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Explicit and implicit reinforcement learning across the psychosis spectrum

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Abstract

Motivational and hedonic impairments are core features of a variety of types of psychopathology. An important aspect of motivational function is reinforcement learning (RL), including implicit (i.e., outside of conscious awareness) and explicit (i.e., including explicit representations about potential reward associations) learning, as well as both positive reinforcement (learning about actions that lead to reward) and punishment (learning to avoid actions that lead to loss). Here we present data from paradigms designed to assess both positive and negative components of both implicit and explicit RL, examine performance on each of these tasks among individuals with schizophrenia, schizoaffective disorder and bipolar disorder with psychosis, and examine their relative relationships to specific symptom domains transdiagnostically. None of the diagnostic groups differed significantly from controls on the implicit RL tasks in either bias towards a rewarded response or bias away from a punished response. However, on the explicit RL task, both the individuals with schizophrenia and schizoaffective disorder performed significantly worse than controls, but the individuals with bipolar did not. Worse performance on the explicit RL task, but not the implicit RL task, was related to worse motivation and pleasure symptoms across all diagnostic categories. Performance on explicit RL, but not implicit RL, was related to working memory, which accounted for some of the diagnostic group differences. However, working memory did not account for the relationship of explicit RL to motivation and pleasure symptoms.

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These findings suggest transdiagnostic relationships across the spectrum of psychotic disorders between motivation and pleasure impairments and explicit RL.

Keywords

reinforcement learning; psychosis; motivation; reward; loss; learning; pleasure; function

Motivational and hedonic impairments are core aspects of a variety of types of psychopathology. These impairments cut across diagnostic categories and may be critical to understanding major aspects of the functional impairments accompanying psychopathology. Given the centrality of motivational and hedonic systems to psychopathology, the RDoC initiative (T. Insel et al., 2010; T. R. Insel, 2014) includes a “positive valence” systems domain outlining a number of constructs that may be key to understanding the nature and mechanisms of motivational and hedonic deficits. Among others, these component constructs include responsiveness to reward, reward anticipation, reinforcement learning, effort valuation, and action selection. Here we focus on reinforcement learning (RL), both implicit (i.e., outside of conscious awareness) and explicit (i.e., including the use of explicit representations about potential reward associations) as well as both positive reinforcement (learning about actions that lead to reward) and punishment (learning to avoid actions that lead to loss) components. The goals of this study are to: 1) present data on the performance among individuals with schizophrenia, schizoaffective disorder and bipolar disorder with psychosis on paradigms designed to assess both positive and negative components of both implicit and explicit RL; and 2) examine relationships between performance and both self-reports and clinical assessments of pleasure and motivation, as well as functional outcome, transdiagnostically.

RL is thought to be mediated by midbrain dopamine (DA) projections to ventral and dorsal regions of the basal ganglia (Berridge, 2004; Schultz, 2007). The degree to which these neurons respond to rewards depends on predictability. Unpredicted rewards induce DA neurons to fire strongly (signaling a positive prediction error), and nonoccurrence of predicted rewards leads to reduced firing (signaling a negative prediction error) (Schultz, 1992, 2004, 2007; Schultz, Apicella, & Ljungberg, 1993; Schultz, Dayan, & Montague, 1997). Over time, DA neurons learn to fire to cues predicting reward, rather than to rewards themselves (Schultz, 2007). In humans, fMRI studies show activity in ventral and dorsal striatum to cues predicting reward (Knutson, Fong, Adams, Varner, & Hommer, 2001; Knutson, Westdorp, Kaiser, & Hommer, 2000) as well as positive and negative prediction error responses (Abler, Walter, Erk, Kammerer, & Spitzer, 2006; McClure, Berns, & Montague, 2003). Such DA/striatal responses are thought to support aspects of RL that may occur *without* conscious awareness, that is *implicit* RL (Dayan & Balleine, 2002; Frank, Seeberger, & O’Reilly R, 2004). While there are common mechanisms that may contribute to implicit RL for both positive (reward) and negative (loss) feedback, there are also dissociable mechanisms. For example, there is evidence for striatal cells that mediate “go” or reward-based learning versus cells that mediate “no-go” or loss based learning, with a hypothesized role for D1 receptors in go learning and D2 receptors in no-go learning (Frank & Hutchison, 2009; Frank & O’Reilly, 2006; Frank, et al., 2004; Hazy, Frank, & O’Reilly R,

2007b). There is also evidence for a role for serotonin in negative implicit RL and punishment (Bari et al., 2010; Crockett, Clark, & Robbins, 2009; Evers et al., 2005).

In addition to these mechanisms thought to influence implicit RL, there is also evidence that the development of explicit representations accessible to conscious awareness can also drive RL, albeit with a potentially different time course and brain mechanism (Frank, Loughry, & O'Reilly, 2001; Frank & O'Reilly, 2006; Gold, Waltz, et al., 2012; Hazy, Frank, & O'Reilly R, 2007a). These more explicit forms of RL also engage neural systems involved in cognitive control and value representations, such as dorsal frontal and parietal regions and the OFC (Frank, et al., 2001; Frank & O'Reilly, 2006; Gold, Waltz, et al., 2012; Hazy, et al., 2007a). By cognitive control, we mean the ability to maintain goal or task representations in working memory in order to guide behavior, focusing attentional resources on task-relevant information while filtering out task-irrelevant information (Braver, 2012; Miller & Cohen, 2001).

Reinforcement Learning in Psychotic Disorders

The literature on RL in schizophrenia is mixed, though there is some evidence that distinguishing between explicit/implicit and positive/negative RL may help clarify these inconsistencies. The evidence suggests relatively intact performance on a range of tasks in which learning is either relatively easy or relatively implicit (Ceaser et al., 2008; Elliott, McKenna, Robbins, & Sahakian, 1995; Heerey, Bell-Warren, & Gold, 2008; Hutton et al., 1998; Jazbec et al., 2007; Joyce et al., 2002; Somlai, Moustafa, Keri, Myers, & Gluck, 2011; Turner et al., 2004; Tyson, Laws, Roberts, & Mortimer, 2004; Waltz & Gold, 2007; Weiler, Bellebaum, Brune, Juckel, & Daum, 2009), though with some exceptions (Oades, 1997; Pantelis et al., 1999). Similarly, several studies using the Weather Prediction task found a relatively intact learning rate, but impairments in maximum performance level, which provides mixed evidence for striatal learning impairments (Beninger et al., 2003; Keri et al., 2000; Keri, Nagy, Kelemen, Myers, & Gluck, 2005; Weickert et al., 2002). However, two studies found lower learning rates in schizophrenia than in controls, suggesting possible impairments in striatally mediated learning (Weickert et al., 2010; Weickert, Leslie, Rushby, Hodges, & Hornberger, 2013). There is also evidence of intact positive RL in schizophrenia using implicit reinforcement learning tasks (Ahnallen et al., 2012; Heerey, et al., 2008). Further, even chronically ill individuals with schizophrenia can learn many new skills under conditions of systematically delivered positive reinforcement and extinction of irrelevant behavior (Glynn & Mueser, 1986; Silverstein et al., 2006).

In contrast, when RL paradigms become more difficult and therefore benefit from the explicit use of representations about stimulus-reward contingencies, individuals with schizophrenia show more consistently impaired RL (Cicero, Martin, Becker, & Kerns, 2014; Gold, Waltz, et al., 2012; Koch et al., 2009; Morris, Heerey, Gold, & Holroyd, 2008; Waltz, Frank, Robinson, & Gold, 2007; Yilmaz, Simsek, & Gonul, 2012). Interestingly, these impairments may be greater when individuals with schizophrenia must learn from reward versus from punishment (Cheng, Tang, Li, Lau, & Lee, 2012; Gold, Waltz, et al., 2012; Reinen et al., 2014; Waltz, et al., 2007), though some studies also find impaired learning from punishment (Cicero, et al., 2014; Fervaha, Agid, Foussias, & Remington, 2013).

Further, there is recent work suggesting that working memory impairments may make a significant contribution to RL deficits in schizophrenia (Collins, Brown, Gold, Waltz, & Frank, 2014), as well as a growing literature suggesting altered activity in cortical regions involved in cognitive control during anticipation/prediction error (Gilleen, Shergill, & Kapur, 2014; Walter, Kammerer, Frasch, Spitzer, & Abler, 2009) and during RL (Culbreth, Gold, Cools, & Barch, in submission; Waltz et al., 2013). Such findings are consistent with the larger literature suggesting altered cognitive control function in schizophrenia, and are also consistent with the growing basic science literature suggesting important interactions between what have been referred to as "model-free" learning systems (e.g., DA in the striatum) and "model-based" learning systems that engage prefrontal and parietal systems that support representations of action-outcome models (Daw, Gershman, Seymour, Dayan, & Dolan, 2011; Doll, Simon, & Daw, 2012; Glascher, Daw, Dayan, & O'Doherty, 2010; Lee, Shimojo, & O'Doherty, 2014; Otto, Skatova, Madlon-Kay, & Daw, 2015). Interestingly, there is robust evidence that explicit RL impairments in schizophrenia are correlated with motivation/pleasure negative symptoms (Farkas et al., 2008; Murray et al., 2008; Polgar et al., 2008; Somlai, et al., 2011; Strauss et al., 2011; Waltz, Frank, Wiecki, & Gold, 2011) and that negative symptoms more broadly are related to positive as compared to negative RL (Gold, Waltz, et al., 2012; Polgar, et al., 2008; Somlai, et al., 2011).

Interestingly, despite evidence that individuals with bipolar disorder describe themselves as overly reward responsive and, at times, appear to engage in high levels of effort toward obtaining rewards (Harmon-Jones et al., 2008; Hayden et al., 2008; Johnson, Edge, Holmes, & Carver, 2012b; Strakowski et al., 2010), a number of studies suggest impairments in both implicit (Mueller et al., 2010; Pizzagalli, Goetz, Ostacher, Iosifescu, & Perlis, 2008) and explicit (Dickstein, Finger, Brotman, et al., 2010; Dickstein, Finger, Skup, et al., 2010; Gorrindo et al., 2005; McKirdy et al., 2009; Murray, et al., 2008; Shamay-Tsoory, Harari, Szepsenwol, & Levkovitz, 2009) RL in bipolar disorder (for exceptions see (Ernst et al., 2004; Rau et al., 2008). To our knowledge there is no research on either implicit or explicit RL in samples comprised solely of schizoaffective. There is, however, evidence that RL deficits are correlated with motivation/pleasure negative symptoms in affective psychosis and in schizophrenia (Murray, et al., 2008; Pizzagalli, et al., 2008). However, few studies have made distinctions between implicit and explicit RL, or between positive and negative RL in bipolar disorder. Individuals with bipolar disorder may have impairments in learning from negative feedback (Minassian, Paulus, & Perry, 2004; Rich et al., 2005), which has important implications for the role of "no-go" learning pathways and the serotonin system. Further, there is evidence that individuals with schizophrenia, schizoaffective disorder and bipolar disorder all experience impairments in cognitive control and working memory functions, albeit with varying levels of severity (Owoso et al., 2013; Reilly & Sweeney, 2014; Tamminga et al., 2014).

The goal of the current study was to use tasks designed to measure both positive and negative components of implicit and explicit RL to understand impairments in these different RL components both within and across the spectrum of psychotic disorders. Given the evidence for deficits in cognitive control and working memory functions across psychotic disorders, we predicted that individuals with schizophrenia, schizoaffective, and bipolar disorder with lifetime psychosis would each show impaired explicit RL, though

potentially more so for positive than negative RL given the prior work suggesting differential impairments for positive RL among individuals with schizophrenia. In contrast, we predicted relatively intact implicit RL across all three diagnostic categories, though with the potential for greater impairment among individuals with bipolar disorder on either or both positive and negative implicit RL given literature cited above. Lastly, given previous findings, we also predicted that the severity of motivation and pleasure-related negative symptoms would be associated with impaired RL, potentially more so with performance on the explicit than implicit RL tasks and with positive versus negative RL.

Methods

Participants

Participants for the study were recruited as part of the Cognitive Neuroscience Test Reliability And Clinical applications for Serious mental illness (CNTRACS) Consortium, which included five different research sites: University of California – Davis, Maryland Psychiatric Research Center at the University of Maryland School of Medicine, Rutgers University, University of Minnesota – Twin Cities, and Washington University in St. Louis. Participants were recruited nearly equally across the five different sites, and were recruited from outpatient psychiatric clinics, community centers and local settings via flyers and online advertisements. Healthy controls were also recruited through community centers, flyers in the community and online advertisements. Recruiting and informed consent procedures for each site were reviewed and approved by that site's Institutional Review Board, as follows: 1) Maryland Psychiatric Research Center; -- Title: Cognitive Neuroscience Task Reliability & Clinical Applications Consortium -- IRB # HP-00052713; 2) University of California at Davis -- Title: 2/5 - Cognitive Neuroscience Task Reliability & Clinical Applications Consortium – IRB # 247889; 3) University of Minnesota -- Title: University of Minnesota Study Measurement of Mental Illness and Mental Health II -- IRB #: 1407S52341; 4) Rutgers University -- Title: 3/5 CNTRAC -- IRB # PRO2013003578; and 5) Washington University -- Title: Cognitive Neuroscience Task Reliability & Clinical Applications Consortium -- IRB #: 201309052.

Across the five sites, we conducted in-person screens on 269 individuals. Sixty healthy controls met all inclusion criteria and attended all testing sessions, as well as 65 with schizophrenia, 53 with schizoaffective and 50 with bipolar disorder with psychosis, for a total of 228 participants. Of the other 41 participants, 17 were excused from the study for testing positive for drugs or alcohol (all patients), 3 for meeting criteria for current drug or alcohol abuse (all patients), 9 for not meeting diagnostic criteria for schizophrenia, schizoaffective or bipolar disorder, 3 for a history of head injuries (1 control and 2 patients), 1 for being outside the age range of 18–65 (patient), 1 for having current major depression (potential control), 1 for a low Wechsler Test of Adult Reading (WTAR) score (control), 1 for a recent medication change (patient), 1 for responding randomly in the first task session (patient) and 4 because they failed to complete all testing sessions (1 control and 3 patients).

The study from which these data are drawn administered a variety of paradigms, including both working memory and RL tasks. The focus of the current manuscript is on two types of RL tasks: The *Explicit Probabilistic Incentive Learning Tasks* (EPILT; 2- and 4-block

versions) and the *Implicit Probabilistic Incentive Learning Tasks* (IPILT, positive and negative versions, IPILT-P and IPILT-N), each of which is described in more detail below. Five healthy controls, six individuals with bipolar, 7 with schizophrenia and 5 with schizoaffective did not pass the practice trials for either or both 2-block or 4-block EPILT. Two patients did not pass the practice for the IPILT-P, but all did for the negative IPILT-N. Thus, across these categories, a total of 25 individuals were excluded, leaving a total of 203 participants with data on all four tasks (55 healthy controls, 57 schizophrenia, 48 schizoaffective and 43 bipolar with psychosis[1]). We focused our analysis on these participants, but the results were not substantively different if we examined all participants with data on any given task. Of the individuals with schizoaffective disorder, 32 had bipolar type and 16 had depressed type.

The inclusion and exclusion criteria were the same as those used in the previous studies from our consortium (Barch et al., 2012; Gold, Barch, et al., 2012; Henderson et al., 2012; Ragland et al., 2012; Silverstein et al., 2012). The general criteria included: 1) age 18–65; 2) no clinically significant head injury (loss of consciousness for 20 minutes or overnight hospitalization) or neurological disease; 3) no diagnosis of mental retardation or pervasive developmental disorder; 4) no substance dependence in the past six months and no substance abuse in the past month; 5) sufficient spoken English so as to be able to complete testing validity; 6) a score of 6 or higher on the WTAR as a measure of premorbid IQ (Wechsler, 2001); 7) ability to give valid informed consent; and 8) passed alcohol and drug testing on each day of testing. Urine drug testing was conducted using the OnTrak Testcard™ 501 by Varian (Palo Alto, CA), which screens for cocaine, THC, methamphetamine, morphine, and amphetamine. Alcohol screenings were done using an Alcohawk Breathalyzer (< .05%). Additional criteria for the patient groups were: 1) DSM-IV diagnosis of schizophrenia, schizoaffective disorder or bipolar with lifetime psychosis, with the definition of lifetime psychosis used in Ivelva et all (Ivleva et al., 2012) (based on SCID interview, see below); 2) no medication changes in the prior month or anticipated in the upcoming month; and 3) stable outpatient or partial hospital status. Additional criteria for controls were: 1) no history of schizophrenia, schizoaffective, or bipolar disorder; 2) no current major depression and 3) no current psychotropic or cognition enhancing medication. The groups were recruited to be matched for gender, age, race, and parental socioeconomic status, measured using the Hollingshead Index (Hollingshead & Redlich, 1958) as updated using occupational prestige ratings based on the 1989 general social survey (Davis, Smith, Hodge, Nakoa, & Treas, 1991). Demographic and clinical characteristics for each group are presented in Table 1. As shown, groups were similar on age, gender, race, and parental SES, although mean levels of personal education and Wechsler Test of Adult Reading scores were significantly higher in the healthy control group than in the three diagnosed groups[2]. The schizophrenia and schizoaffective groups were on higher doses of olanzapine equivalent medication doses than

[1]Of the 43 individuals with bipolar disorder, 13 were not currently symptomatic, 8 met criteria for mania, 10 mixed, 4 hypomanic, 7 depressed, and one unspecified.

[2]There were no significant associations in any group between education and Wechsler Test of Adult Reading scores and performance on either of the IPILT tasks. There were some significant correlations with performance on some of the EPILT conditions in the healthy controls, bipolar with psychosis and schizoaffective, but no significant correlations in the schizophrenia. Like covarying for working memory, the results as a function of Motivation and Pleasure symptom severity hold when covarying for Wechsler Test of Adult Reading.

the bipolar with psychosis group [3](Gardner, Murphy, O'Donnell, Centorrino, & Baldessarini, 2010). The groups differed on smoking rates, but the main findings presented below remain when controlling for smoking status.

Diagnosis and Clinical Assessment

A masters-level clinician conducted or supervised diagnostic assessments using the Structured Clinical Interview for DSM-IV-TR[4] (First, Spitzer, Miriam, & Williams, 2002), the 24-item Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962; Ventura, Green, Shaner, & Liberman, 1993; Ventura et al., 1993), the Young Mania Rating Scale (YMRS; (Young, Biggs, Ziegler, & Meyer, 1978), the Bipolar Depression Rating Scale (BDS; (Berk et al., 2007), and the Clinical Assessment Interview for Negative Symptoms (CAINS) (Kring, Gur, Blanchard, Horan, & Reise, 2013). In addition to on-site standardized SCID instruction and supervision, raters were trained by teleconferences in which ratings and anchor points for all scales were discussed and six training videos were rated and discussed. Certified raters achieved agreement with the "gold" standard ratings (those of the trainers, which were highly skilled clinicians from either the St. Louis or Maryland sites or Sheri Johnson for the YMRS/BDRS or Ann Kring for the CAINS) for at least six interviews. Agreement was defined as no more than 2 items with a difference of more than 1 rating point from the gold standard. Raters added after the start of the study went through a similar process to achieve the same agreement level. To maintain reliability across the course of the study, the St. Louis site created a videotaped interview to rate every 2–4 weeks and all raters participated in a teleconference to resolve discrepancies.

Procedure, Session Composition and Order

During the first session, participants completed the diagnostic interview, symptom ratings, WTAR (Wechsler, 2001), demographic assessment, and assessments of community function using the participant and informant versions of the Specific Levels of Functioning Scale (SLOF) (Schneider & Struening, 1983). Participants then completed 2 additional cognitive testing sessions within approximately one month. Session one included one version each of the IPILT-P and IPILT-N (with different stimuli), either the 2- or 4-block EPILT, 1 change detection task, 1 change localization task, 1 running span task, and three subtests from the MATRICS battery (Hopkins Verbal Learning, BACS Symbol Coding and Letter Number Sequencing). Session two include another version each of the IPILT-P and IPILT-N (with different stimuli), the other version of the EPILT, another change detection task, another change localization task, and the UCSD-Performance Based Skills Assessment (UPSA) (Harvey, Velligan, & Bellack, 2007; Patterson, Goldman, McKibbin, Hughs, & Jeste, 2001; Twamley et al., 2002). Thus, across the two sessions, participants performed two versions of the EPILT with different stimuli (2 and 4 block versions); 2 versions of the IPILT-P with different stimuli, and two versions of the IPILT-N with different stimuli.

[3]There were no significant correlations between task performance and olanzapine equivalents in the combined patient sample or among the individuals with schizophrenia or the bipolar. There were only two nominally significant associations among individuals with schizoaffective disorder, with higher olanzapine equivalents associated with lower average IPILT-P bias and with worse performance on the EPILT-2 block AVOID LOSS, but neither of these would pass multiple comparison correction.

[4]All but one of the individuals diagnosed with DSM-IV schizophrenia would have met DSM-5 criteria, all individuals with bipolar disorder would have met DSM-5 criteria, and 46 of the individuals with schizoaffective disorder would have met DSM-5 criteria.

Tasks

All tasks were administered using E-prime (Schneider, Eschman, & Zuccolotto, 2012) and are available for download at cntracs.ucdavis.edu.

Implicit Probabilistic Incentive Learning Tasks (IPILT)—Participants completed two modified versions of the implicit probabilistic reward task based on the work of Pizzagalli (Heerey, Bell-Warren, & Gold, 2008; Pizzagalli et al., 2005), here termed **IPILT-Positive** (IPILT-P) and **IPILT-Negative** (IPILT-N), to assess gain and loss responsiveness respectively (Figure 1). Before beginning each task participants were given instructions and completed at least 20 practice trials as in (Heerey, et al., 2008). To generate multiple parallel versions that could be used in longitudinal or treatment studies, we developed six different sets of stimuli, with the stimulus type counterbalanced across subjects and sessions. As shown in Figure 1, the six sets were: 1) mouth long or short (the original stimulus type in Pizzagalli et al (Pizzagalli, Jahn, & O'Shea, 2005); 2) nose long or short (Bogdan & Pizzagalli, 2006); 3) mouth thick or thin; 4) nose thick or thin; 5) eyes far or near; and 6) eyes big or small. Analyses of stimulus set effects are provided in Supplemental Materials.

On each trial, participants performed a perceptual discrimination in which they indicated which of two variants of a stimulus was briefly presented (e.g., short or long mouth). For the IPILT-P, ~40% of correct responses received gain feedback while, for the IPILT-N, a portion of incorrect responses received loss feedback. Critically, for both tasks, one of the two responses (termed the RICH response) was scheduled to receive three times the amount of feedback as the alternative (LEAN) response. Healthy adults preferentially select the RICH response across IPILT-P task blocks (positive response bias) (Luking, Neiman, et al., 2015; Luking, Pagliaccio, et al., 2015; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008; Pizzagalli et al., 2005) and preferentially avoid the RICH response across IPILT-N task blocks (negative response bias) (Luking, Neiman, et al., 2015; Luking, Pagliaccio, et al., 2015). As shown in Figure 1, each trial started with a fixation cross for 500 ms, followed by a face without the critical stimulus for 500 msec. The critical stimulus was presented for 100 ms, followed by a noise mask (#######). Participants had up to 8000 ms from onset of the critical stimulus to respond. On the IPILT-P, if it was a feedback trial and they responded correctly, they saw "Correct! You win!," which the initial instructions indicated that they earned $0.05. On the IPILT-N, participants were told that they started with an endowment of $3.60. If it was a feedback trial and they responded incorrectly, they saw "Sorry. You Lose," which the initial instructions indicated that they lost $0.05. In both versions, if they did not respond within 8000 ms, they saw "Too slow – please respond faster." Instructions about the response mappings remained on the bottom of the screen throughout the task. In both tasks, feedback was presented in a pseudorandom order, such that no more than three trials in a row could receive feedback. A counter, reshuffled for each block, determined which RICH or LEAN response was scheduled for feedback. If a correct/incorrect response (IPILT-P/N respectively) was not made on a trial scheduled to receive feedback, feedback was delivered on the next available trial of that type. The button (left or right) used for the RICH or LEAN response was counterbalanced across participants, as was the variant of the stimulus (e.g., short or long mouth) that was designated as RICH or LEAN. Trials were presented in three

blocks of 60 trials each, with a brief break in between blocks and the same ratio of RICH to LEAN trials within each block.

Explicit Probabilistic Incentive Learning Tasks (EPILT)—Following previous work (Gold, Waltz, et al., 2012; Kim, Shimojo, & O'Doherty, 2006; Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006), we used a task in which participants were explicitly asked to simultaneously learn discriminations for four pairs of stimuli (Figure 2). In two of the pairs, the choice of the optimal stimulus was probabilistically associated with the receipt of money, and the choice of the non-optimal stimulus was associated with no reward ("Win or Not Win" or gain approach). In the other two pairs, the choice of the optimal stimulus result was probabilistically associated with no loss of money, while the choice of the non-optimal stimulus was probabilistically associated with the loss of money ("Not Lose or Lose" or loss avoidance). As shown in Figure 2, stimuli were color images of landscapes or other types of nature scenes appearing on a white background, one pair at a time. On "Win or Not Win" trials, if the optimal item was selected, participants saw an image of a nickel coupled with the word "Win!" If the non-optimal item was selected, they saw "Not a winner, Try again!" On "Not Lose or Lose" trials, the optimal response received the feedback "Keep your money!" If the of non-optimal item was selected, participants saw an image of a nickel with a red line through it, coupled with the word "Lose!". The optimal response was reinforced on 90% of trials in one pair and on 80% of trials in the other pair within each type of trial. Thus, there were a total of four types of trials: 1) Win/Not Win at 90/10 probability distribution; 2) Win/Not Win at 80/20 probability distribution; 3) Not Lose/Lose at 90/10 probability distribution; and 4) Not Lose/Lose at 80/10 probability distribution. To generate multiple parallel versions that could be used in longitudinal or treatment studies, we developed four different sets of stimuli, with the stimulus type counterbalanced across subjects and sessions (Figure S1). Analyses of stimulus set effects are provided in Supplemental Materials.

The task started with a 20 trial session (10 trials each "Win or Not Win" and "Lose or Not Lose" at the 90/10 probability distribution) to ensure task comprehension, using different stimuli than the actual task. The first trial was always "Win or Not Win" and participants were guaranteed to experience a win on the first trial by mapping that stimulus to the optimal stimulus category. Participants had to achieve 60% accuracy for both types of trials in order to proceed to the real task. If they did not achieve this accuracy, there were asked to repeat the practice (with the same stimuli and mappings) for up to a total of six practice sets. If they still did not achieve the target accuracy, the task was terminated.

As described in the Supplemental Materials, we developed versions with differing lengths of **training** (2 block versus 4 blocks) to determine if effects could be achieved in a shorter time than the standard version. Here we present data from the original 4-block version used in the Gold et al study, and analyses of the 2-block version are provided in Supplemental Materials. In this version, participants were presented with 160 trials in four blocks of 40 trials, with a brief break after the first two blocks, for a total of 40 trials of each of the four trial types.

Following training a **transfer** test phase was presented. In these 72 trials, the original 4 training pairs were each presented 4 times, and novel pairings were presented on 58 trials. For novel pairings, each trained item was presented with every other trained item. Of most interest were pairings that pitted stimuli that had experienced different types of reinforcement histories against each other (referred to as pairings). Participants were instructed to pick the item in the pair that they thought was “best” based on their earlier learning. No feedback was administered during this phase. Following Gold and colleagues (Gold, Waltz, et al., 2012), we focused on the pairings outlined in Table 2.

Data Processing and Analysis

IPILT: As in previous studies (Luking, Neiman, et al., 2015; Luking, Pagliaccio, et al., 2015; Pizzagalli et al., 2005), individual trials with reaction time (RT) either outside of the range of 150–2500 msec post-stimulus onset or beyond +/− 3 standard deviations from the participant’s mean RT were excluded, after which discriminability and response bias were calculated for each of the three blocks of 60 trials. Greater discriminability (log d) indicates improved ability to distinguish between stimuli. Response bias (log b) assesses behavioral responsiveness to feedback, and so was the primary focus of analyses (analyses of d-prime are presented in the supplemental analyses). Higher log b values during the PILT-P indicate a greater propensity to select the more frequently rewarded (RICH) stimulus. Higher log b values during the PILT-N indicate a greater propensity to select the LEAN stimulus, i.e. to avoid the more frequently punished response.

$$Discriminability\ (\log d\ or\ dprime) = \frac{1}{2}\log\left(\frac{RICHcorrect * LEANcorrect}{RICHincorrect * LEANincorrect}\right)$$
$$Response\ Bias\ (\log b) = \frac{1}{2}\log\left(\frac{RICHcorrect * LEANincorrect}{RICHincorrect * LEANcorrect}\right)$$

We analyzed the IPILT-P and IPILT-N (in separate analyses) using repeated-measures ANOVAs with Block as a within subject factor, and Stimulus Set and Diagnostic Group as between subject factors. We then followed-up with analyses as a function of negative symptom severity, conducting a similar ANOVA just in the patient groups, but adding the CAINS Motivation and Pleasure symptom score as a covariate to the ANOVAs (which still included diagnostic group as a factor). Analyses investigating response bias focused on overall bias (the overall degree to which the individual was sensitive to a particular response being rewarded or punished), and the change in bias from the initial (block 1) to the final (block 3) task block (Luking, Neiman, et al., 2015; Luking, Pagliaccio, et al., 2015; Pizzagalli et al., 2005).

EPILT: For the **training phase**, accuracy was computed for each block for each of the 4 trial types: 1) Win/Not Win at 90/10; 2) Win/Not Win at 80/10; 3) Not Lose/Lose at 90/10; and 4) Not Lose/Lose at 80/10. We analyzed the training phase data using a repeated measures ANOVA with Block (4), Condition (Win/No Win vs. Lose/No Lose) and Probability (90/10 vs. 80/20) as within-subject factors, and Stimulus Set and Diagnostic Group as between-subject factors. For the **transfer** phase, the percentage of times the participant chose the first item in the pairings is described in Table 2, along with the

meaning of each comparison: 1) Frequent Winner versus Infrequent Winner [FWvsIW]; 2) Frequent Winner versus Frequent Loser [FWvsFL]; 3) Frequent Winner versus Frequent Loser [FWvsFL]; and 4) Frequent Lose Avoider versus Infrequent Winner [FLAvsIW]. We analyzed the transfer phase data using a repeated-measures ANOVA with Pairing as a within-subject factor, and Stimulus Set and Diagnostic Group as between-subject factors. We used planned contrasts to compare groups on each of the four pairings, to compare our results to those from Gold (Gold, Waltz, et al., 2012). We then followed up analyses for both training and transfer phases with analyses as a function of negative symptom severity, conducting similar ANOVAs just in the patient groups, but adding the CAINS Motivation and Pleasure symptom score as a covariate to the ANOVAs (which still included diagnostic group as a factor). Due to the different nature of the tasks, no direct comparisons between implicit and explicit learning could be made. There were no significant main effects or interactions with site, and all results remained the same when site was included as a factor. Thus, the analyses below do not include site as a factor for ease of presentation.

Results

IPILT

Diagnostic Group Effects

IPILT-P: As presented in Supplemental Materials, analyses of stimulus sets indicated that one set (Eyes Far or Near) showed much higher bias and much lower accuracy, suggesting that the discrimination was too hard. As such, for the analysis of hypotheses examining diagnostic group and negative symptoms below, we excluded participants who did the Eyes Far or Near set (N = 39 for IPILT-P and N = 38 for IPILT-N, distributed relatively equally across groups), though the results were not substantively different if those stimulus sets were retained. Thus, for IPILT-P, we had 48 healthy controls, 39 bipolar with psychosis, 35 schizoaffective and 46 schizophrenia. As shown in Figure 3a, all groups showed the expected overall positive bias on the IPILT-P (model intercept: $F(1,164) = 59.85$, $p < .001$, $\eta^2_p = .267$), though the main effect of Block (i.e., increase across blocks) was not significant ($F(2,328) = 1.25$, $p = .29$, $\eta^2_p = .008$). Consistent with our predictions, the ANOVA on bias from the IPILT-P (see Figure 3a) indicated no significant main effect of Diagnostic Group ($F(3,164) = 1.46$, $p = .23$, $\eta^2_p = .026$), and no interaction between Diagnostic Group and Block ($F(6,328) = 0.19$, $p = .98$, $\eta^2_p = .008$).

IPILT-N: For IPILT-N, we had 46 healthy controls, 35 bipolar with lifetime psychosis, 40 schizoaffective and 49 schizophrenia. As shown in Figure 3b, all groups showed the expected overall bias away from the punished stimulus (plotted as positive in Figure 3b for ease of presentation) on the IPILT-N (model intercept: $F(1,166) = 25.76$, $p < .001$, $\eta^2_p = .134$), and the main effect of Block was significant ($F(2,332) = 7.61$, $p = .001$, $\eta^2_p = .044$), indicating an increase in bias across blocks. Also consistent with predictions, the ANOVA on IPILT-N bias (see Figure 3b) indicated no significant main effect of Diagnostic Group ($F(3,166) = 1.09$, $p = .35$, $\eta^2_p = .019$), and no interaction between Diagnostic Group and Block ($F(6,332) = 0.56$, $p = .76$, $\eta^2_p = .01$).

Motivation/Pleasure Symptom Effects

IPILT-P: As described in the methods, we also examined the effects of motivation and pleasure negative symptom severity by conducting a similar ANOVA in just the patient groups, but adding the CAINS Motivation and Pleasure subscale as a covariate (retaining diagnostic group as a between subject factor). This analysis indicated a significant main effect of Motivation and Pleasure symptom score ($F(1,116) = 4.373$, $p = .039$, $\eta^2_p = .036$), and a trend level main effect of Diagnostic Group ($F(2,116) = 2.751$, $p = .068$, $\eta^2_p = .045$), but no significant interactions (all $ps > .10$ and all η^2_ps < .022). Follow up regression analyses examining the correlation between Motivation and Pleasure scores and average IPILT-P bias indicated a trend level positive relationship ($t = 1.837$, $p = .069$, $\beta = .20$), with *higher* Motivation and Pleasure scores being associated with *greater* bias. The trend level main effect of diagnostic group indicated greater bias among the bipolar with psychosis as compared to schizophrenia and schizoaffective (ps <.05) when accounting for Motivation and Pleasure scores.

IPILT-N: This analysis indicated a significant main effect of Motivation and Pleasure symptom score ($F(1,116) = 5.785$, $p = .018$, $\eta^2_p = .046$), but no main effect of Diagnostic Group ($F(2,116) = 0.028$, $p = .97$, $\eta^2_p = .099$), and no significant interactions (all $ps > .50$ and all η^2_ps < .013). Follow up regression analyses examining the association between Motivation and Pleasure scores and average IPILT-N bias indicated a positive relationship ($t = 2.10$, $p = .038$, $\beta = .22$), with *higher* Motivation and Pleasure scores being associated with *greater* bias.

Correlations with Clinical Symptoms—We also examined whether there were any individual difference relationships with any symptoms other than the CAINS Motivation and Pleasure with performance on either the IPILT-P or IPILT-N in the patient groups. We conducted parallel analyses of the average bias across blocks and the change in bias from block 1 to block 3. We computed a series of linear regressions in which we included dummy variables to code for diagnostic group, average d prime performance (to control for accuracy), and the clinical predictor of interest (BPRS scores for negative and positive symptoms, YMRS, BDRS and CAINS Expression). We also included interaction terms between group and the clinical predictor to determine if there were significant diagnostic group differences in any effects of symptom scores. We corrected the alpha level for the test of each dependent variable based on inclusion of five symptom predictors ($p = .05/5 = .01$).

We found no significant main effects of clinical predictors, but we found one clinical predictor (mania) that showed a significant interaction with diagnostic group for average bias: BPRS Mania ($F(6,113) = 3.15$, $p = .007$)[5]. The YMRS ($F(6,113) = 2.77$, $p = .015$ showed the same pattern. For both mania measures, the interactions of the mania scores with the dummy code for schizophrenia were significant ($t = -2.26$, $p = .026$, $\beta = -.67$ & $t = -3.12$,

[5]When we visualized the relationships between the BPRS Mania and YMRS variables and the average bias score, we noted some potential outliers. We computed the Mahalanobis test for outliers, and recomputed these relationships excluding six potential outliers. The results held even with exclusion of these potential outliers, including both the significant group X mania rating scale interactions, as the significant within group relationships in the individuals with bipolar disorder. There were also three potential univariate outliers in the average Bias scores (> 3 SDs from mean) and all results held with exclusion of these outliers as well. In addition, the relations to mania in the bipolar disorder group hold when control for Motivation and Pleasure symptom scores.

$p = .002$, $\beta = -.54$ respectively), as well as the interactions with the dummy code for schizoaffective disorder ($t = -2.66$, $p = .009$, $\beta = -.79$ & $t = -2.42$, $p = .017$, $\beta = -.43$ respectively), indicating that the relationships in schizophrenia and schizoaffective differed from the relationships in bipolar with psychosis. Follow-up analyses computing correlations separately for each group indicated that both mania measures were related to significantly higher average positive bias on the IPILT-P ($r(36) = .65$, $p < .001$ & $r(36) = .59$, $p < .001$ respectively) in the bipolar with psychosis group, but not in the schizoaffective $r(32) = . -.09$, $p = .60$ & $r(32) = . -12$, $p = .50$) or schizophrenia $r(43) = -.04$, $p = .76$ & $r(43) = -.14$, $p = .36$) groups.[a] There were no significant relationships between the clinical variables and IPILT-P change in bias or IPILT-N change in bias or average bias. In addition, using the formulas from Meng, Rosenthal and Rubin (Meng, Rosenthal, & Rubin, 1992), BPRS Mania was significantly more strongly correlated with average IPILT-P bias than with average IPILT-N bias ($Z = 2.81$, $p < .05$), with a similar trend for YMRS ($Z = 1.34$, $p = .09$). For completeness, we also include a table of relationships to all clinical variables assessed in this study (see Supplemental Table 1).

EPILT

Training Phase

Diagnostic Group Effects: We observed significant main effects of Block, Probability, and Valence, with better performance across the blocks, in the 90% than the 80% conditions, and in avoiding loss versus gain conditions (see Table S2 and Figure 4). We also found a significant main effect of Diagnostic Group (Table S2). Post hoc tests indicated that the schizophrenia and schizoaffective groups performed worse than the healthy controls, and schizoaffective worse than bipolar with psychosis, but the bipolar individuals did not differ significantly than the healthy controls.

These main effects were qualified by significant interactions between Diagnostic Group, Block and Valence, as well as between Diagnostic Group, Block and Probability (Table S2). To identify the source of the interaction between Diagnostic Group, Block and Valence, we first asked whether the schizophrenia and schizoaffective groups differed from healthy controls in both valence conditions (all ps ≤ .06, see Figure 4). We then computed ANOVAs comparing each of the three patient groups to controls. The source of the interaction was the comparison of healthy controls to schizoaffective (see Figure 4), as the magnitude of the group differences was larger in blocks 1 and 4 for avoid loss, but larger in blocks 2 and 3 for gain. Similarly, we confirmed that the pattern of group differences described above held for both 80% and 90% probability conditions, finding that the schizophrenia and schizoaffective groups differed from healthy controls in these conditions (all ps ≤ .04, Figure 4). We then computed a follow up ANOVAs comparing each of the three patient groups to controls and determined that the source of the interaction was (see Figure 4) that the schizophrenia and schizoaffective groups differed from the bipolar with psychosis group only in blocks 1 and 2 for the 90% condition. Thus, the interactions with Block were not particularly meaningful, with the primary finding being a main effect of diagnostic group and some evidence for greater diagnostic group effects in the 90% versus 80% conditions.

Motivation/Pleasure Negative Symptom Effects—Like the IPILT, we also examined the effects of motivation and pleasure and negative symptom severity by conducting a similar ANOVA in just the patient groups, but adding the CAINS Motivation and Pleasure symptom score as a covariate (retaining diagnostic group as a between subject factor). This analysis indicated a significant main effect of Motivation and Pleasure score (F(1,144) 7.90, p = .006, η^2_p = .052), and no main effect of Diagnostic Group (F(2,144) = 1.36, p = .26, η^2_p = .019). There were no significant interactions of Motivation and Pleasure score with any of the other factors (all *ps > .19,* all η^2_ps < .011). Follow up regression analyses examining the association between Motivation and Pleasure scores and average accuracy indicated a significant negative relationship (*t = 2.45, p= .*015*, β= . −231),* with *higher* Motivation and Pleasure scores being associated with *reduced* accuracy.

Transfer Phase

Diagnostic Group Effects: As shown in Figure 5, this analysis revealed a significant main effect of Pairing (F(3,597) = 59.65, p <.001, η^2_p = .231) and a significant Diagnostic Group x Pairing interaction (F(9,597) = 2.45, p = .025, η^2_p = .036). As shown in Figure 5, post hoc contrasts indicated that the groups differed significantly on choosing stimuli associated with frequent winning over stimuli associated with infrequent winning (FW-IW; p=.004; healthy control = bipolar with psychosis > schizophrenia = schizoaffective) and on choosing stimuli associated with frequent loss avoidance versus stimuli associated with infrequent winning (FLA-IW; p=.031; healthy control = schizophrenia = bipolar with psychosis > schizoaffective). The groups also differed at the trend level on choosing stimuli associated with frequent winning versus frequent loss avoidance (FW-FLA; p = .089; healthy control > bipolar with psychosis), but did not differ on choosing stimuli associated with frequent winning versus frequent losing (FW-FL; p = .46).

Motivation/Pleasure Symptom Effects: There was no significant main effect of Motivation and Pleasure symptom score (F(1,144) = 1.234, p = .27, η^2_p = .009) and no significant main effect of Diagnostic Group (F(2,144) = 0.36, p = .72, η^2_p = .055). However, the significant interaction between Diagnostic Group and Pairing remained (F(2,144) = 2.48, p = .023, η^2_p = .033). As in the analysis above, the groups differed on choosing stimuli associated with frequent loss avoidance versus stimuli associated with infrequent wining (FLA-IW; p=.021; schizophrenia = bipolar with psychosis > schizoaffective).

Correlations with Clinical Symptoms—We again examined whether there were any effects of clinical symptom scores on EPILT performance within the patient groups, and whether these effects differed by diagnostic group. We focused on average training accuracy for the GAIN and AVOID LOSS conditions and transfer performance for FWvsIW, FLAvsIW and FWvsFLA. We again adjusted alpha level to control for the presence of five symptom predictors (*p <.05/5 < .01).* There were two significant main effect predictors of FWvsFLA. Individuals with higher depression on both the BPRS Depression subscale (*t =* −2.664*, p =* .009*, β=* −.28) and BDRS Depression (*t =* −3.68*, p =* .001*, β=* −.38) were less likely to choose stimuli associated with frequent winning versus frequent loss avoidance. For completeness, we also include a table of relationships to all clinical variables assessed in this study (see Supplemental Table 1).

Relationship to Working Memory—Some prior literature has suggested that working memory impairments make a significant contribution to reinforcement learning deficits in schizophrenia (Collins, et al., 2014). In the current study, we administered the Letter Number Sequencing Task from the MATRICS Consensus Cognitive Battery. Thus, we asked whether there was a relationship between working memory and learning in the EPILT tasks, using overall GAIN or AVOID LOSS accuracy, as well as performance in the transfer phase. Among controls, working memory was significantly correlated with GAIN accuracy (r = .31, p = .02), FWvsFL (r = .36, p = .007), and FWvsIW (r = .36, p = .007). Among the patients, working memory was significantly correlated with GAIN (r = .26, p = .002), and LOSS (r = .29, p = .001), accuracy, as well as with FLAvsIW (r = .20, p = .016), FWvsFL (r = .23, p = .005), and FWvsIW (r = .30, p = .001). We then asked whether the diagnostic or Motivation and Pleasure symptom score effects remained if we controlled for working memory. For the training phase analyses as a function of Diagnostic Group, the main effect of group continued to be significant (F(3,194) = 2.76, p = .043, η^2_p = .041), though only the individuals with schizoaffective disorder continued to be worse than the healthy controls. However, importantly, the analysis as a function of Motivation and Pleasure score remained significant (F(3,194) = 4.59, p = .034, η^2_p = .032), with individuals with worse Motivation and Pleasure scores having worse performance. For the transfer phase analyses as a function of Diagnostic Group, the interaction between Diagnostic Group and Pairing also continued to be significant (F(9,582) = 2.49, p = .023, η^2_p = .037), with group differences only present for FLA-IW (p=.016; healthy controls = schizophrenia = bipolar with psychosis > schizoaffective). Thus some diagnostic differences observed in explicit RL may be a function of working memory (or even cognitive deficits more generally), whereas this was less likely to be the case for the Motivation and Pleasure symptom effects.

For comparison, we also examined the relationship between working memory and IPILT performance. Among controls, there were no significant relationships with either average bias or change in bias from block 1 to block 3 in either the positive or negative versions (all rs < |.11|). Among patients, there was only one significant association (r = −.26, p = .002), with better working memory associated with overall lower bias on the IPILT-N. None of the other correlations were significant (all rs < |.11|).

Correlations Between IPILT and EPILT and Differential Relationships to Motivation and Pleasure Symptoms and Working Memory—There were no significant correlations between performance on the IPILT and EPILT tasks, either in the sample as a whole or when the sample was split by healthy control and patient, or into each diagnostic group separately. However, given the very different structure of the tasks, direct comparisons are difficult. Nonetheless, we can ask whether the presence of relationships to Motivation and Pleasure symptoms scores and working memory for the explicit RL task and not the implicit RL tasks reflect significant differences in the magnitude of these relationships. Using the formulas from Meng, Rosenthal and Rubin (Meng, et al., 1992), we found that GAIN accuracy was more strongly associated with Motivation and Pleasure symptoms scores that either average bias on the IPILT-P (Z = 2.42, p =.007), or the IPILT-N (Z = 3.46, p <.001). Similarly, LOSS accuracy was more strongly associated with Motivation and Pleasure symptoms scores that either average bias on the IPILT-P (Z = 2.19,

p =.01), or the IPILT-N ($Z = 3.30$, p <.001). GAIN accuracy was significantly more strongly positively associated with letter number sequencing scores than average bias IPILT-N ($Z = -4.15$, p <.001). LOSS accuracy was significantly more strongly positively associated with letter number sequencing scores than average bias IPILT-N ($Z = -4.36$, p <.001), with a similar trend for average bias on the IPILT-P ($Z = -1.57$, p =.057).

Discussion

The goal of the current study was to use tasks that measure both positive and negative components of implicit and explicit RL to examine reinforcement learning within and across the spectrum of psychotic disorders. As predicted, we found relatively intact performance across diagnostic groups on the implicit RL tasks, but evidence for impairment on the explicit RL tasks. However, contrary to our predictions, we did not see strong evidence for greater impairment in learning from reward versus learning to avoid loss on the explicit RL tasks. At the diagnostic level, individuals with bipolar with lifetime psychosis were less impaired on explicit RL than other patients, though higher mania symptoms among individuals with bipolar disorder were associated with greater positive bias in the positive implicit RL task. At the symptom level, more severe motivation and pleasure negative symptoms were related to worse performance in both negative and positive explicit RL learning across diagnostic boundaries. Each of these findings will be discussed in more detail below.

Across all participants, we saw the predicted bias effects in both the positive and negative versions of the implicit learning task, with a bias towards the rewarded response in the IPILT-P and a bias towards the non-punished response in the IPILT-N. As predicted, we did not find any significant diagnostic group differences from healthy controls on either the positive or negative version of the IPILT. This result is consistent with prior literature in schizophrenia (Ahnallen, et al., 2012; Heerey, et al., 2008). However, two previous studies of bipolar disorder did find some evidence for impaired implicit RL, though these studies were not focused on bipolar disorder with psychosis (Pizzagalli, et al., 2008). One potential interpretation of the observed lack of diagnostic group differences is relatively intact striatal slow learning systems among individuals with psychosis, at least among medicated patients. However, it may also reflect the fact that the influence of reward and punishment on this RL task paradigm is through bias to choose one response or another, rather than through accuracy, and thus may in some sense be less “difficult” than paradigms that use reward and punishment to drive learning. Another putative task of implicit RL is the Weather Prediction Task, which does involve using feedback to drive learning. On this task, there is mixed evidence in schizophrenia with findings of both relatively intact learning rates (Beninger, et al., 2003; Keri, et al., 2000; Keri, et al., 2005; Weickert, et al., 2002) as well as impaired learning rates (Weickert, et al., 2010; Weickert, et al., 2013). However, a number of studies have provided evidence suggesting that explicit learning can play a major role in the Weather Prediction Task (Kemeny, 2014; Kemeny & Lukacs, 2013; Newell, Lagnado, & Shanks, 2007; Price, 2005). For example, Newell et al found that performing a concurrent memory task reduced learning on the Weather Prediction Task, which is consistent with the idea that performance is not purely based on implicit learning. To our knowledge, this has not been evaluated with the IPILT, and would be an important direction for future work to

establish whether the bias effects indeed reflect implicit learning and to determine whether a secondary this differentially disrupts bias development on the IPILT in psychosis. Our prediction would be that a secondary task does not disrupt bias development in the IPLIT either in controls or in patients.

We did find some evidence for relationships between performance on the implicit RL tasks and motivation or pleasure negative symptoms. However, these relationships were modest and were in the direction of higher motivation and negative symptoms being associated with greater sensitivity to reward and loss, which was not the expected direction. Interestingly however, we did see a relationship between more severe mania symptoms and greater bias towards reward, but only among individuals with bipolar disorder with lifetime psychosis. This finding is consistent with prior work in bipolar disorder suggesting increased striatal responses to rewards (Dutra, Cunningham, Kober, & Gruber, 2015), and with theories about reward hypersensitivity as a risk factor and/or characteristic of bipolar disorder (Alloy, Nusslock, & Boland, 2015; Johnson, Edge, Holmes, & Carver, 2012a). It is intriguing that we only saw this relationship among individuals with bipolar disorder with psychosis and not in schizophrenia or schizoaffective. This significantly different relationship in bipolar disorder cannot be explained by greater levels of mania symptoms among the individuals with bipolar disorder, as the individuals with schizoaffective actually had the highest mean values of mania symptoms and the greatest range. As such, it is possible that this finding reflects a differential relationship that may exist in individuals with bipolar disorder that is not shared across the psychosis spectrum.

In the explicit RL task, consistent with our predictions, we saw evidence for impaired explicit reinforcement learning during the training phase in both people with schizophrenia and schizoaffective disorder. However, contrary to expectations, we did not see evidence for impaired learning during the training phase in bipolar disorder. Importantly however, when we examined the relationships to motivation and pleasure symptoms, we saw significantly greater impairment in explicit RL learning among patients with higher symptoms across diagnostic groups. This finding is consistent with prior work suggesting greater impairments in explicit RL among patients with schizophrenia who have more severe negative symptoms and is consistent with an RDoC transdiagnostic dimensional approach to understanding psychopathology symptoms.

In contrast to our predictions, we did not see significant interactions with valence (GAIN or AVOID LOSS) or probability (80/20 or 90/%) and either diagnostic group or Motivation and Pleasure symptom severity, with evidence for impaired learning on both GAIN and AVOID LOSS among people with schizophrenia and schizoaffective disorder and among patients with worse Motivation and Pleasure symptom scores. This is somewhat inconsistent with previous studies showing greater impairments among people with schizophrenia who have worse Motivation and Pleasure scores when they must learn from reward versus from punishment (Cheng, et al., 2012; Gold, Waltz, et al., 2012; Reinen, et al., 2014; Waltz, et al., 2007), though several other studies have also found impaired learning from punishment (Cicero, et al., 2014; Fervaha, et al., 2013). Thus, these results add to the literature documenting impaired explicit RL in psychosis, at least those with more severe negative

symptoms, but are more consistent with a general impairment in explicit RL, rather than a specific impairment in learning from reward.

Importantly, our follow up analyses examining the relationship with working memory suggested, consistent with prior literature (Collins, et al., 2014), that some of the group level variance in RL performance, at least in schizophrenia, is accounted for by working memory function. As such, one interesting speculation is that the evidence for impairment on the explicit RL tasks but not the implicit RL tasks among individuals with schizophrenia and schizoaffective reflects the greater working memory demands associated with the explicit RL tasks. We did not find any association between working memory and implicit RL performance among controls, and only one significant association in patients. However, we continued to see impairments among patients with high Motivation and Pleasure scores even when accounting for working memory, suggesting that at least some of the variance in explicit RL among patients with more severe motivation and pleasure symptoms is not secondary to working memory deficits. This of course also raises the question of why more severe motivation and pleasure symptoms were related to worse performance on explicit RL and not implicit RL. We would argue that this is consistent with the evidence in the literature that amotivation and anhedonia are not related to impairments in reward responsiveness or reward experience per se (which may be more captured by implicit RL), but more to the ability to use reward or incentive information to guide motivated behavior (which may be better captured by explicit RL) (Kring & Barch, 2014).

In the transfer phase, all patient groups showed intact sensitivity to the frequency of losing versus winning, as all groups were similar in their greater choice of frequent winners over frequent losers. However, individuals with schizophrenia and schizoaffective showed less sensitivity to the frequency of winning, as they were less likely than controls to chose frequent winners over infrequent winners. This reduction in sensitivity to winning remained, at least in the schizoaffective disorder group, when controlling for working memory function. Further, the individuals with schizoaffective disorder showed reduced sensitivity to loss avoidance, as they were less likely than controls and individuals with bipolar disorder to choose stimuli associated with frequent loss avoidance over stimuli associate with wining infrequently. Taken together, these data indicate some evidence of being less sensitive to frequent reward amongst the patient groups, with the most consistent effects present for the individuals with schizoaffective disorder. This finding is generally consistent with the prior work of Gold, who also found impaired FW-IW performance among patients, only among those with worse Motivation and Pleasure symptoms. In contrast, we did not find that transfer task performance varied as a function of Motivation and Pleasure symptom severity. Also consistent with Gold (Gold, Waltz, et al., 2012), we found that schizophrenia patients were similar to controls in the FLA vs. IW pairing, hinting at somewhat more intact learning to avoid loss, but we did see reduced sensitivity to frequent loss avoidance in the schizoaffective disorder patients. However, we did not find evidence for reduced choice of frequent winners over frequent loss avoiders, which is not consistent with the findings of Gold (Gold, Waltz, et al., 2012). Thus, the transfer phase results provided only partial replication of the prior findings of Gold, though they did provide some modest evidence of greater impairment in learning about items associated with reward versus those associated with avoiding loss.

There are a number of important limitations that must be kept in mind when interpreting these results. First, all of the patients were taking medications that influence neurotransmitter systems thought to be important for RL, such as dopamine. As such, it is possible that that the impairment on the explicit RL tasks reflected a negative impact of antipsychotic medication. However, the people with bipolar disorder were as likely to be on antipsychotic medications as the people with schizophrenia and schizoaffective disorder, but did not show impairment in explicit RL learning. This pattern argues against the impaired performance in schizophrenia and schizoaffective disorder simply being secondary to antipsychotic medications. Nonetheless, examination of performance on these tasks among individuals with psychosis not taking antipsychotic medications will be necessary to clarify this issue. Second, the majority, though not all, of the patients were in a chronic, stable phase of their illness. Thus, we cannot rule out the possibility that we might see greater evidence for impairments in implicit RL in early phase or more acutely ill individuals.

Taken together, these data also provide evidence for greater impairment on tasks designed to assess explicit as compared to implicit RL, both as a function of diagnosis and as a function of negative symptom severity. However, this finding must be moderated by the fact that the task structures were quite different, and not directly comparable in terms of key factors such as task difficulty and discriminating power given their differing designs. Further, these findings provide strong evidence for a relationship between the severity of motivation and pleasure negative symptoms and impaired performance on explicit RL tasks. Importantly, these relationships transcended diagnostic category, and suggest that variation in symptom severity is a key factor driving explicit RL performance across diagnostic boundaries among individuals with psychotic disorders. Interestingly however, we saw relationships between the severity of manic symptoms and greater bias on the implicit RL tasks, but only among individuals with a diagnosis of bipolar disorder. This suggests a symptom-behavior relationship that may be more diagnostically specific.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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General Scientific Summary

Individuals with different forms of psychosis, such as schizophrenia, schizoaffective disorder, and bipolar disorder with lifetime psychosis often have difficulties with motivated behavior and processing incentive information. However, it is not clear whether the same impairments are present across psychotic disorders, and whether they relate to symptoms in the same way. Here we show that individuals with psychotic disorders have relatively intact performance on tasks measuring "implicit (i.e., outside of conscious awareness)" learning about incentives. In contrast, individuals with psychotic disorders, particularly schizophrenia and schizoaffective disorder, have more problems with "explicit" learning about incentives, which is related to the severity motivation and pleasure symptoms across psychotic disorders.

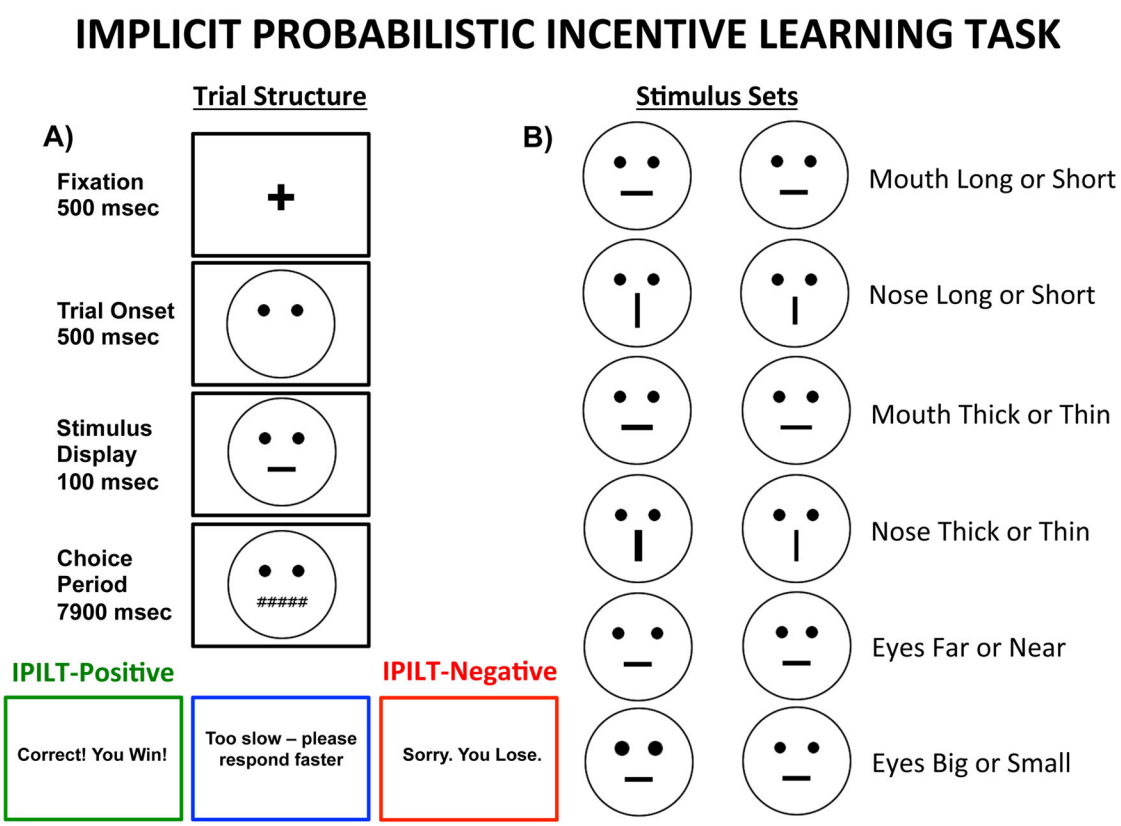

Figure 1.
Schematic and Stimulus Examples for the Implicit Probabilistic Incentive Learning Tasks (IPILT)

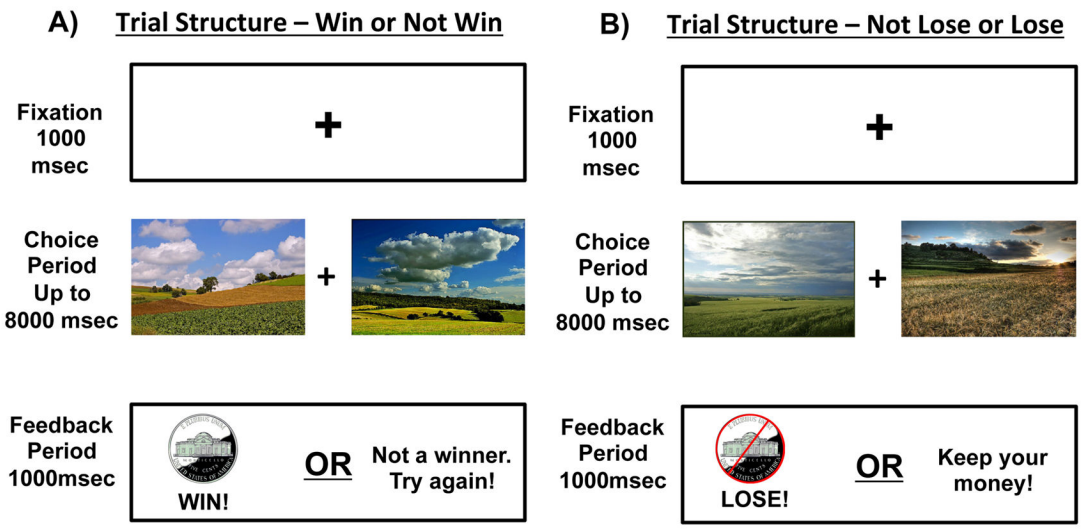

Figure 2.
Schematic and Stimulus Examples for the Explicit Probabilistic Incentive Learning Task (EPILT)

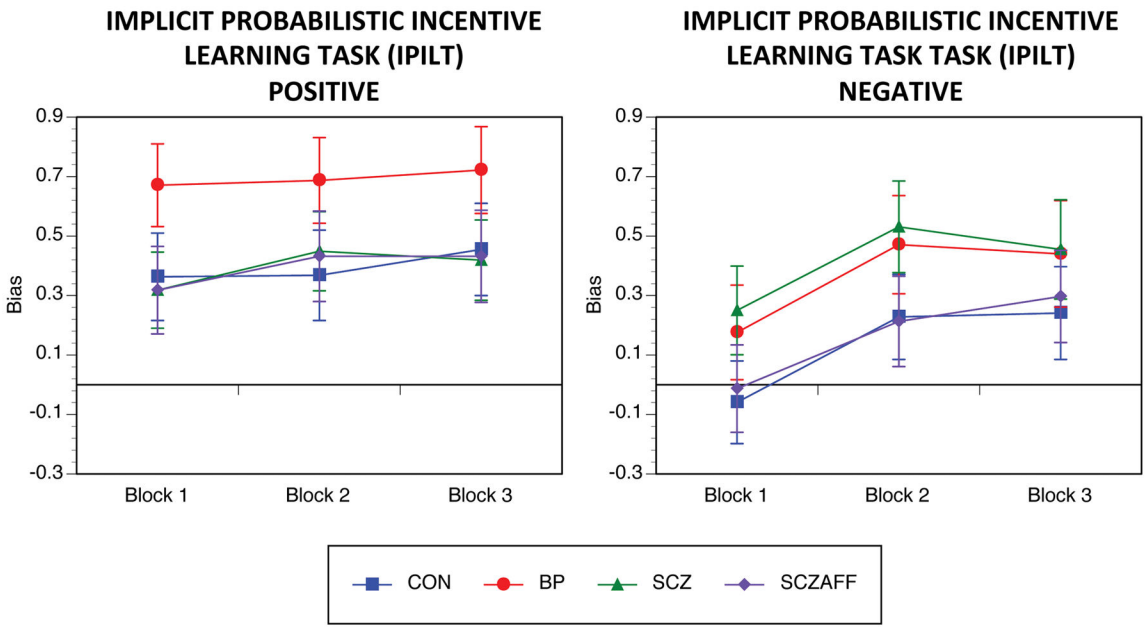

Figure 3.

Diagnostic Group Differences on the Implicit Probabilistic Incentive Learning Tasks (IPILT) Tasks. Panel A is for the Positive I-PILT version and Panel B is for the Negative IPILT version. Bias scores in Panel A reflect bias *towards the rewarded* responses and bias scores in Panel B reflect bias away from the punished response, but are plotted as positive values for ease of graphing.

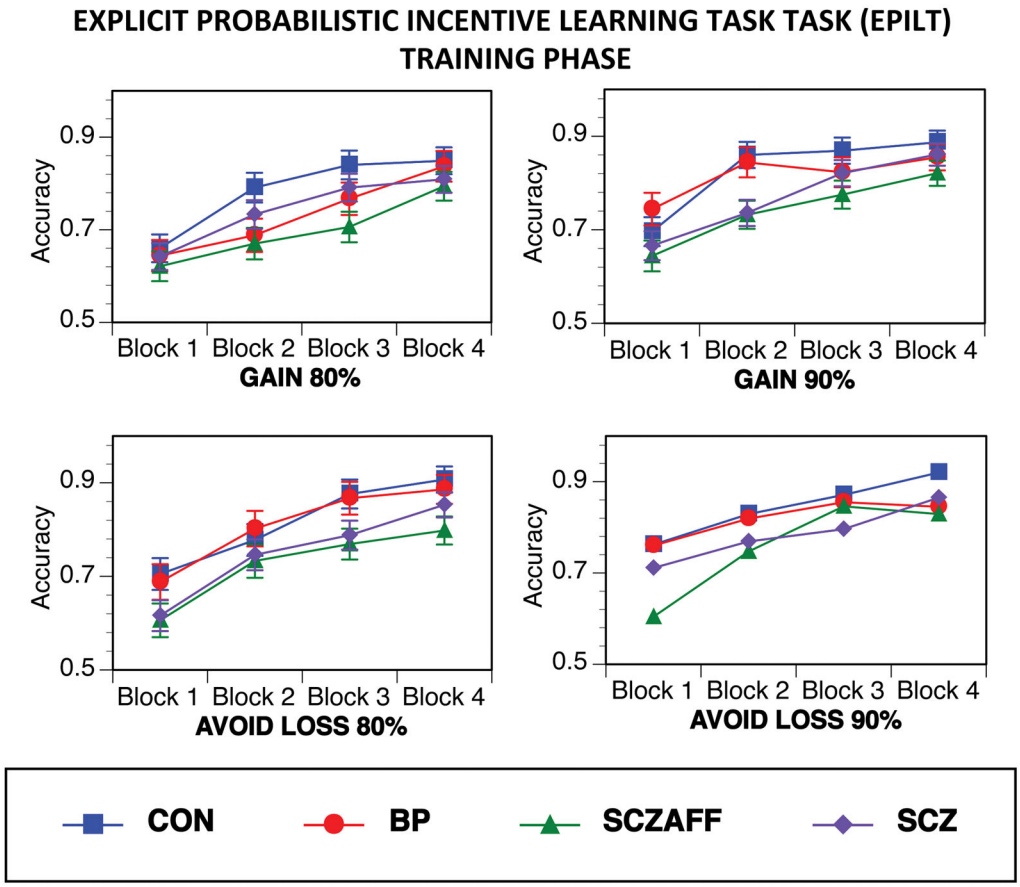

Figure 4.
Training Performance in the Explicit Probabilistic Incentive Learning Task (EPILT) as A Function of Diagnostic Group.

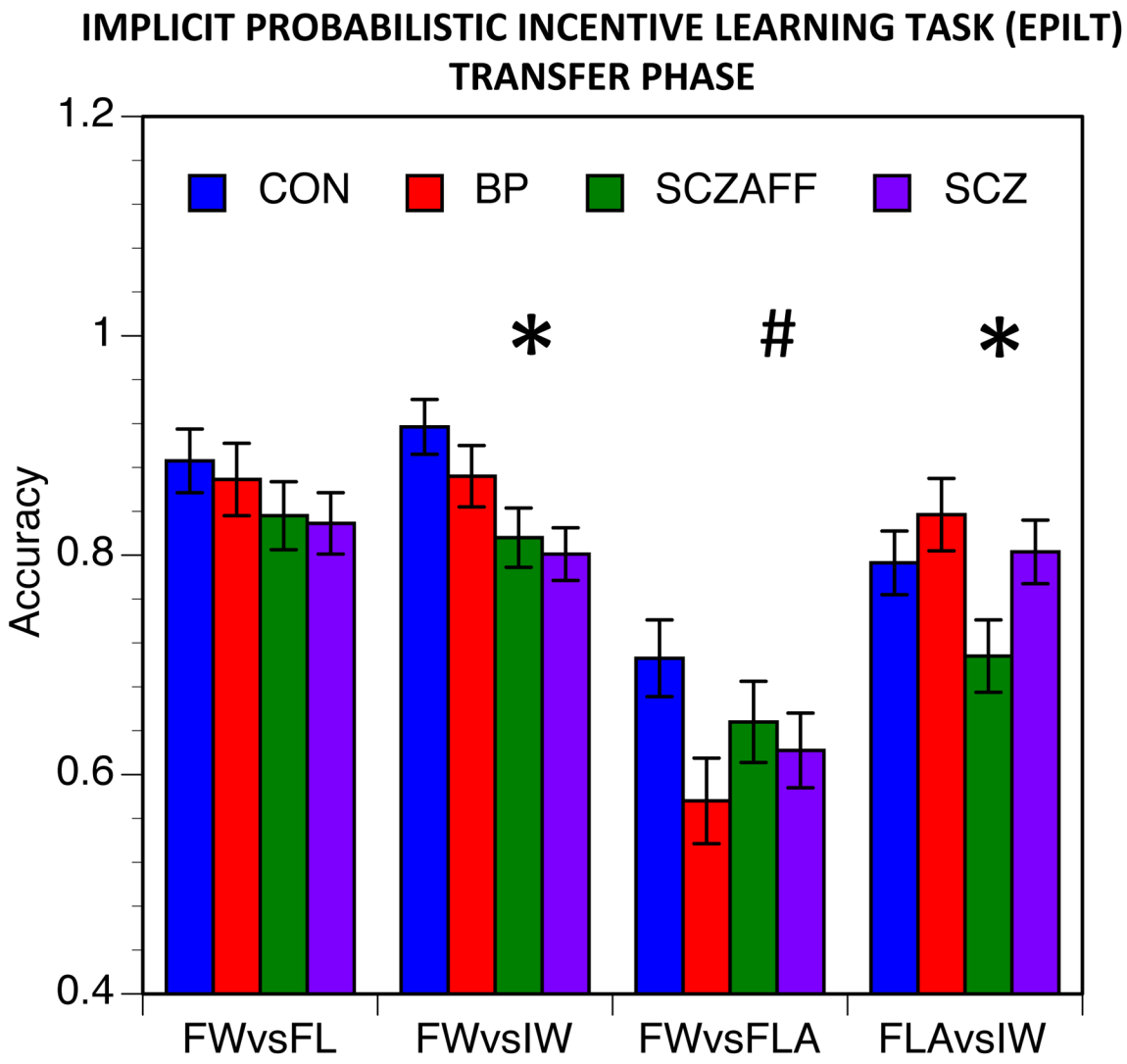

Figure 5.
Transfer Performance in the Explicit Probabilistic Incentive Learning Task (EPILT) as A Function of Diagnostic Group.

Table 1

Demographic and Clinical Characteristics of the Sample

	Healthy Controls (HC)		Schizophrenia (SCZ)		Schizoaffective Disorder (SCZAFF)		Bipolar with Lifetime Psychosis (BP)		Group Differences
	M	SD	M	SD	M	SD	M	SD	
Age	36.0	11.1	37.9	11.6	39.5	11.7	35.4	10.0	NS
Gender (% Female)	46%		40%		48%		56%		NS
Race (% Black)	27%		40%		25%		26%		NS
Personal Education	14.8	2.0	13.3	2.3	13.6	2.8	13.7	2.6	HC > SCZ; SCZAFF; BP
Parental SES	44.6	13.6	44.4	14.1	44.7	16.3	47.0	17.0	NS
Wechsler Test of Adult Reading	39.5	8.7	31.7	9.3	36.3	10.5	33.6	11.8	HC > SCZ; SCZAFF; BP
BPRS Positive	--		7.4	4.4	8.2	3.4	4.2	2.0	SCZ; SCZAFF > BP
BPRS Negative	--		7.7	3.2	7.3	2.3	6.0	2.2	SCZ; SCZAFF > BP
BPRS Disorganization	--		5.0	1.6	4.9	1.4	4.5	0.9	NS
BPRS Depression	--		7.5	3.5	11.0	4.4	9.3	4.4	SCZAFF > SCZ; BP
BPRS Mania	--		6.7	2.3	7.0	2.6	6.7	2.6	NS
Young Mania Rating Scale	--		8.2	6.6	11.8	7.4	7.2	7.3	SCZAFF > SCZ; BP
Bipolar Depression Rating Scale	--		9.6	6.2	14.6	7.6	11.5	7.5	SCZAFF > SCZ; BP
CAINS Motivation & Pleasure	--		10.6	6.1	11.7	5.9	7.74	4.9	SCZ; SCZAFF > BP
CAINS Expression	--		3.7	3.4	2.3	2.1	1.3	2.1	SCZ > SCZAFF > BP
SLOF Self Report	--		4.3	0.5	4.2	0.4	4.3	0.5	NS
SLOF Informant	--		4.3	0.6	4.2	0.6	4.3	0.4	NS
Olanzapine Equivalents	--		20.09	20.7	15.52	12.13	8.3	8.44	SCZ; SCZAFF > BP
Typical Antipsychotic	--		8.8%		6.3%		2.3%		NS
Atypical Antipsychotic			75.4%		66.7%		67.4%		NS
Both Typical and Atypical	--		8.8%		12.5%		2.3%		NS
Clozapine	--		17.5%		8.3%		2.3%		SCZ > BP

BPRS = Brief Psychiatric Rating Scale; CAINS = Clinical Assessment Interview for Negative Symptoms; SLOF = Specific Levels of Function Scale

Table 2

Pairings Used for Analysis in Transfer Phase of EPILT

Pairing Type	Acronym	Description
Frequent Winner [FW] vs. Frequent Loss Avoider [FLA] **Meaning**: Relative sensitivity to gain versus loss avoidance	FW-FLA	16 trials, with 4 of each pairing: 90%-FW vs. 90%-FLA 90%-FW vs. 80%-FLA 80%-FW vs. 90%-FLA 80%-FW vs. 80%-FLA
Frequent Winner [FW] versus Infrequent Winner [IW] **Meaning**: Relative sensitivity to frequency of feedback about gain	FW-IW	12 trials with 4 each of the original pairings: 90%FW vs. 10%-IW 80%-FW vs. 20%-IW]; + 2 each of: 90%-FW vs. 20%-IW 80%-FW vs. 10%-IW
Frequent Winner [FW] vs. Frequent Loser [FL] **Meaning**: Relative sensitivity to gain versus loss	FW-FL	8 trials, with 2 trials each of: 90%-FW vs. 90%-FL 90%-FW vs. 80%-FL 80%-FW vs. 90%-FL 80%-FW vs. 80%-FL
Frequent Loss Avoider [FLA] vs. Infrequent Winner [IW] **Meaning**: Relative sensitivity to frequent loss avoidance versus less frequent gain	FLA-IW	8 trials, with 2 trials each of: 90%-FLA vs. 90%-IW 90%-FLA vs. 80%-IW 80%-FLA vs. 90%-IW 80%-FLA vs. 80%-IW