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Corticostriatal Control of Goal-Directed Action Is Impaired in Schizophrenia

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ABSTRACT

BACKGROUND: Goal-directed actions depend on our capacity to integrate the anticipated consequences of an action with the value of those consequences, with the latter derived from direct experience or inferred from predictive stimuli. Schizophrenia is associated with poor goal-directed performance, but whether this reflects a deficit in experienced or predicted value or in integrating these values with action-outcome information is unknown, as is the locus of any associated neuropathology.

METHODS: We assessed the contribution of these sources of value to goal-directed actions in people with schizophrenia (SZ) (n = 18) and healthy adults (n = 18). Participants learned to use specific actions to liberate snack foods from a vending machine. They also learned about the reward value of the foods, changes in reward value, and the relationship between various predictive stimuli and food delivery. We then evaluated the ability of subjects to use experienced or predicted value to guide goal-directed actions while undergoing functional magnetic resonance imaging.

RESULTS: Acquisition and sensitivity to experienced changes in outcome value did not differ in SZ and healthy adults. The SZ were, however, deficient in their ability to integrate action-outcome learning with outcome values to guide choice, more so when actions were guided by experienced than by predicted values. These effects were differentially associated with reductions in activity in caudate and limbic structures, respectively.

CONCLUSIONS: This novel assessment of goal-directed learning revealed dysfunction in corticostriatal control associated with a profound deficit in integrating changes in experienced value with the action-outcome association in schizophrenia.

Keywords: Choice, Decision-making, Executive dysfunction, Predictive learning, Reinforcement learning, Reward

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The performance of goal-directed actions depends on the ability to integrate knowledge of the causal consequences of specific actions with the experienced value of those consequences (1,2). The importance of this integrative capacity has been recognized in animal and computational models of goal-directed action (2–4) and its dysfunction has been thought to play a critical role in psychiatric disorders, most notably schizophrenia (5–9).

Historically, these deficits in goal-directed action were regarded as secondary to the anhedonia reported to accompany schizophrenia, resulting in a decreased motivation to attain goals (10–12). Multiple studies have observed, however, that patients with schizophrenia report surprisingly normal experiences to hedonic stimuli (13–15), suggesting that deficits in goal-directed action are unrelated to their immediate experience of reward. Alternatively, poor goal-directed action may reflect a failure to integrate reward values with the causal consequences of specific actions, whether related to problems maintaining the experienced value of rewarding events in memory (16,17)—associated with pathology in prefrontal cortex (PFC) (18,19)—or to predicting values from cues that anticipate future reward—often attributed to the mesoaccumbal dopamine pathway (8,12,20–25).

Recent studies have distinguished the influence of experienced and predicted reward value on the control of goal-directed actions. The ability of reward-related cues to motivate and guide actions is demonstrated by Pavlovian-instrumental transfer in which Pavlovian cues that predict a particular reward bias choice toward actions that earn that reward (26). This specific transfer effect engages a circuit involving the orbitofrontal cortex (OFC), amygdala, and nucleus accumbens in humans (27–30), and damage to this circuit renders choices indifferent to predictive stimuli (31–33). Outcome devaluation tests have established that experienced reward values also influence choice: devaluing a food reward can reduce the performance of actions associated with that food relative to other actions (34,35). Such goal-directed actions engage a prefrontal cortical–dorsomedial striatal circuit in humans (36–41), and damage to this circuit renders choices insensitive to changes in outcome value and abolishes goal-directed action control (42,43).

In this study, we sought to establish whether deficits in goal-directed action associated with schizophrenia are due to an inability to use reward-related cues or previous experiences of reward value to select the best action. We assessed the influence of 1) cues predicting food rewards in a Pavlovian-instrumental transfer test; and 2) an outcome devaluation test in people with schizophrenia (SZ) and in healthy adults (HA). Neural hemodynamic responses were assessed (functional magnetic resonance imaging [fMRI]) during each test. We predicted that

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SZ would be unable flexibly to update their choices on the basis of changes in either predicted or experienced reward values. Furthermore, we predicted deficits in transfer associated with aberrant hemodynamic responses in the limbic and medial OFC (mOFC) regions, described above and known to be critical for cue-guided action selection. In contrast, we predicted deficits in outcome devaluation associated with abnormal responses in the prefrontal cortex–dorsomedial striatal circuit.

METHODS AND MATERIALS

All participants provided written informed consent according to the approval requirements of the Human Research Ethics Committee of Sydney University (HREC #12812).

See Supplement 1 for a full description of the methods and results.

Participants

Eighteen healthy adults and 18 people with schizophrenia ($n = 12$) or schizoaffective disorder ($n = 6$) and no other Axis 1 disorder (Table 1) were included after meeting the inclusion criteria (cf. Supplementary Methods in Supplement 1). Participants were assessed with the Diagnostic Interview for Psychosis to establish a lifetime diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV criteria (44,45).

Stimuli

Visual stimuli during the scan were presented via a projector positioned at the back of the MRI scanner. A Lumina MRI-compatible two-button response pad (Cedrus, California) recorded each response. Food rewards consisted of sweet and salty snack foods (chocolate candy, chocolate chip cookies, and barbecue flavored crackers).

Procedure

Instrumental Training. Before the MRI scan, participants rated the desirability of the three different snack foods by answering the question "How much do you want this snack right now?" on a 7-point Likert scale and were then trained to liberate two of the snack foods from a virtual vending machine presented on a laptop computer (Figure 1A). Left and right button presses earned a different snack food (food A and food B, respectively). Participants were provided with the relevant snack food and allowed to eat it. After every three rewards, a probe question to assess knowledge of the instrumental contingencies was posed on the screen. After getting six questions correct in a row, instrumental training ended. For further details, see Supplementary Methods in Supplement 1.

Pavlovian Training. In the next stage (Figure 1B), the virtual snack machine was presented and participants learned the predictive relationship between colored lights (red, green, blue, or yellow) presented on the front of the virtual machine and snack food delivery (foods A, B, C, and empty, respectively). Each cue lasted for 6 seconds, after which a snack fell out of the virtual machine. Participants were allowed to eat each snack when it appeared. After every four trials, a probe question was posed to test knowledge of the Pavlovian contingencies. Feedback was provided and training ended when six correct answers in a row occurred.

The next two stages took place during the fMRI scan.

Table 1. Clinical and Neuropsychological Results, Mean (SD)

	Schizophrenia ($n = 18$)[a]	Healthy ($n = 18$)	t Value ($df = 34$)	p Value
Age	45.3 (11.4)	39.9 (12.9)	1.36	.18
Female Subjects	9	9		
Edinburgh Handedness Score	73.9 (27.7)	79.1 (29.7)	.56	.58
Years of Education	14.4 (3.4)	15.1 (2.3)	.71	.48
WASI IQ	99.2 (15.5)	112.3 (14.5)	2.69	.01
WTAR IQ	102.4 (15.9)	108.2 (7.8)	1.43	.16
DASS-21 Scores				
Depression	13.1 (8.9)	4.4 (4.8)	3.60	.00
Anxiety	12.0 (9.1)	3.2 (2.5)	4.10	.00
Stress	14.7 (10.7)	6.0 (5.4)	3.09	.00
BIS/BAS Scores				
BIS	16.5 (5.4)	16.3 (4.3)	.15	.89
BAS-reward subscale	11.3 (4.8)	12.1 (3.9)	.52	.60
BAS-drive subscale	9.5 (2.6)	11.5 (2.4)	2.31	.03
BAS-fun-seeking subscale	9.9 (3.2)	10.1 (2.3)	.17	.87
SAPS	25.1 (14.6)			
SANS	34.4 (14.2)			

BAS, Behavioral Approach System; BIS, Behavioral Inhibition System; DASS-21, Depression Anxiety Stress Scale-21; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; WASI, Wechsler Abbreviated Scale of Intelligence; WTAR, Wechsler Test of Adult Reading.

[a]Antipsychotic drug treatment of schizophrenia: aripiprazole $n = 2$; clozapine $n = 4$; olanzapine $n = 6$; paliperidone $n = 2$; quetiapine $n = 1$; risperidone $n = 1$; ziprasidone $n = 2$.