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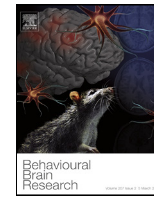

Research report

A microstructural analysis of schedule-induced polydipsia reveals incentive-induced hyperactivity in an animal model of ADHD☆

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HIGHLIGHTS

- Similar rate of licking induced by FT 30-s schedule in SHR, Wistar, and WKY rats.
- FT 90-s lengthened drinking episodes in SHR, reduced rate of licking in Wistar, WKY.
- Schedule-induced drinking occurred in bouts separated by pauses.
- SHR episodes comprised shorter, more frequent bouts of drinking.

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ABSTRACT

Recent research has suggested that frequent short bursts of activity characterize hyperactivity associated with attention deficit hyperactivity disorder (ADHD). This study determined whether such pattern is also visible in schedule-induced polydipsia (SIP) in the spontaneously hypertensive rat (SHR), an animal model of ADHD. Male SHR, Wistar Kyoto (WKY) and Wistar rats were exposed to 40 sessions of SIP using a multiple fixed-time (FT) schedule of food delivery with FT 30-s and FT 90-s components. Stable performance was analyzed to determine the extent to which SIP-associated drinking is organized in bouts. The Bi-Exponential Refractory Model (BERM) of free-operant performance was applied to schedule-induced licks. A model comparison analysis supported BERM as a description of SIP episodes: licks were not produced at a constant rate but organized into bouts within drinking episodes. FT 30-s induced similar overall licking rates, latencies to first licks and episode durations across strains; FT 90-s induced longer episode durations in SHRs and reduced licking rate in WKY and Wistar rats to nearly baseline levels. Across schedules, SHRs made more and shorter bouts when compared to the other strains. These results suggest an incentive-induced hyperactivity in SHR that has been observed in operant behaviour and in children with ADHD.

1. Introduction

Recent research suggests that children with attention deficit hyperactivity disorder (ADHD) engage in frequent but short bouts of operant behaviour [1]. The spontaneously hypertensive rat (SHR), an animal model of ADHD [2,3], shows a similar pattern of operant performance [4]. It thus appears that this pattern of behaviour constitutes a key component of the behavioural phenotype of ADHD.

The present study was aimed at determining whether frequent but short bouts of responding were also observed in SHRs in a non-operant behavioural preparation, schedule-induced polydipsia (SIP). SIP consists of excessive drinking that occurs on a schedule in which food is intermittently delivered, usually observed in partially food-deprived rats [5]. SIP can be produced in a wide range of behavioural schedules, including conditions in which animals are exposed to intermittent delivery of food regardless of their behaviour, such as fixed time (FT) schedules [6,7].

The principal characteristic of SIP is its excessiveness, which distinguishes it from others behaviours performed throughout inter-food intervals. Thus, SIP serves as the prototype of so-called

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adjunctive behaviour ([8]; also referred to as interim behaviour [9]). In relation to ADHD, SIP successfully selects among experimental subjects those that display characteristics associated with excess behaviour [10,11] and other disorders associated with deficient impulse control [12,13], such as substance abuse [14], obsessive compulsive behaviour [15–19], and schizophrenia [20,21].

Comparisons of SIP between SHR, Wistar and Wistar Kyoto (WKY) rats have shown that (a) there is no significant difference in SIP among strains when the inter-food interval is short (30 s), but (b) whereas SIP declines with longer inter-food intervals (approximately 60 s) in WKY and Wistar rats, SIP in SHR remains relatively high [22,23]. Reduced SIP in control strains may occur because of (a) a reduction in the proportion of inter-food intervals that contain drinking episodes, (b) an increase in the latency to initiate drinking episodes, (c) a reduction in the duration of drinking episodes, and/or (d) a reduction in the rate of licking during a drinking episode. To the extent that licking rate is, like operant behaviour, organized in bouts [24,25], licking rate may decline because (a) licking bouts occur less often, (b) licking bouts are shorter, and/or (c) licking rate within bouts declines.

The present study aimed at examining these potential differences in SIP performance across three strains of rats, SHR, Wistar and WKY, and two food schedules, FT 30-s and FT 90-s. The organization of drinking episodes in bouts of licks was of particular interest, not only because of its ostensible link to ADHD, but also because parameters of bout organization have been associated with motor, motivational and learning variables [25]. Therefore, differences in parameter estimates across strains may suggest novel hypotheses about the behavioural mechanisms that underlie the differences in performance across strains, as well as on the behavioural mechanisms involved in SIP and related phenomena.

2. Method

2.1. Subjects

Twenty-four male rats of three strains – 8 SHR, 8 WKY and 8 Wistar – obtained from Charles River Laboratories (Lyon, France) were used. On arrival at the laboratory, animals were 10 weeks old; they were housed in groups, in an environmentally controlled room with a 12-h light–dark cycle (light from 08:00 to 20:00 h), ambient temperature of 17–23 °C, and 60% relative humidity. Once habituated to the animal facility, rats were housed singly in 18 cm × 32.5 cm × 20.5 cm transparent Plexiglas cages, with a metal-grid detachable roof that allowed for food to be deposited and a water bottle to be fitted.

Rats were 12 weeks old at the start of the experiment. Their average weights were, for SHR, 292 g (range: 277–302 g); for WKY, 339 g (range: 306–361 g); for Wistar, 373 g (range: 359–384 g). Weights were reduced to 80–85% of free-feeding weight by a controlled diet, and then maintained throughout the experiment in proportion to standard growth curves for each strain. Each rat was weighed daily before the experimental session. Twenty minutes after the experimental session, each animal received the appropriate food supplement to maintain its weight within the criterion-based range.

2.2. Apparatus

Eight Letica LI-836 conditioning chambers, measuring 29 cm × 24.5 cm × 35.5 cm, enclosed in soundproofed housing, equipped with its own ventilation and a small observation window at the front. The front panel of each conditioning chamber was made of aluminium, the left wall of transparent Plexiglas and the remaining walls of black Plexiglas. On the exterior of the chamber' right-hand wall, a water bottle was fitted, and the rat had access to the spout from the interior of the chamber, through a 3.2 cm × 3.9 cm aperture in the wall, situated 20 cm from the front panel and 7 cm from the floor. The spout was placed 2 cm towards the interior of the aperture to allow for licks rather than continuous drinking. Contact between the animal's tongue and the metal spout completed the electric circuit between the 12-bar metal grid that served as the floor and the water-bottle spout. Licks were recorded using a MED-PC-IV application under a Windows XP environment. Forty-five mg food pellets were dispensed (Bio-Serv, Frenchtown, NJ, USA) in an aperture in the chamber's front wall situated 3.7 cm from the floor, between the panel's two levers, which were retracted throughout the experiment. The chambers were lit by two 3 W lamps situated on the front panel at either side of the food hopper and by an indirect 25 W light fitted to the interior of the soundproof housing that insulated each chamber. Exterior noise was masked by a fan that produced an ambient noise of approximately 60 dB in each chamber. At the top of the front wall of each chamber was a speaker that produced sound signals when necessary.

2.3. Procedure

The SIP procedure was carried out using a multiple FT schedule, in which a food pellet was delivered at regular intervals regardless of the animal's behaviour. Every experimental session contained two schedule components, FT 30-s and FT 90-s, and the first component to start each session was determined randomly. Rats were given 20 food pellets/session in each component. One of the components was always signalled with a continuous tone of 60 dB (while the other was signalled by its absence); assignment of tone-signalled component was randomized across animals. The experimental chamber lights were turned off for 60 s between FT components.

Forty experimental sessions were conducted, until SIP performance was stable in both schedules in terms of lickingrate (licks/min) and volume of water consumed. Data from the last 8 sessions was used for the estimation of bout parameters. All data were collected with a resolution of 20 ms.

2.4. Estimation of bout parameters

Bout-parameter estimation was conducted only on rats that, during the last 8 sessions, drank more than the average daily level of prandial water consumption (2.75 ml). A total of 19 rats (all SHR rats, 6 WKY rats and 5 Wistar rats) were included in the analysis.

The following measures were obtained from each trial in which a rat produced at least two licks: latency to the first lick, duration of the drinking episode (i.e., time between first and last lick), and 3 parameters of the distribution of inter-lick intervals (ILIs): the rate at which licking bouts were initiated (b), the rate of licking within bouts (w), and the probability that a lick was not the last one in a bout [p; mean bout length = $1/(1-p)$]. These parameters were estimated using the Biexponential Refractory Model (BERM) of free-operant performance [26],

$$\begin{aligned} &p(\text{ILI}=t|t<\delta)=0 \\ &p(\text{ILI}=t|t\geq\delta)=pw\exp[-w(t-\delta)]+(1-p)b\exp[-b(t-\delta)] \end{aligned} \quad (1)$$

This equation indicates that there is a minimum time between consecutive licks, δ, and that ILIs longer than δ are sampled with probability p from an exponential distribution with mean $(1/w)+\delta$ (the within-bout lick rate), and with probability $1-p$ from another exponential distribution with mean $(1/b)+\delta$ (the bout-initiation rate). Estimates of p, w and b were obtained using the method of least squares [27], with δ fixed at 10 ms (half of the data resolution)