Schizophrenia Research 206 (2019) 277–283

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Reward-driven decision-making impairments in schizophrenia

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ARTICLE INFO

Article history:
Received 23 February 2018
Received in revised form 1 November 2018
Accepted 3 November 2018
Available online 12 November 2018

Keywords:
Schizophrenia
Decision-making
Reward learning
Motivation
Depression

ABSTRACT

The ability to use feedback to guide optimal decision-making is essential for goal-directed behaviour. While impairments in feedback-driven decision-making have been associated with schizophrenia and depression, this has been examined primarily in the context of binary probabilistic choice paradigms. In real-world decision-making, however, individuals must make choices when there are more than two competing options that vary in the frequency and magnitude of potential rewards and losses. Thus, the current study examined win-stay/lose-shift (WSLS) behaviour on the Iowa Gambling Task (IGT) in order to evaluate the influence of immediate rewards and losses in guiding real-world decision-making in patients with schizophrenia and major depressive disorder. Fifty-one patients with schizophrenia, 43 patients with major depressive disorder, and 51 healthy controls completed the IGT, as well as a series of clinical and cognitive measures. WSLS was assessed by quantifying trial-by-trial behaviour following rewards and losses on the IGT. Multivariate analyses of variance revealed that patients with schizophrenia demonstrated intact lose-shift behaviour, but significantly reduced win-stay rates compared to healthy controls. In contrast, no WSLS impairments emerged in the depressed group. Win-stay impairments in the schizophrenia group were significantly related to deficits in motivation and cognition. Patients with schizophrenia exhibit impaired reward-driven decision-making in the context of multiple choices with concurrent rewards and losses, and this appears to be driven by a reduced propensity for advantageous win-stay behaviour. With the importance of reward learning and decision-making in generating goal-directed behaviour, these findings suggest a potential mechanism contributing to the motivation deficits seen in schizophrenia.

1. Introduction

Goal-directed decision-making is a central component of the broader reward and motivation system, and requires the ability to dynamically integrate both positive and negative feedback from the environment in order to maximize rewards and minimize loss over time. Accordingly, impaired motivation- and goal-directed decision-making may arise from abnormal reinforcement learning (Gold et al., 2008), such that reward feedback is not properly learned, integrated and/or translated into goal-directed behaviour. Such impairments may contribute to the loss of motivation seen in the context of illnesses such as schizophrenia (SZ) and major depressive disorder (MDD), where these motivation deficits significantly contribute to poor functional and treatment outcomes for affected individuals across these disorders (Foussias et al., 2009; Strauss et al., 2013; Uher et al., 2012; Vrieze et al., 2013). Indeed, dysfunctional reinforcement learning, with altered sensitivity to reward and punishment linked to impaired feedback-driven decision making and overall diminutions in motivation has been demonstrated in SZ (Barch et al., 2016; Gold et al., 2008), and to some extent in MDD (Eshel and Roiser, 2010; Martin-Soelch, 2009).

A more nuanced approach to understanding alterations in reward-driven decision-making is possible by examining the immediate influence of positive and negative feedback on decision-making within the framework of win-stay/lose-shift (WSLS) behaviour (Paulus et al., 2001; Waltz et al., 2007; Young and Markou, 2015). From an operant learning perspective, WSLS posits that a rewarded or positively reinforced behaviour should be repeated (i.e. win-stay), while an action that yields a negative outcome should subsequently be adjusted on the next trial (i.e. lose-shift). This paradigm has been examined in SZ using behavioural measures such as Go/NoGo (Chang et al., 2016; Waltz et al., 2011), probabilistic reversal learning (Culbreth et al., 2016; Reddy et al., 2016; Waltz et al., 2013), probabilistic reward learning and choice tasks (Chang et al., 2016; Kim et al., 2007; Ludewig et al., 2003; Waltz et al., 2007), as well as the Wisconsin Card Sorting Task

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https://doi.org/10.1016/j.schres.2018.11.004
0920-9964/

(WCST; Prentice et al., 2008). The findings, however, are mixed with some evidence for impairments on both win-stay and lose-shift (Chang et al., 2016; Reddy et al., 2016; Waltz et al., 2013, 2007), on win-stay only (Culbreth et al., 2016), on lose-shift only (Prentice et al., 2008; Waltz et al., 2011), or no impairments at all (Chang et al., 2016; Ludewig et al., 2003). Examinations of WSLS in MDD are more limited, though a recent study found that MDD patients made fewer lose-shift responses on a probabilistic learning task compared to healthy controls (Bakic et al., 2017).

To date, WSLS behaviour in SZ and MDD has been examined primarily in the context of binary probabilistic choice paradigms, with the exception of Prentice et al. (2008) who examined the first four pre-shift trials of the WCST. In real-world decision-making, however, individuals must also make choices when there are more than two competing options that vary in the frequency and magnitude of potential rewards and losses. To this end, the Iowa Gambling Task (IGT), one of the most commonly used measures of goal-directed decision-making, involves learning from multiple rewards and punishments, and simulates real-world choices under conditions of uncertainty and risk (Bechara et al., 1994). Moreover, the IGT taps into 'hot' affective decision-making (Buelow and Suhr, 2013), which affords the opportunity to evaluate behavioural responses as a function of emotionally loaded rewards and losses. Performance on the IGT, however, has typically been evaluated using a net score of total advantageous minus disadvantageous card selections, which does not provide insight into the specific influence of positive and negative feedback on trial-by-trial decision-making (Cassotti et al., 2014), or the process by which rewards and losses are learned, integrated, and translated into goal-directed behaviour. Thus, the purpose of the current study was to examine WSLS behaviour by way of performance on the IGT in order to investigate the influence of immediate rewards and losses in guiding real-world decision-making in SZ and MDD. More specifically, we sought to address the following questions: 1) Do patients with SZ and MDD experience difficulties using feedback to guide trial-by-trial decision-making on the IGT, and moreover, are these impairments specific to positive or negative feedback; and 2) What are the clinical and/or cognitive correlates of these impairments? We hypothesized that patients with SZ would exhibit deficits in both win-stay and lose-shift behaviour, whereas patients with MDD would only demonstrate impaired lose-shift behaviour.

2. Methods

2.1. Participants

The participants recruited for this study consisted of 51 patients with SZ, 43 patients with MDD, and 51 demographically-matched healthy controls (HC), all between the ages of 18–55. As confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First et al., 1997), participants with SZ met criteria for a diagnosis of schizophrenia or schizoaffective disorder, and MDD participants met criteria for major depressive disorder in a current depressive episode. Participants in the SZ and MDD groups were clinically stable outpatients with no change in treatment for at least 4 weeks. Patients were not eligible if they met criteria for any other Axis I disorder, with the exception of comorbid anxiety disorders for the MDD group. Further, all participants were excluded if they had a history of substance abuse or dependence in the past 6 months (with the exception of nicotine); a history of neurological disease; significant akathisia (a rating of >2 on the Barnes Akathisia Rating Scale Global item (Barnes, 1989)); or significant extrapyramidal symptoms (a rating of >2 on >2 items of the Simpson Angus Rating Scale (Simpson and Angus, 1970)). HC participants were also administered the SCID, and were excluded if they met criteria for any Axis I disorder, were taking psychotropic medications, or had a family history of mood or psychotic disorders in first-degree relatives. This study was approved by the local research ethics board, and all participants provided written informed consent.

2.2. Instruments and procedures

A battery of clinical measures was administered to assess for psychopathology and symptom severity. The Scale for the Assessment of Positive Symptoms (SAPS; (Andreason, 1984) was used to evaluate positive symptoms for individuals in the SZ group, and all participants were administered the Scale for the Assessment of Negative Symptoms (SANS; (Andreasen, 1982), with the total score calculated as the sum of the amotivation subdomain (Avolition-Apathy and Anhedonia-Asociality subscales, excluding global items) and the diminished expression subdomain (Affective Flattening subscale and the poverty of speech item, excluding inappropriate affect, poverty of content of speech, blocking, response latency, and global items) (Foussias et al., 2009). Amotivation was assessed using the Apathy Evaluation Scale — Clinician version (AES; (Marin et al., 1991), specifically chosen over the SANS amotivation subdomain as it does not rely exclusively on functional proxies, but also evaluates the behavioural, emotional, and cognitive aspects of motivation. The Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) was used to measure depressive symptom severity. Participants also completed self-report questionnaires including the Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2006) as a measure of consummatory and anticipatory pleasure, and the Barratt Impulsiveness Scale (BIS; Patton et al., 1995) to assess for impulsivity given its relationship with risky decision-making. For a subset of the sample ($n = 80$), we also administered the Beck Anxiety Inventory (BAI; Beck and Steer, 1993) as anxiety has been shown to impair decision-making on the IGT (Miu et al., 2008); as well as the Defeatist Beliefs subscale of the Dysfunctional Attitudes Scale (DAS; Weissman and Beck, 1978) which measures the extent to which one endorses defeatist beliefs about their ability to perform goal-directed tasks. In addition, neurocognition was evaluated using the Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004), with composite and domain Z scores calculated based on age and sex normative data. Antipsychotic dosages were converted to chlorpromazine (CPZ) equivalents (Gardner et al., 2010; Leucht et al., 2016)

2.2.1. Computerized tasks

The Iowa Gambling Task (IGT; Bechara et al., 1994) requires participants to make selections from four decks of cards, labelled 'A', 'B', 'C', and 'D'. Specific instructions were provided as outlined by Bechara et al. (2000). In the current study, selections from decks A and B yield $50 rewards, cards from decks C and D offer $100, and unbeknownst to the participants, each deck differs in loss magnitude and frequency. Specifically, the losses in deck A are frequent, occurring five times for every 10 selections, with low magnitudes ranging from $25 to $75, and in deck B, there is an infrequent, high magnitude penalty of $250 that occurs once for every 10 selections. The losses in deck C are frequent (i.e., in 5/10 selections), with low magnitudes ranging from $100 to $350, and in deck D, there is an infrequent (i.e., in 1/10 selections), high magnitude loss of $1250. Decks A and B are considered advantageous as they net $200 for every 10 selections, whereas decks C and D are considered disadvantageous as they net a loss of $350. The task consisted of 100 trials, and each card selection was immediately followed by feedback. A reward was depicted by a cartoon happy face and a slot machine sound, while this feedback was replaced with a sad face, and an error sound effect for a loss. Net wins and losses were depicted on a bar at the top of the screen. This computerized task was programmed and administered on Open Sesame v. 2.9.4 (Mathôt et al., 2012).

The Wisconsin Card Sorting Task (WCST; Heaton et al., 1993) was administered as a measure of perseveration in order to ensure that win-stay/lose-shift performance on the IGT was not related to inflexible set shifting. In this computerized version of the task, participants are instructed to match a series of cards according to different stimulus parameters such as colour, form, and number. Participants are not informed how to match the cards, but are given verbal feedback from the computer after each trial as to whether they are correct or incorrect.

After 10 consecutive correct answers, a new sorting rule is implemented without notice, and participants must deduce the new rule and continue matching the cards correctly. The variable of interest is the age-corrected standardized percentage of perseverative errors.

2.3. Statistical analysis

2.3.1. Demographic and clinical characteristics

Statistical analyses were conducted using SPSS v.24 (SPSS Inc.) software. Analyses of variance (ANOVAs) or chi-square tests were used to compare groups across demographic, clinical, and cognitive characteristics, as appropriate.

2.3.2. Win-stay/lose-shift

Our primary outcome of interest was differences in win-stay/lose-shift behaviour across groups, which was evaluated using a multivariate analysis of variance (MANOVA). WSLS on the IGT was assessed by quantifying trial-by-trial choice behaviour following immediate wins and losses, with total win-stay referring to the proportion of times the same deck was chosen immediately after a reward was received in the absence of a concurrent loss, and total lose-shift as the proportion of times a different deck was chosen after receiving a loss of any magnitude. Thus, the win-stay variable represents decision-making behaviour that is positively reinforced by rewarding feedback, whereas lose-shift is the tendency to modify choice behaviour in response to losses or negative feedback. The MANOVA was conducted with diagnostic group as the independent variable, and total win-stay and total lose-shift as the dependent variables.

Given that a reward may also occur in the presence of a loss (i.e., where a participant may receive a small loss but still have a net monetary gain), we also calculated net WSLS rates by defining any net outcome greater than or equal to zero as a win, and any net outcome less than zero as a loss (Cassotti et al., 2011). In contrast to the total WSLS variables above, the net win-stay/lose-shift variables represent reward-driven decision-making behaviour as a function of monetary gains or losses rather than just positive or negative feedback. An additional MANOVA was subsequently computed to compare net WSLS group differences.

2.3.3. Clinical and cognitive correlates of win-stay/lose-shift impairments

Based on the results of the first MANOVA, exploratory bivariate correlational analyses were conducted to determine if specific deficits that emerged in win-stay and/or lose-shift behaviour were related to positive or negative symptoms, amotivation, depression, neurocognitive function or perseveration, or to self-report measures of consummatory and anticipatory pleasure, impulsivity, anxiety, or defeatist beliefs.

2.3.4. Overall IGT performance

To enable comparisons with previously published studies using the IGT, we also conducted secondary analyses on the traditional IGT performance variables. Specifically, a one-way ANOVA was conducted to assess group differences in IGT net score (consisting of the total number of advantageous minus disadvantageous card choices: [(A + B) − (C + D)]), as well as a 3 (group) × 5 (bin) mixed-model ANOVA to evaluate task learning across 5 bins of 20 trials.

The following findings are based on secondary analyses of data collected for a larger parent study examining the multiple facets of the reward system in SZ and MDD.

3. Results

3.1. Demographics and clinical characteristics

Summary demographic and clinical variables are shown in Table 1. Groups did not significantly differ in age or sex; however, education level was significantly lower in the SZ group. Further, illness duration was comparable between patient groups. Not surprisingly, in relation to the HC group both SZ and MDD participants exhibited significantly higher severity of clinical amotivation, depressive symptoms, as well as self-reported anxiety and impulsiveness. Additionally, the SZ group demonstrated greater levels of diminished expression than the HCs, and the MDD group endorsed lower levels of consummatory and anticipatory pleasure, as well as greater severity of defeatist beliefs compared to the HC group.

3.2. Win-stay/lose-shift

The MANOVA for WSLS revealed a significant main effect of diagnostic group ($F(4, 284) = 2.538$, $p = .040$, $\eta^2 = 0.035$), specifically for win-stay rates ($F(2,142) = 5.242$, $p = .006$). Post-hoc comparisons revealed significant pairwise differences, such that the SZ group demonstrated reduced win-stay behaviour in comparison to the HC group ($p = .003$), as well as the MDD group ($p = .017$). In contrast, the main group effect for lose-shift was not significant ($p = .116$) (Fig. 1). An exploratory mixed-model ANOVA was subsequently conducted in order to determine if win-stay rates differed according to deck type (i.e. advantageous vs. disadvantageous) or loss magnitude-frequency contingencies (i.e. low-magnitude/high-frequency (LMHF) vs. high-magnitude/low-frequency (HMLF)). Specifically, a 2 (advantageous vs. disadvantageous × 2 (LMHF vs. HMLF) × 3 (group) mixed-model ANOVA revealed a non-significant trend for an effect of deck type ($F(1,141) = 3.764$, $p = .054$), with higher rates on advantageous decks, as well as a significant main effect of magnitude-frequency ($F(1,141) = 23.305$, $p < .001$), such that win-stay rates were higher on HMLF decks. There was also a significant deck type × magnitude-frequency interaction ($F(1,141) = 13.317$, $p < .001$), driven by higher win-stay rates on the disadvantageous HMLF deck. Additionally, the deck type × group interaction was significant ($F(2,142) = 6.333$, $p = .002$), with post-hoc one-way ANOVAs revealing a main effect for the advantageous decks only ($F(2,142) = 4.443$, $p = .013$), such that the SZ group exhibited significantly lower win-stay rates for advantageous decks compared to the HC group ($p = .007$) and MDD group ($p = .021$). Further, there were no significant magnitude-frequency × group, or deck type × magnitude-frequency × group interactions.

The results of the second MANOVA for net wins and losses similarly revealed a main effect of group ($F(4, 284) = 2.705$, $p = .031$, $\eta^2 = 0.037$), driven by net win-stay rates ($F(2,142) = 5.425$, $p = .005$), such that patients with SZ exhibited significantly reduced net win-stay behaviour in relation to individuals in the HC group ($p = .002$) and MDD group ($p = .015$).

3.3. Clinical and cognitive correlates of win-stay deficits in schizophrenia

The win-stay deficits in the SZ group were significantly correlated with amotivation ($r = -0.30$, $p = .03$) and global neurocognition ($r = 0.28$, $p = .048$), with a non-significant trend for a correlation with depressive symptoms ($r = -0.26$, $p = .07$). An exploratory evaluation of the cognitive correlates of win-stay deficits in SZ revealed no significant relationship with working memory, executive function, or verbal fluency; however, significant correlations emerged for verbal memory and learning ($r = 0.31$, $p = .03$) and motor function (token motor: $r = 0.30$, $p = .04$; symbol coding: $r = 0.33$, $p = .02$). In contrast, win-stay behaviour was not correlated with positive symptoms, diminished expression, anticipatory or consummatory pleasure, impulsiveness, anxiety, defeatist beliefs, perseverative errors, or chlorpromazine equivalents.

Lastly, optimal IGT performance was significantly correlated with win-stay rates in the SZ group ($r = 0.37$, $p = .008$), as well as in the entire sample ($r = 0.47$, $p < .001$).

Table 1
Demographic & clinical characteristics.

	SZ	MDD	HC	*p* value	Group differences
	(*n* = 51)	(*n* = 43)	(n = 51)		
Sex (M:F)	28:23	20:23	25:26	0.700	
Age M (SD)	34.5 (10.4)	32.3 (11.2)	31.7 (11.0)	0.391	
Education	14.9 (3.6)	16.9 (2.5)	17.2 (2.5)	<0.000	SZ < HC = MDD
Parental education	15.2 (5.4)	15.6 (4.9)	16.5 (4.7)	0.390	
Illness duration (years)	11.8 (7.3)	11.6 (9.0)		0.884	
CPZ	529.8 (306.3)				
Medications					
Antipsychotics (n)	51	4	–		
Antidepressants (n)	11	33	–		
SAPS	23.4 (16.8)				
SANS total	24.6 (12.2)	21.5 (7.6)	3.4 (5.4)	<0.001	SZ = MDD > HC
AES	39.7 (6.7)	37.3 (4.7)	25.3 (4.6)	<0.001	SZ > MDD > HC
HDRS	10.8 (5.6)	17.2 (5.0)	1.8 (1.9)	<0.001	MDD > SZ > HC
TEPS-Ant	4.5 (0.8)	3.5 (0.9)	4.5 (0.6)	<0.001	MDD < SZ = HC
TEPS-Con	4.4 (0.8)	4.1 (1.0)	4.7 (0.9)	0.005	MDD < HC
BIS	63.3 (8.6)	66.3 (13.5)	54.1 (8.0)	<0.001	HC < SZ = MDD
DAS defeatist beliefs[a]	48.4 (18.7)	60.6 (15.6)	40.1 (11.0)	<0.001	MDD > SZ = HC
BAI[a]	11.5 (13.5)	22.3 (11.6)	3.3 (5.2)	<0.001	MDD > SZ > HC
BACS composite	−1.6 (1.3)	−0.3 (0.9)	0.2 (1.0)	<0.001	SZ < MDD < HC
Working memory[b]	−1.1 (1.0)	−0.3 (1.1)	0.1 (1.0)	<0.001	SZ < MDD < HC
Executive function[c]	−0.5 (1.4)	0.3 (0.7)	0.06 (0.8)	0.001	SZ < MDD = HC
WCST perseverative errors	93.5 (24.4)	93.5 (18.4)	90.8 (18.2)	0.756	

Abbreviations – CPZ: Chlorpromazine; SAPS: Scale for the Assessment of Positive Symptoms; AES: Apathy Evaluation Scale; SANS: Scale for the Assessment of Negative Symptoms; HDRS: Hamilton Depression Rating Scale; TEPS-Ant: Temporal Experience of Pleasure Scale – Anticipatory Pleasure; TEPS-Con: Temporal Experience of Pleasure Scale – Consummatory Pleasure; BIS: Barratt Impulsiveness Scale; DAS: Dysfunctional Attitudes Scale; BAI: Beck Anxiety Inventory; BACS: Brief Assessment of Cognition in Schizophrenia; WCST: Wisconsin Card Sorting Task.

[a] Subset of $n = 80$.
[b] BACS Digit Sequencing.
[c] BACS Tower of London.

3.4. Overall IGT performance

The results of the ANOVA for the IGT net score revealed a main effect of group ($F(2,142) = 5.916$, $p = .003$), such that participants in the SZ group ($M = 1.13$, $SE = 3.67$) made significantly fewer advantageous deck selections compared to participants in both the MDD group ($M = 16.23$, $SE = 4.39$) and HC group ($M = 17.96$, $SE = 3.63$). However, there was no significant main effect of bin ($F(4,139) = 1.644$, $p = .167$) or group × bin interaction ($F(8,280) = 0.555$, $p = .814$). A summary of IGT performance variables is presented in Table 2.

4. Discussion

The purpose of the current study was to investigate feedback-driven decision-making in individuals with schizophrenia, major depressive disorder, and healthy control participants by evaluating win-stay/lose-shift behaviour on the Iowa Gambling Task. Our primary goal was to determine if patients with SZ and MDD demonstrate trial-by-trial decision-making impairments on the IGT, and whether these impairments were associated with specific abnormal responses to positive or negative feedback. The examination of WSLS behaviour revealed that patients with SZ demonstrated significant feedback-driven decision-making impairments in comparison to both MDD and HC participants, and this was specifically driven by reduced win-stay rates. In contrast, lose-shift behaviour was intact in the SZ group, which aligns with a previous study examining WSLS using a probabilistic reversal learning task (Culbreth et al., 2016). A similar effect emerged for net WSLS rates, perhaps suggesting that irrespective of how the reward is defined – that is, whether the monetary gain is in the presence or absence of concurrent losses – individuals with SZ experience difficulties using positive feedback to optimize behaviour. Given that the type of reward learning required for optimal IGT performance has been shown to rely on prediction error processes (Nestor et al., 2014), it is possible that these win-stay deficits are related to impairments in reward prediction error signalling that have been demonstrated in individuals with SZ (Murray et al., 2008b). Though speculative, impaired reward prediction error signalling, resulting in a reduced ability to anticipate positive outcomes, learn from prediction errors, and use rewarding feedback to guide decision-making, represents a potential mechanism underlying win-stay deficits in SZ that warrants further investigation. Overall, these findings add to a growing body of evidence for selective reward-driven deficits in schizophrenia (Cheng et al., 2012; Deserno et al., 2013; Murray et al., 2008a; Nestor et al., 2014; Waltz et al., 2007; Weiler et al., 2009; Whitton et al., 2015).

Further examination of win-stay behaviour, however, revealed a more complex pattern of impaired reward learning in SZ, such that patients only demonstrated significant win-stay reductions on advantageous decks. These impairments, therefore, cannot simply be attributed to reward insensitivity as the win-stay rates on disadvantageous decks (i.e. high rewards) were comparable between SZ and HC groups. Instead, these findings may be better understood in the context of intact reward responsiveness, with impairments emerging in the translation

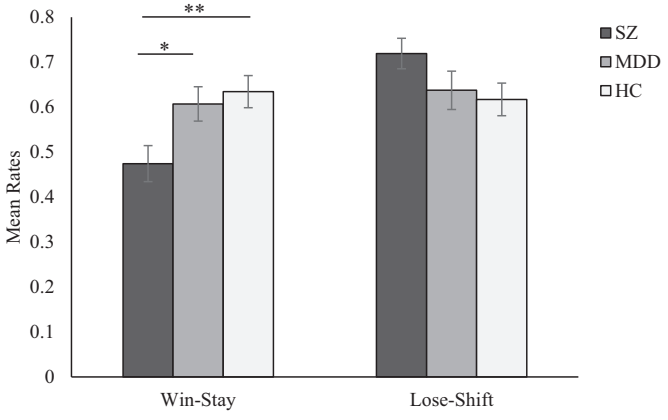

Fig. 1. Total Win-Stay/Lose-Shift group differences on the IGT. Error bars represent standard error of the mean. *$p < .05$, **$p < .01$.

Table 2
Summary of IGT performance across groups.

	SZ	MDD	HC	p	Group Diff.
Total money earned	−402.9 (707.9)	−28.5 (912.6)	68.6 (896.0)	0.014	SZ < HC = MDD
Total number cards selected:					
Advantageous					
Deck A	21.4 (8.6)	24.1 (10.5)	24.6 (10.4)	–	
Deck B	29.1 (8.1)	34.1 (8.3)	34.4 (7.6)	0.001	SZ < HC = MDD
Disadvantageous					
Deck C	22.4 (6.6)	19.1 (7.4)	17.4 (6.2)	0.001	SZ > HC = MDD
Deck D	27.1 (9.5)	22.8 (9.9)	23.7 (9.5)	0.073	
Net scores:					
Bin 1	−1.1 (7.2)	1.3 (10.7)	2.0 (8.4)	–	
Bin 2	−0.4 (6.7)	3.4 (8.9)	2.9 (9.5)	0.055	
Bin 3	0.8 (9.5)	4.8 (9.1)	5.2 (10.6)	0.049	SZ < HC = MDD
Bin 4	0.3 (9.3)	5.0 (9.5)	3.5 (9.8)	0.053	
Bin 5	1.6 (9.5)	1.8 (12.9)	4.4 (10.8)	–	
Total wins (in the absence of losses)	72.7 (3.0)	72.6 (3.2)	73.4 (3.2)	–	
Total net wins	74.8 (2.4)	75.2 (2.4)	76.0 (2.2)	0.033	SZ < HC
Total shifts	56.8 (25.7)	44.9 (24.5)	42.2 (23.9)	0.008	SZ > HC = MDD

of reward feedback into motivated goal-directed behaviour (Barch et al., 2017) – that is, selecting and *staying* on the advantageous decks which result in smaller immediate rewards, but greater long-term outcomes. To this end, SZ patients' reduced win-stay behaviour was significantly correlated with severity of clinical amotivation, which aligns with previous studies that have similarly found reward-driven learning impairments to be related to motivation deficits and negative symptoms, more broadly (Gold et al., 2012; Waltz et al., 2011). Thus, our findings fit well within the current conceptualizations of motivation, which position reinforcement learning and goal-directed decision-making as central components of the broader multi-faceted reward system (Barch and Dowd, 2010; Cuthbert and Insel, 2013). Moreover, while deficits in working memory and executive function have previously been implicated in driving reinforcement learning impairments and poor IGT performance (Collins et al., 2014; Gold et al., 2008; Manes et al., 2002) these cognitive domains were not associated with reduced win-stay rates in the SZ group. It is important to note, however, that global cognition was significantly correlated with win-stay behaviour for these individuals, which is not entirely surprising given the higher-order cognitive processes involved in reward learning and preference-based decision making. Our results suggest an interconnected and potentially bidirectional relationship between cognitive and motivation deficits in the context of feedback-driven decision-making that may influence goal-directed behaviour in schizophrenia.

Contrary to our hypotheses, the MDD group did not demonstrate any WSLS impairments. Given that depression is typically associated with reward hyposensitivity and punishment hypersensitivity (Eshel and Roiser, 2010), it is somewhat surprising that we found no evidence of reduced win-stay rates or excessive lose-shift behaviour in the MDD group, despite these individuals also experiencing significant depressive symptoms, amotivation, and hedonic deficits. That being said, it is important to note that other studies have similarly failed to find evidence for abnormal responses to feedback in MDD, as well (Chase et al., 2010; Dalgleish, 2004; Dickstein et al., 2010; Shah et al., 1999). These findings may suggest that individuals with MDD can experience blunted reward responsiveness, while still maintaining the capacity to learn from rewards and integrate feedback into goal-directed decision-making, providing further support for the distinction between reward sensitivity and learning in depression (Huys et al., 2013).

We also evaluated overall IGT performance using the traditional measure of net card selections, and found that patients with SZ made significantly fewer advantageous choices compared to the MDD and HC group. This finding is in line with a number of studies demonstrating IGT impairments in SZ (Beninger et al., 2003; Brown et al., 2015; Kester et al., 2006; Kim et al., 2012; Nestor et al., 2014; Premkumar et al., 2008; Ritter et al., 2004; Shurman et al., 2005), though not consistently (Cavallaro et al., 2003; Evans et al., 2005; Matsuzawa et al., 2015; Rodríguez-Sánchez et al., 2005; Sevy et al., 2007; Turnbull et al., 2006; Wilder et al., 1998). In contrast, individuals with MDD performed comparably to healthy controls, which is consistent with some studies (Dalgleish, 2004; Gorlyn et al., 2013; Han et al., 2012), but not others (Cella et al., 2010; Must et al., 2006; Smoski et al., 2008).

To our knowledge, the current study is the first to examine WSLS behaviour on the IGT concurrently in SZ and MDD. Nevertheless, this work should be interpreted within the context of the following limitations. First, patient groups were taking a range of antipsychotic and antidepressant medications, both of which have been found to influence reward and punishment sensitivity. We computed chlorpromazine equivalents for the SZ group and confirmed that they were not statistically related to WSLS behaviour, but we recognize that although CPZ equivalents are routinely used for this purpose, they represent a crude measure of the potential effects of antipsychotic medications on reward process. At present, however, we are not aware of other routinely used measures that are able to more comprehensively capture the effects of antipsychotics on reward system processes. Similarly, to our knowledge there is not a corresponding approach for dose equivalents in terms of antidepressant medications that can adequately capture the potential reward system effects of these medications. In addition, the use of the HDRS in the SZ group serves as another limitation as it does not evaluate depressive symptoms independently of negative symptoms. Further, there are likely individual differences associated with WSLS behaviour on the IGT that we did not measure such as risk aversion and personality, though we did examine impulsivity which was not associated with WSLS across groups. While the groups were matched by age, sex, and parental education, another limitation is that there were group differences in participant education. Though there is inconsistent evidence for a relationship between education and IGT performance, it may be necessary to consider how these differences may have influenced WSLS behaviour in the current study. Additionally, while there are other decision-making strategies and reinforcement learning models, such as expectancy valence and prospect valence learning that can be applied to IGT performance, the WSLS strategy has been shown to account for a large proportion of participants' behaviour (Worthy et al., 2013). Finally, given the cross-sectional design of the current study, we cannot fully disentangle the specific influence of cognition versus motivation on WSLS behaviour. Going forward, it will be important to evaluate these processes longitudinally in order to better understand how feedback-driven decision-making impairments develop and evolve over time.

Taken together, our findings suggest that individuals with MDD demonstrate intact WSLS behaviour, whereas patients with SZ experience selective reward-driven decision-making deficits in the context of multiple choices with concurrent gains and losses. This impairment appears to be driven by a reduced propensity for advantageous win-

stay behaviour, suggesting that individuals with SZ experience specific difficulties using positive feedback to optimize goal-directed behaviour. With the importance of reward learning and decision-making in generating goal-directed behaviour, these findings suggest a potential mechanism contributing to clinical amotivation in schizophrenia.

Conflict of interest

SS, SDS, IS, AR, ANV, and KKZ declare no conflicts of interest. OA has received research support from Pfizer Inc., Janssen-Ortho, Otsuka, Boehringer Ingelheim, Neurocrine Biosciences, Sunovion, serves on the advisory board for Janssen-Ortho, Sepracor, Sunovion, Roche, Novartis, BMS, Otsuka, Lundbeck, Eli Lilly and Sumitomo Dainippon Pharma, and has received speaker's fees from Janssen-Ortho, Novartis, Sepracor, Sunovion, Lundbeck, Eli Lilly, Mylan Pharmaceuticals and Otsuka. ZJD has received research support from Brainsway Inc. and Magventure Inc., has served on the advisory board for Sunovion, Hoffmann-La Roche Limited and Merck, and has received speaker support from Eli Lilly. GR has received consultant fees from Neurocrine Biosciences and Synchroneuron, as well as research support from Novartis. GF has served as an investigator on research sponsored by Medicure Inc., and Neurocrine Bioscience. He has also served on advisory boards for Hoffman-La Roche and Takeda, and received speaker's fees from Hoffman-La Roche, Lundbeck and Novartis.

Contributors

SS and GF designed the study, and SS led the data collection, statistical analyses and preparation of the first draft of the manuscript. SDS and IS contributed to the data collection and statistical analyses. All other authors subsequently made significant contributions to the interpretation of the findings, and have approved the final manuscript.

Role of funding source

This work was supported by a research grant through the Ontario Mental Health Foundation (GF). This source had no further role in the analysis or interpretation of the data, development of the manuscript or the decision to submit for publication.

Acknowledgements

We thank the participants who took part in this study.

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