.

Body Image and Multiculturalism Lab Fall 2008
University Of Nevada, Las Vegas Advisor: Cortney S. Warren, Ph.D.
Project: Studying Personality in Juvenile Prostitutes: Aren’t all Delinquents the Same?

Auditory Cognition Research Program Fall 2008
University of Nevada, Las Vegas Advisor: Joel S. Snyder, Ph.D.
Project: Effects of prior experience are distinct from stimulus encoding during auditory and visual perception.

Mojave Adult, Child, and Family Services
Las Vegas, NV

SERVICE

National Academy of Neuropsychology
Professional Affairs and Information Committee Member April 2011–Present
Responsibilities: Advocacy for neuropsychologists, providing practice-related information to neuropsychologists in the form of resources and information, dictate quarterly conference call meeting minutes, monitor national neuropsychology listserv for practice related issues.

Student Volunteer at Annual Conferences Fall 2009–Fall 2011
NAN Annual Conference, Marco Island, FL November 2011
NAN Annual Conference, Vancouver, BC, Canada November 2010
NAN Annual Conference, New Orleans, LA October 2009
Responsibilities: Registration of conference attendees, scheduling of interviews for on-site Job Fair, and checking attendees in and out to ensure continuing education credits.

Outreach Undergraduate Mentoring Program Fall 2011–Present
Undergraduate student mentor
Responsibilities: Mentor an underrepresented undergraduate student through graduate school preparation, applications, and potential career paths in psychology.

UNLV Clinical Psychology Doctoral Student Committee Fall 2010–August 2011
Cohort Representative and Treasurer
Responsibilities: Serving as a liaison between clinical faculty and graduate students, coordinating and assisting with interview weekend activities, organizing student-focused events, and managing the committee’s funds.

Ad Hoc Reviewer
Schizophrenia Bulletin 2010

American College of Professional Neuropsychology
Student Volunteer at 2nd Annual Conference February 2010
Responsibilities: Registration of conference attendees, monitoring of seminars, and checking attendees in and out to ensure continuing education credits.

Reitan Society Meeting
Student Volunteer at Conference February 2010
Responsibilities: Registration of conference attendees, and monitoring of seminars.
National Alliance of Professional Psychology Providers  
Student Volunteer at Continuing Education Conference  
Responsibilities: Registration of conference attendees, monitoring of seminars, and checking attendees in and out to ensure continuing education credits.

Psi Chi National Honor Society in Psychology  
Vice-President, University of Nevada, Las Vegas Chapter  
Fall 2008–Spring 2009

Psychology Club  
Secretary, University of Nevada, Las Vegas  
Spring 2008

PROFESSIONAL AFFILIATIONS AND HONOR SOCIETIES

National Academy of Neuropsychology, Student Affiliate  
Summer 2007–Present
American Psychological Association, Student Affiliate  
Fall 2007–Present
Nevada Psychological Association, Student Affiliate  
Fall 2010–Present

Phi Kappa Phi National Honor Society  
Fall 2008 – Present
Golden Key Honor Society  
Fall 2008 – Present
Psi Chi, National Honor Society in Psychology  
Fall 2006 – Present

OTHER RELEVANT WORK AND TRAINING EXPERIENCE

Psychological Testing Clinic  
August 2009–August 2010
Las Vegas, NV  
Supervisor: Michelle G. Carro, Ph.D.
Graduate Assistant responsible for conducting telephone intakes, scheduling and case assignments for 6-10 graduate students, auditing files, bookkeeping, and other administrative functions at the department-sponsored community psychological assessment training clinic. (20 hours per week).

The Collaborative IRB Training Initiative (CITI) Program  
Spring 2005–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).

Symptoms Ratings Training Program  
Fall 2010
University of Nevada, Las Vegas  
Training Supervisor: Daniel N. Allen, Ph.D.
Completed a training program for administration of the Brief Psychiatric Rating Scale, Hamilton Depression Rating Scale, Scale for the Assessment of Negative Symptoms, Scale for the Assessment of Positive Symptoms and Young Mania Scale. Training was comprised of a series of workshops across a two month period for a total of approximately 40 workshop hours. Training culminated in a final mock interview conducted with Dr. Daniel Allen in order to assess proficiency.
SCID Training Program
University of Nevada, Las Vegas

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 across a two week period for a total of approximately 40 workshop hours. Training culminated in a final mock interview conducted with Dr. Daniel Allen in order to assess proficiency. Approximately 35 SCIDs have since been administered with a variety of populations, including individuals being screened for substance abuse and dependence, bipolar disorder, and schizophrenia. An additional training has been held in which workshop and mock interview assistance was provided.