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Research report

# Effects of delayed reinforcers on the behavior of an animal model of attention-deficit/hyperactivity disorder (ADHD)

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**Abstract**

Attention-deficit/hyperactivity disorder (ADHD), affecting 3–5% of grade-school children, is a behavioral disorder characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity. It has been suggested that the symptoms are caused by altered reinforcement and extinction processes, behaviorally described as an abnormally short and steep delay-of-reinforcement gradient in ADHD.

The present study tested predictions from the suggested shortened and steepened delay gradient in ADHD in an animal model, the spontaneously hypertensive rats (SHRs). It was predicted that SHR responding during baseline would mainly consist of responses with short interresponse times, and that responding would be more rapidly reduced in the SHR than in the controls by the introduction of a time interval between the response and reinforcer delivery. Effects of a resetting delay of reinforcement procedure with water as the reinforcer were tested on two baseline reinforcement schedules: variable interval 30 s (VI 30 s) and conjoint variable interval 60 s differential reinforcement of high rate 1 s (VI 60 s DRH 1 s).

The results showed a higher rate of responses in the SHR than in the controls during baseline, mainly consisting of responses with short interresponse times. The statistical analyses showed that response rates decreased more rapidly as a function of reinforcer delay in the SHR than in the controls. The analyses of the estimates of the reinforcer decay parameter showed no strain differences during the VI 30 s schedule but showed a significant strain difference at the end, but not at the start, of the sessions during the VI 60 s DRH 1 s schedule.

In general, the results support predictions from the suggested steepened delay gradient in SHR. However, the predictions were only partly confirmed by the analyses of the decay parameter.


*Keywords:* Catecholamine; Reward; Hyperkinesis; Hyperkinetic disorder; IRT

## 1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) [2] is the most common behavioral disorder of childhood affecting between 3 and 5% of grade-school children [1,61,63,64]. The core symptoms include a persistent pattern of inattention and/or a developmentally inappropriate level of hyperactivity. Age of onset is usually before the child is 7-year old [3,6]. ADHD is a highly persistent disorder and 50–70% of children diagnosed with ADHD will experience difficulties related to social adjustment and functioning and/or have psychiatric problems as adolescents and young adults [9,67].

ADHD is currently defined as a developmental disorder where all clinical criteria are behavioral. The cause of ADHD has not yet been ascertained and there is no biological marker distinguishing ADHD from normality. However, a strong genetic basis for ADHD has been recognized [14,29,62], and dopamine dysfunction seems to be an important factor in its etiology [19,60,66].

Reinforcers affect the behavior of children with ADHD and normal children differently [18,28,37,42,57], and children with ADHD are less sensitive to changes in reinforcement contingencies compared to normal controls [65].

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Altered reinforcement processes have been suggested as a factor in producing ADHD symptoms [8,17,18,23,42–44,55,68]. ADHD children show aversion to delayed reinforcers and generally prefer immediate reinforcers, even when these are less attractive than reinforcers that may be obtained after a delay [56,57].

Reinforcement and extinction have been demonstrated to be associated with dopamine neuron activity in primates [22,52]. The neurobiological basis for the delay-of-reinforcement gradient may be the time window available for coincidence detection of new response–reinforcement or stimulus–response–reinforcement relations [31]. Dopamine release may, at a neuronal level, increase the time window for coincidence detection. Consequently, reduced dopamine function associated with ADHD may produce narrower than normal time windows for coincidence detection resulting in a shorter than normal delay gradient [23,45].

We have suggested that there might be three underlying factors causing ADHD: a shorter than normal delay-of-reinforcement gradient, deficient extinction of previously reinforced behavior, and poor motor control [23,45]. An abnormally short delay gradient in ADHD implies that only responses in close proximity to reinforcer delivery can be strengthened by the reinforcer [23,39,42,43,49]. A shorter delay gradient may be the source of ADHD children's aversion to delayed reinforcers and their preference for immediate reinforcers, even when more attractive reinforcers may be obtained after a delay, cf. [56,57].

A reinforcer acts not only on the response that produced it but to a lesser degree also on responses emitted earlier [10]. Also relations between responses (e.g. interresponse times, IRTs) are strengthened and maintained by reinforcers [10,13,42]. In contrast to the normal delay gradient, only short IRTs may be reinforced and maintained by a short delay gradient.

The present studies investigated behavioral effects of delayed reinforcers in an animal model of ADHD using a resetting delay-of-reinforcement procedure. The spontaneously hypertensive rat (SHR) is possibly the best-validated animal model of ADHD [40,41]. Bred from normotensive progenitor Wistar Kyoto rats (WKY), SHR have demonstrated attention problems [27,47,48], impulsiveness and hyperactivity (see [40,41]). Also, as in children with ADHD [42], hyperactivity is not present in novel situations, but develops after some time in the new setting [27,48].

In the first part of the present study, predictions derived from a hypothetical shorter and steeper delay gradient in the SHR were experimentally tested. A short and steep delay-of-reinforcement gradient will mainly reinforce responses with short IRTs (burst responding). Consequently, it was predicted that the SHR would develop a high rate of responses with short IRTs when the reinforcers were delivered without any delay. Further, in the resetting delay procedure, the consequence of the lever press (delivery of a drop of water) was delayed for a specified time interval (i.e. the effect of the reinforcer is "blocked"). Thus, a greater proportion of a steep and short delay gradient would be "blocked" as compared to a long and less steep normal delay gradient. Therefore, we also predicted that responding would be more affected by delayed reinforcement in SHR than in control WKY rats.

## 2. General methods

### 2.1. Subjects

The subjects in each experiment were eight male NIH-strain spontaneously hypertensive rats (SHR) and 8 male NIH-strain Wistar Kyoto (WKY) control rats bred by a commercial supplier (Møllegaard Breeding Center, Denmark). The subjects were experimentally naive and weighed 180–250 g at the start of each experiment. In experiment 1, the rats were housed in groups of four of the same strain in opaque plastic cages 35 cm × 26 cm × 16 cm (height). During experiment 2, the rats were housed individually in the same type of cages. In both experiments, the animals had free access to food (Beekay Feeds, Rat and Mouse Autoclavable Diet, B&K Universal Ltd.).

A 22 h drinking water-deprivation schedule was used throughout both experiments except during weekends when the animals had free access to water. Access to water in the home cage was limited to 30 min immediately following each session. The animal quarters were temperature and humidity controlled (20 ± 2 °C and 55 ± 10%, respectively). Light was on between 0800 and 2000 h.

The experiment was approved by the Norwegian Animal Research Authority (NARA), and was conducted in accordance with the laws and regulations controlling experiments/procedures in live animals in Norway.

### 2.2. Apparatus

Eight identical Campden Instruments rodent test cages, 26 cm × 25 cm × 30 cm (height), were located in Campden Instruments small environment cubicles. One 2.8 W house light illuminated each test chamber. The chambers were equipped with two retractable levers requiring 3 g (0.03 N) to close. Only the left lever was used; the right lever remained retracted throughout the experiments. One liquid dipper delivered 0.01 ml of tap water when activated. It was housed in a small cubicle with a 2.8 W cue light and located halfway between the two levers. A 7 cm × 5 cm transparent, top-hinged plastic flap separated this cubicle from the animal's working space. Light pushing by the nose or the paw was sufficient to open the flap and activated a microswitch. A computer and an on-line system (Spider, Paul Fray Ltd., UK) recorded lever presses and tray visits, and scheduled reinforcers and lights. Behavior was also recorded by cumulative recorders.

### 2.3. General procedure

#### 2.3.1. Response shaping

During the combined 15 min habituation and magazine training sessions, the animals received water according to a variable time 3 s schedule (VT 3 s). This schedule presents a reinforcer on average every 3 s independent of the animal's behavior. In these sessions, the flap in front of the water dipper remained open.

The habituation and magazine training sessions were followed by two sessions where opening of the flap into the water cubicle