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Reinforcement learning deficits in people with schizophrenia persist after extended trials

David C. Cicero [a,*], Elizabeth A. Martin [b], Theresa M. Becker [c], John G. Kerns [d]

[a] Department of Psychology, University of Hawaii at Manoa, Honolulu, HI, United States
[b] Department of Psychology, University of California, Irvine, Irvine, CA, United States
[c] Institute for Learning and Brain Sciences, University of Washington, Seattle, WA, United States
[d] Department of Psychology, University of Missouri, Columbia, MO, United States

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ABSTRACT

Previous research suggests that people with schizophrenia have difficulty learning from positive feedback and when learning needs to occur rapidly. However, they seem to have relatively intact learning from negative feedback when learning occurs gradually. Participants are typically given a limited amount of acquisition trials to learn the reward contingencies and then tested about what they learned. The current study examined whether participants with schizophrenia continue to display these deficits when given extra time to learn the contingences. Participants with schizophrenia and matched healthy controls completed the Probabilistic Selection Task, which measures positive and negative feedback learning separately. Participants with schizophrenia showed a deficit in learning from both positive feedback and negative feedback. These reward learning deficits persisted even if people with schizophrenia are given extra time (up to 10 blocks of 60 trials) to learn the reward contingencies. These results suggest that the observed deficits cannot be attributed solely to slower learning and instead reflect a specific deficit in reinforcement learning.

1. Introduction

One common deficit associated with schizophrenia is reinforcement learning (Waltz and Gold, 2007; Ziauddeen and Murray, 2010; Dowd and Barch, 2012). This deficit is thought to be associated with dopamine dysregulation (Guillin et al., 2007), and a long line of research suggests that dopamine dysregulation plays an important role in schizophrenia and psychosis (Seeman, 1987; Davis et al., 1991; Laruelle and Abi-Dargham, 1999; Abi-Dargham et al., 2000; Howes and Kapur, 2009; Heinz and Schlagenhauf, 2010). Understanding deficits in reward processing deficit may provide insight into important motivational deficits that may be a future target of treatment in schizophrenia-spectrum disorders (Gold et al., 2008; Ziauddeen and Murray, 2010).

In previous work, one common strategy for assessing reinforcement learning deficits is to give participants a relatively limited number of "acquisition" trials in which participants learn the reinforcement contingencies prior to a "testing" phase in which participants choose among the stimuli (Frank et al., 2004). Several previous studies using this paradigm have shown that people with schizophrenia have difficulty learning from positive feedback, but tend to have intact learning from negative feedback (Waltz et al., 2007; Strauss et al., 2011; Waltz et al., 2011). At the same time, some research has found that people with schizophrenia tend to learn reward contingencies more slowly in rapid learning situations, but to have relatively intact gradual or long-term learning (Gold et al., 2008; Morris et al., 2008; Weiler et al., 2009).

Rapid learning is thought to be mediated by the prefrontal cortex (PFC), while gradual learning is thought to be mediated by the basal ganglia (BG; Frank and Claus, 2006). Previous work has found that patients with schizophrenia seem to have relatively normal basal ganglia-mediated gradual learning, but impairments in rapid trial-to-trial learning mediated by the PFC (Gold et al., 2012). If people with schizophrenia have intact BG-mediated gradual learning, then it is possible that they would "catch up" to healthy controls if given enough trials to learn the reward contingencies. If this is the case, then participants with schizophrenia should show similar learning on both positive feedback and negative feedback to comparison participants if they are given more trials during the acquisition phase to gradually learn the reward contingencies. However, if participants are unable to learn the reward contingencies after extended trials, then we can conclude that the deficit is not simply related to slower learning, but is a deficit related to reward learning specifically.

* Correspondence to: Department of Psychology, University of Hawaii at Manoa, 2530 Dole Street, Sakamaki D-406, Honolulu, HI 96822-2294, United States. Tel.: +1 808 956 3695.
E-mail address: dcicero@hawaii.edu (D.C. Cicero).

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The primary goal of the current research was to examine whether participants with schizophrenia would continue to show a deficit in positive feedback learning even if given enough trials to ensure gradual learning of the reward contingencies. In previous research using the same task as the current research, participants are usually given up to 180 trials (three blocks of 60 trials) to acquire reward contingencies. In the current research, participants were given up to 600 trials (10 blocks of 60 trials) to learn reward contingencies before progressing to the testing phase of the study. In addition, to test the pace at which participants learned reward contingencies, we conducted a survival analysis to see if healthy controls learned the reward contingencies more quickly than did participants with schizophrenia.

2. Methods

2.1. Participants

Participants were 54 people with a diagnosis of schizophrenia and 32 non-psychiatric controls. Participants in the schizophrenia group all met criteria for either schizophrenia or schizoaffective disorder and were recruited from a state mental hospital with a largely forensic population. They were 49.1% White, 36.4% African-American, and 10% mixed ethnicities. 87.3% of these participants were male. Participants in the comparison group were recruited via online advertisements on Craigslist and an email sent to all university employees. These comparison participants had no history of Axis I mental disorders, and were 93.9% White, 3% African-American, and 3% other. 90.9% of the control group was male. Participants were matched on sex, age, and parental education. Demographic characteristics for both groups of participants are presented in Table 1. All participants received $30 for participating in the study.

2.2. Materials

2.2.1. Reinforcement learning

The Probabilistic Selection Task (PSS; Frank et al., 2004) was used to measure reinforcement learning. In particular, the PSS assesses participants' ability to learn from positive feedback as well as from negative feedback. Following previous research (Waltz et al., 2011), the PSS was modified for use with participants with schizophrenia. Instead of using unfamiliar Hiragana characters as in the original paper (Frank et al., 2004), more familiar pictures were used (i.e., an egg, bus, wrench, clock, leaf, and cow). Familiar characters were used due to reports in the literature that patients had difficulty learning reward contingencies with unfamiliar symbols (Waltz et al., 2007). The PSS contains two phases: the acquisition and testing phase. In the acquisition phase, participants choose the correct stimulus from stimulus pairs, which are reinforced probabilistically. In the AB pair, A is rewarded 80% of the time, while B is rewarded only 20% of the time. In the CD pair, C is rewarded 70% of the time while D is rewarded only 30% of the time, and in the EF pair, E is rewarded 60% of the time while F is rewarded 40% of the time. Each block of the acquisition phase consists of 60 trials. Participants continue the acquisition phase of the task until they learn to reliably choose A over B (at least 70% of the time), C over D (at least 60% of the time), and E over F (at least 50% of the time) before moving on to the testing phase. Participants were instructed in the task following Frank et al. (2004). No practice trials were done prior to the first acquisition block. In the current research, participants completed the acquisition block up to ten times.

In the testing phase, participants are presented with novel combinations of stimuli (e.g., AD, AF, BC, BF) and asked to choose a stimulus in the absence of feedback. The dependent variables are the percentage of time participants choose A (i.e., positive feedback learning) and the percentage of times participants avoid B by choosing the stimulus paired with B (i.e., negative feedback learning) in the testing phase.

Table 1
Demographic and clinical information.

Variable	Schizophrenia group ($n=54$)	Control group ($n=32$)
Sex (% male)	87.3%	90.9%
Ethnicity (% Caucasian)	49.1%	93.9%
Mean (S.D.) age (years)	41.46 (11.55)	43.00 (9.63)
Mean (S.D.) education (years)	12.61 (7.83)	16.11 (1.76)
Mean (S.D.) parental education	11.82 (1.75)	12.70 (2.07)
Mean (S.D.) BPRS (total)	37.34 (9.13)	
Thought disturbance	13.94 (4.93)	
Negative symptoms	8.53 (2.94)	
Depression/anxiety	9.94 (3.81)	
Disorganization	5.44 (1.81)	
Negative symptoms		
Social anhedonia	15.39 (6.43)	10.36 (7.69)
Physical anhedonia	16.37 (7.21)	11.60 (6.91)

2.2.2. Diagnosis and symptom ratings

Diagnoses were made with the Structured Clinical Interview for the DSM-IV (SCID; First et al., 1998). The SCID has high test–retest and inter-rater reliability (Zanarini et al., 2000; Zanarini and Frankenburg, 2001). Symptoms were rated with the Brief Psychiatric Rating Scale (Overall and Gorham, 1962), and scores are presented in Table 1. Following McMahon et al. (2002), we calculated factor scores for Reality Distortion, Negative Symptoms, Anxiety/Depression, and Disorganization. The intraclass correlation coefficient for BPRS total scores was 0.87.

In addition to BPRS ratings, negative symptoms were measured with the Social Anhedonia Scale (RSAS; Eckbald et al., 1982) and the Physical Anhedonia Scale (PhysAnh; Chapman et al., 1976). The RSAS is a 40-item true-false questionnaire designed to measure lack of relationships and lack of pleasure from relationships. The PhysAnh is a 61-item true/false questionnaire designed to measure a lack of pleasure from or interest in physical sensations. In the current research, the RSAS and PhysAnh both had internal reliabilities of alpha $=0.83$.

2.2.3. Mental status

Participants completed the Mini-Mental Status Exam (MMSE). The MMSE is one of the most commonly used screening measures for cognitive impairment and dementia (Hodges, 1994; Manning et al., 2007). MMSE scores have been found to have high inter-rater reliability (Tombaugh and McIntyre, 1992), internal consistency, and well-established normative data (Tombaugh et al., 1996). In the current research, the MMSE was used to screen for and exclude participants with dementia.

2.3. Procedure

First, participants read and signed the informed consent form. Then, they were given the Mini Mental Status Exam. All participants exceeded the cutoff of 22 on the Mini Mental Status Exam, which suggests that all participants did not have dementia. Then participants completed the Probabilistic Selection Task. Next, the Structured Clinical Interview for the DSM-IV was conducted.

3. Results

3.1. Group comparisons for reward learning

First, we examined the pace at which participants learned the reward contingencies during the acquisition phase. As can be seen in Tables 1, 40.4% of schizophrenia participants and 34.4% of comparison participants did not meet learning criteria (i.e., choose A 70% of the time, C 60% of the time, and E 50% of the time) even after up to 10 blocks of trials. To test whether participants in the comparison group met criteria more quickly than did schizophrenia participants, we conducted a survival analysis with meeting criteria as the status category. As can be seen in Fig. 1, there was a non-statistically significant trend for comparison participants to meet criteria more quickly than did participants with schizophrenia (Wald Statistic$=2.70$, $\beta=0.17$, OR$=1.18$, CI 0.97–1.45). The trend is evident in that the confidence interval of the odds ratio is 0.97–1.45, which nearly does not include 1.00. However, there was not a significant difference between groups in the number of participants who met criteria by the end of 10 blocks ($\chi^2(1)=0.48$, $p=0.49$). Thus, by the end of 10 blocks, there was no significant difference in the percentage of people with schizophrenia and comparison participants who met learning criteria. Participants who met criteria did not differ from participants who did not meet criteria in MMSE scores ($M=27.08$, S.D.$=2.84$ vs. $M=27.23$, S.D.$=2.11$. $t(80)=0.25$, $p=0.80$), and MMSE scores were not correlated with positive feedback ($r=0.08$, $p=0.48$) or negative feedback learning ($r=0.08$, $p=0.48$).

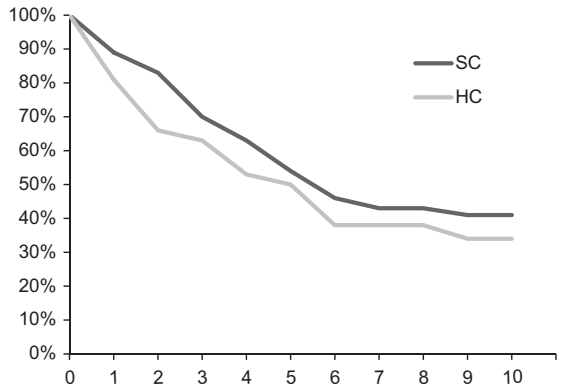

Fig. 1. Survival analysis of the block in which participants met learning criteria. SC=schizophrenia, HC=healthy control.

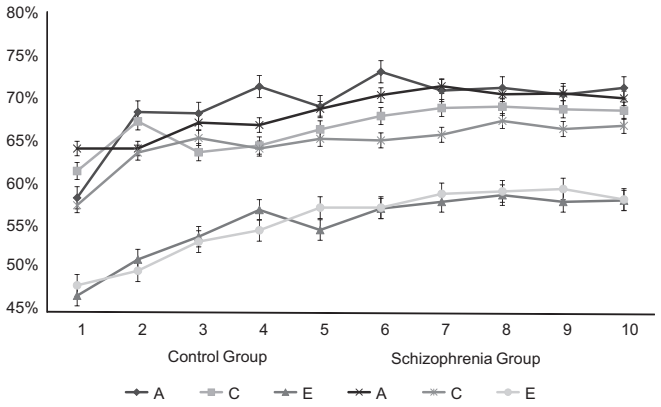

Fig. 2. Learning curves for participants with schizoprhenia and healthy controls for AB, CD, and EF pairs during the acquisition trials.

To test whether the two groups learned at different paces during the acquisition phase, a repeated measures ANOVA was computed with group and block entered as fixed factors and percentage of trials in which participants chose A instead of B during each block as the outcome variable. Since participants varied in how many blocks they completed, we used a Last Observation Carried Forward method. The group by block interaction was not significant ($F(1, 9)=1.42$, $p=0.17$), which suggests that there was no significant difference in learning pace between groups across all 10 blocks. As mentioned, however, few participants improved their learning after the sixth block. Thus, we ran this same analysis for just the first six blocks. There was a trend for group by block interaction ($F(1, 5)=1.99$, $p=0.08$), which suggests that participants with schizophrenia learned more slowly than did healthy controls. Fig. 2 shows the learning pace by block for all three pairs of stimuli. To further examine whether participants in the schizophrenia group learned more slowly than did participants in the healthy control group, we examined whether the schizophrenia and healthy control group differed in the mean percentage of time when they chose A during the first two blocks. There was no significant difference in Block 1 for the schizophrenia and healthy control groups ($M=0.64$, S.D.$=0.24$ vs. $M=0.58$, S.D.$=0.26$, $F(1,84)=1.38$, $p=0.24$) or in Block 2 ($M=0.64$, S.D.$=0.26$ vs. $M=0.68$, S.D.$=0.27$, $F(1,84)=0.56$, $p=0.57$).

Second, we examined whether participants with schizophrenia were impaired in positive or negative feedback learning during the testing phase of the PSS. Participants with schizophrenia chose the rewarded stimulus (A) less in the testing phase than did control participants ($M=0.58$, S.D.$=0.20$, vs. $M=0.67$, S.D.$=0.20$; $t(84)=2.02$, $p=0.047$; *Cohen's* $d=0.45$). However, participants with schizophrenia and control participants did not significantly differ in the percentage of the time that they avoided the non-rewarded stimulus ($M=0.55$, S.D.$=0.25$, vs. $M=0.63$, S.D.$=0.24$; $t(84)=1.25$, $p=0.22$; *Cohen's* $d=0.33$). To examine whether this was a specific learning deficit in relation to learning from positive feedback, we ran a factorial ANOVA including a group by valence interaction effect. There was not a significant interaction between group and valence of reward ($F(1, 82)=0.01$, $p=0.93$). There was a significant main effect for group ($F(1, 82)=4.11$, $p=0.046$).[1] Taken together, these results suggest that people with schizophrenia displayed a deficit in reward learning in general that is potentially not specific to learning from rewards compared to learning from negative feedback.

In addition, we examined whether the deficits in learning from positive feedback and negative feedback were associated with negative symptoms. Neither positive reinforcement learning nor negative reinforcement learning was associated with BPRS negative symptom ratings ($r=-0.10$, $p=0.40$, $r=0.11$, $p=0.35$), Revised Social Anhedonia ($r=-0.07$, $p=0.63$, $r=0.10$, $p=0.58$), or Physical Anhedonia scores ($r=-0.05$, $p=0.76$, $r=-0.05$, $p=0.76$).

Finally, we examined whether the nonsignificant difference in parental education between the two groups could have accounted for learning deficits observed in people with schizophrenia. There was no difference in parental education among people who reached criterion and people who did not ($p=0.61$), and parental education was not correlated with either choosing A ($r=0.02$, $p=0.86$) or Avoiding B($r=-0.12$, $p=0.36$) in the testing phase. Thus, it is unlikely that the reinforcement learning deficit observed in people with schizophrenia is a result of lower parental education.

4. Discussion

The results of the current research are similar to previous work which has shown that participants with schizophrenia have deficits in reinforcement learning. However, most previous research has found that this deficit is primarily in learning from positive feedback, and that people with schizophrenia have relatively intact learning from negative feedback (Somlai et al., 2011; Strauss et al., 2011; Waltz et al., 2011). Although the *t*-tests did not reveal a difference between people with schizophrenia and healthy controls in the percentage of time they avoided B in the testing phase, there was not a significant group by valence interaction, which suggests that the observed deficit was related to learning from both positive feedback and negative feedback. Moreover, when collapsed across both choosing the most rewarded stimulus (i.e., A) and avoiding the least rewarded stimulus (i.e., B), there was a main effect for group, which suggests that participants with schizophrenia were impaired in choosing the "correct" stimulus, whether this was the rewarded or non-rewarded stimulus. These findings are somewhat consistent

[1] In some studies using the PSS, only participants who meet criterion for choosing A are included in the transfer analysis. If we excluded participants who did not reach criterion for choosing A, the effect sizes were similar, but not statistically significant due to a reduction in statistical power due to the reduction in the sample size. Participants with schizophrenia were less likely than controls, albeit not statistically significantly, to choose A: ($M=0.62$, S.D.$=0.21$ vs. $M=0.72$, S.D.$=0.18$, $t(60)=1.96$, $p=0.055$; Cohen's $d=0.51$) and to avoid B: ($M=0.57$, S.D.$=0.27$ vs. $M=0.65$, S.D.$=0.21$, $t(60)=1.16$, $p=0.25$; Cohen's $d=0.33$). Like the analysis including all participants, there was not a significant group by valence effect ($F(1, 60)=0.20$, $p=0.66$), but there was a trend for a main effect of group ($F(1, 60)=3.88$, $p=0.054$).

with neurocomputational models of dopamine dysregulation that suggest go-learning (i.e., reward learning) is associated with rapid learning in the orbital frontal cortex and is impaired in schizophrenia (Waltz et al., 2007). Moreover, the current results suggest that the deficit seen in schizophrenia is not due simply to slower learning, but remains even when participants are given up to 600 trials to learn the reward contingencies.

In addition to supporting neurocomputational models of dopamine functioning, the current research is consistent with previous work showing that people with schizophrenia tend to learn reward contingencies at a slower pace than healthy controls (Weiler et al., 2009). Although not statistically significant, the survival analysis in the current research suggests that people with schizophrenia tend to need more time to learn the reward contingencies than did the comparison participants. Thus, participants with schizophrenia could be classified as "slower" learners than are healthy controls. However, the results after the 10th block suggest that there was not a significant difference in the percentage of people with schizophrenia who met reward learning criterion compared to the percentage of healthy reward learning criterion. One explanation for this finding, which is consistent with computational models, is that participants with schizophrenia "catch up" to the healthy controls via gradual learning in the basal ganglia (Waltz et al., 2011). In addition, the current research suggests that, even after 10 blocks, participants with schizophrenia still underperform healthy controls on reward learning during the testing phase of the study. Again, the finding that these deficits persist after this many trials suggests that the reward learning deficits found in the current and previous research works are not simply the result of slower learning, but are specific to deficits in learning from rewards.

As mentioned, the testing phase analysis suggests that participants with schizophrenia had a reinforcement learning deficit in transferring what they learned to a new stimulus. However, not all results were consistent with a reinforcement learning deficit. Participants with schizophrenia did not differ from healthy controls in early learning (i.e., the first two blocks), and there were no significant group differences in overall acquisition. Thus, an alternative explanation of the results could be that people with schizophrenia did not display a reinforcement learning deficit that persisted across the session.

The results of the current research may have implications for the treatment of schizophrenia. Many treatments for schizophrenia, particularly for people with severe impairment, are based on behaviorist principles (Corrigan, 1995). For example, social learning/token economy programs are built on a foundation of positive/negative feedback (Dickerson et al., 2005). The current research suggests that people with schizophrenia my benefit from the repetition of positive feedback and negative feedback provided in these treatment environments. However, the finding that an equal percentage of schizophrenia and control participants met criteria in the acquisition phase, but participants with schizophrenia did worse in the testing phase suggests that people with schizophrenia may have trouble generalizing positive feedback learning to new environments.

One limitation of the current research is that IQ was not assessed. Although participants meeting criterion did not differ from participants who did not on MMSE scores, and MMSE scores were not correlated with learning from either positive feedback or negative feedback, it is possible that cognitive functioning or IQ could have been related to the finding that participants with schizophrenia had a general learning impairment. Another limitation of the current research is that the groups were not matched on race, and the findings could have been related to group differences in race. Moreover, most of the participants in both groups were male, and were from an inpatient facility with a largely forensic population. Thus, it is not clear if the results from the current research can be generalized to other inpatient or outpatient populations.

Another potential limitation of the current research is that we were unable to determine the cause of the learning deficit. For example, these deficits in rapid and gradual learning could be a result of deficits in learning from prediction error signaling, greater stochasticity, or deficits in value representation. However, we were unable to isolate there variables during the acquisition phase of this study because the choice of stimulus in the PSS confounds prediction error learning with value representation learning. In other work, Gold et al. (2012) developed a reinforcement learning task that was specifically designed to isolate these aspects of learning and found that patients with severe avolition seemed to base their judgments on the history of prediction errors (thought to be mediated by the basal ganglia) and to have a deficit in the representation of value (thought to be mediated by the orbital frontal cortex). This result was supported with computational models. Future research could allow participants extended trials in the Gold et al. (2012) task and see if participants are able to overcome the value representation deficit if given extended trials to do so.

The results of the current research may also have implications for the use of the Probabilistic Selection Task in studying reward learning mechanisms in people with schizophrenia. As mentioned, most previous research has given participants three blocks of 60 trials to learn the reward contingencies. The survival analyses in the current research suggest that people with schizophrenia are slower to reach criterion and may benefit from additional trials. However, healthy controls also have trouble learning the reward contingencies and may also benefit from additional trials. Although most participants who met criterion did so in the first three blocks of trials, some participants continued to learn the contingencies up through the 6th block. Only three participants with schizophrenia and one healthy control reached criterion after the 6th block, which suggests that it may not be worth the potential frustration to ask participants to complete more than six blocks. Even with 10 blocks, a large percentage of both healthy controls and people with schizophrenia have difficulty learning the reward contingencies, since 40% of participants with schizophrenia and 34% of healthy controls did not reach criterion even after up to 10 blocks. Future research could examine whether people with schizophrenia continue to display positive feedback learning deficits with less difficult reward learning tasks.

One concerning aspect of the current research is that many participants, both people with schizophrenia and healthy controls, did not reach criterion even after up to 10 blocks of trials. Previous research has shown that results of the Probabilistic Selection Task may vary based on the instructions given to participants (Doll et al., 2009). Since PSS measures both approach and avoidance learning, it is important that instructions are not given in such a way as to influence whether participants are more likely to learn from rewards or the absence of rewards. From our anecdotal experience, it seemed that some participants had trouble understanding the concept of choosing a "correct" (i.e., rewarded) stimulus from innocuous stimuli, and that many of these participants did not figure out this concept, even after completing the acquisition block up to 10 times. Future research could examine whether more explicit instructions could be used to help participants learn the reward contingencies. For example, participants could be informed that the six stimuli are rewarded at rates of 80%, 70%, 60%, 40%, 30%, and 20%, and that their task it to figure this out. Moreover, participants could be given feedback about their performance in between acquisition blocks.

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