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Research report

Response acquisition with signaled delayed reinforcement in a rodent model of ADHD

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ABSTRACT

Previous research by Hand et al. [10] showed that acquisition of lever pressing was retarded in spontaneously hypertensive rats (SHRs) relative to Wistar-Kyoto rats (WKYs) when unsignaled delays of 15 s separated lever presses from food delivery. The SHRs took longer to begin responding, exhibited a slower increase in response rates, responded at a lower asymptotic response rate and earned fewer reinforcers than the WKYs. The present experiment examined whether similar strain differences in acquisition would be observed if the same delay to reinforcement was signaled. Signaled delays of reinforcement typically result in lesser disruption of steady-state operant behavior than unsignaled delays, presumably because the signals function as conditioned reinforcers. Under a response-acquisition procedure, signals might be expected to facilitate acquisition which could minimize SHR–WKY strain differences. The present study exposed SHR and WKY rats to a procedure where a single lever press illuminated the houselight and delivered a food pellet 15 s later. Response acquisition was similar between SHR and WKY rats under 15-s signaled delays of reinforcement; the responses emitted, delay resets and pellets earned by both strains were similar. Removal of the delay signal immediately decreased responding for both strains with the SHRs showing a significantly slower recovery over time. Overall the results suggest that signals occurring during response-reinforcer delays can mitigate the response-weakening effects of delayed reinforcement in a rodent model of ADHD.

1. Introduction

The spontaneously hypertensive rat (SHR) exhibits behavior consistent with humans diagnosed with ADHD including hyperactivity [13] and inattention [23,24]. The SHRs also exhibit heightened sensitivity to delayed reinforcement manifested as weakly maintained free-operant responding under conditions of delayed reinforcement [11], preference for smaller, immediate reinforcers over larger, delayed ones [1,7,9], and difficulties acquiring a new response with delayed reinforcement [10]. Such sensitivity to delayed reinforcement has been suggested as a critical component of ADHD [25]. Hand et al. [10] adapted a procedure developed by Lattal and Gleeson [15] for studying response acquisition with delayed reinforcement and found that SHRs exhibited retarded acquisition of lever pressing for delayed food reinforcers. In Hand et al. [10], a single lever press led to a 15-s, unsignaled, resetting delay to reinforcement. Responses that occurred during the delay reset the delay by another 15 s. Thus, the reinforcer was always separated from the last lever press by 15 s. Relative to the control strain, Wistar-Kyoto (WKY), the SHRs exhibited a slower increase in responding across sessions, and responded at a lower asymptotic response rate at the end of the experiment. Additionally, the SHRs emitted more lever presses on an inactive lever and earned fewer reinforcers throughout the entire experiment.

With clear strain differences in the acquisition of lever pressing between SHRs and WKYs, efforts must be directed at identifying behavioral and neurological variables that modulate response acquisition. Understanding acquisition-modulating variables will provide information pertaining to the mechanisms underlying previously observed strain differences in behavior. Signaling the response-reinforcer delay is a variable that has been shown to modulate sensitivity to delayed reinforcement. In Hand et al. [10], there was no stimulus change associated with the delay. An important follow-up, therefore, is to determine the effect of delay signals on response acquisition. Might the addition of a delay signal, such that the response that starts the delay also produces an immediate stimulus change, improve learning in this procedure? Furthermore, if a rodent model of impulsivity or ADHD can be shown to be less impulsive with the addition of such a stimulus, then the outcome

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could have implications for the development of intervention strategies.

The effects of response-reinforcer delay signals have been studied extensively in the context of steady-state procedures [14,21,22,27,28]. Unlike response-acquisition procedures where responding is established with delayed reinforcement from the beginning, steady-state procedures begin by establishing baseline responding under conditions of immediate reinforcement. Upon this baseline, response-reinforcer delays are imposed either across conditions or within a session. Typically, response rates are inversely related to delay length, and signals generally reduce the response rate-decreasing effects of delayed reinforcement [21]. The effect of these signals is consistent with the notion that they acquire reinforcing function by reliably preceding food; however, this might be only one of many possible explanations.

Extending the results obtained from signaling the delays in steady-state procedures to a response acquisition with delayed reinforcement procedure, one might predict that the immediate, response-contingent presentation of a signal indicating the beginning of the delay would facilitate response acquisition. Critchfield and Lattal [6] examined the effects of a delay signal on response acquisition with 30-s delays to reinforcement. In their study, rats obtained delayed reinforcers by breaking an infrared photobeam, a response chosen by the researchers because unlike a lever press, it has no tactile or auditory feedback that could function as a signal. Two groups of rats were exposed to a 30-s delay of reinforcement acquisition procedure. The beginning of each delay was signaled by a 0.75-s tone for one of the groups. Both groups showed similar patterns of acquisition in terms of response rates, which were roughly equal and increased at the same rate across the study. The group with the signaled delays to reinforcement, however, earned more reinforcers and emitted fewer responses during the delay to reinforcement, results that can be interpreted as reflecting greater efficiency in response acquisition.

Given the above discussion, it is reasonable to expect that signaling the delays to reinforcement would enhance response acquisition for SHRs, perhaps such that strain differences would not be observed. To this end, the present study examined acquisition of lever pressing by SHRs and WKYs using a resetting, signaled 15-s delay to reinforcement. First, based on Hand et al. [10] we predicted that both strains would acquire lever pressing. Second, we predicted that signaling the delay to reinforcement would facilitate response acquisition in SHRs to the extent that there would be no differences in response acquisition between the strains. Finally, we predicted that removing the delay signal would weaken responding to a greater extent in the SHRs.

2. Method

2.1. Subjects

Subjects were eight male SHRs and eight male WKYs (strains SHR/NCrl and WKY/NCrl; Charles River Laboratories, Portage, MI). Upon delivery, the 1-month-old rats were separated into individual wire cages and provided free access to food and water. They were housed in the colony room on a 12-h reversed light–dark schedule (lights off at 8:00 a.m.). Free access to food continued for 10 weeks at which time they were food restricted and maintained at 85% of their free-feeding weights. From then on, supplemental feedings were provided at least 1 h following sessions to maintain each rat's experimental weight. All rats were 4 months old at the beginning of the experiment and were experimentally naïve.

2.2. Apparatus

Four identical Coulbourn Instruments (Allentown, PA) operant chambers measuring 29 cm high by 28.5 cm long by 25 cm deep were used. The work panel contained a rolled steel lever measuring 3.5 cm wide, protruding 2 cm from the wall and required a minimum force of approximately 0.25 N to operate. The center of the lever was located 4.5 cm from the left chamber wall and 6.5 cm above the floor. Three LED stimulus lights (red, yellow and green) were arranged horizontally directly above the lever and were programmed to illuminate in unison. Horizontally centered on the front panel 2 cm from the floor was a 3 cm wide by 4 cm tall by 2 cm deep recess into which 45-mg Bio-Serv® Dustless Precision Pellets (Bio-Serv, Frenchtown, NJ; Product #F0021) were delivered. A houselight module equipped with a 14.4-V miniature bulb was located directly in the middle of the back panel 1.5 cm from the ceiling. All chambers were housed in large sound and light attenuating chambers. An IBM®-compatible computer running Microsoft Windows XP® and Graphic State v. 3.01 software provided control of stimuli and recording of data.

2.3. Procedure

2.3.1. Magazine training

Prior to the beginning of the experiment the rats were trained to eat the food pellets from the food tray in the operant chamber. For these magazine training sessions the stimulus lights and response lever were removed to prevent incidental pairing of lever presses with food delivery. Food pellets were delivered according to a variable-time (VT) 60-s schedule where the individual inter-pellet delivery times were calculated using a constant-probability algorithm described by Catania and Reynolds [5]. Two sessions of magazine training were conducted, each lasting until 30 food pellets were delivered. At this point, all the rats were eating the food pellets immediately upon delivery and the experiment began.

2.3.2. Delayed reinforcement procedure

Each session and trial began with the illumination of the three LEDs above the lever. Following a single press of the lever, the houselight was illuminated and remained on for the duration of the delay preceding pellet delivery. Lever presses during this delay reset the time to pellet delivery to ensure that the response-reinforcer delay was always 15 s. Technically, the schedule of reinforcement was a chain FR 1, DRO 15 s. When a pellet was delivered the houselight and LEDs turned off for 1 s and then the LEDs were turned back on. Twenty sessions, each lasting 30 min, were conducted 5 days per week at approximately the same time every day.

After these 20 sessions the unsignaled condition began. The only difference in the procedure was that the delay signal (houselight) was absent, resulting in a tandem FR 1, DRO 15-s schedule, the same schedule as in Hand et al. [10]. Twenty sessions under this schedule, each lasting 30 min, were conducted 5 days per week at approximately the same time every day.

2.3.3. Data analysis and statistics

The dependent measures were response rate (calculated as the total number of responses divided by the 30-min session time), pellets earned, and the number of lever presses during the DRO component of the schedule (delay resets). Each dependent measure was analyzed using a mixed-model ANOVA with strain as the between-subjects factor and sessions as the repeated, within-subjects factor. Separate ANOVAs were conducted for each dependent measure from the signaled and unsignaled delays.

Acquisition in the signaled condition was modeled using Eq. (1). The model describes acquisition at the group level in terms of response rates (B). Four free-parameters represent the operant level or beginning response rates ($O_{\min}$), the asymptotic response rate ($O_{\max}$), the number of sessions to reach half of the asymptotic response rate (k), and the rate of the ascending portion of the function (λ):

$$B = O_{\min} + \frac{O_{\max} - O_{\min}}{1 + e^{(k-x)/\lambda}} \quad (1)$$

The model was not applied to response rates from the unsignaled condition because lever pressing had already been acquired.

3. Results

3.1. Signaled delays

The mean response rates in each session for both strains in the signaled delay condition are displayed in the top panel of Fig. 1. Response rates for both strains increased until the 5th session. For the remaining 15 sessions response rates oscillated around 3.5 and 2.5 responses per minute for the SHRs and WKYs, respectively. Furthermore, the SHRs showed greater within-group variability than the WKYs. The ANOVA revealed a significant main effect of session on response rates [$F(19, 266) = 14.71$, $p < .001$] indicating that response rates changed for both strains over the course of the experiment. The ANOVA revealed no significant session by strain interaction [$F(19, 266) = 0.79$, $p = .72$] which corroborates the visual evidence that there were no differences in the pattern of response acquisition between the strains. The SHRs emitted somewhat higher response rates across the 20 sessions, although the