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Using an adjusting amount procedure to investigate impulsivity in spontaneously hypertensive rats (SHR)

Phillip Andrew Halsey
James Madison University

Using an Adjusting Amount Procedure to Investigate Impulsivity in Spontaneously Hypertensive Rats (SHR)

Phillip Andrew Halsey

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Table of Contents

List of Tables

List of Figures

Abstract

This experiment compared impulsivity in spontaneously hypertensive rats (SHRs), a putative animal model of Attention Deficit/Hyperactivity Disorder (ADHD), with two control strains. One definition of impulsive behavior that appears in the literature is preference for smaller sooner (SS) reinforcers over larger later (LL) reinforcers when both are concurrently available in the context of discrete trial choice procedures. Adopting that definition, the current experiment used an adjusting amount procedure to measure changes in the subjective value of delayed reinforcers. The LL reinforcers varied across 5 conditions (5 pellets, each evaluated at 5 delays: 2, 4, 8, 16, and 32-s). From the data at each delay, I determined the best-fit curves using Mazur's (1987) hyperbolic-decay model and Green's (1994) hyperbola-like model to demonstrate the extent to which the rats discounted the delayed reinforcers. As an additional measure, I calculated the area-under-the-curve. The discounting functions based on the hyperbolic-like model described the rats' data well and revealed that the SHRs discounted more steeply than rats in both control strains, which were more similar to each other than either was to the SHRs. Although there are limitations to the current study, the SHRs demonstrated a decreased subjective value for larger, delayed reinforcers across the delay conditions. According to their usage as a nonhuman animal model of ADHD, the current data support the SHRs as a valid model of ADHD and their continued use as a nonhuman animal model of this disorder and suggest that Wistar rats might be a more appropriate control strain than the typically employed Wistar-Kyoto rats.

Background

Attention Deficit Hyperactivity Disorder (ADHD), a disorder more commonly diagnosed in boys than girls, first appears childhood or adolescence and includes behaviors such as increased inattentiveness relative to individuals at a similar level of development. Even though, the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 2000) considers the inability to attend to or to complete a task the most defining feature of ADHD, it also includes additional characteristics such as hyperactivity, which manifests in terms of increased and often excessive motor activity, and impulsivity, which is defined as an inability to tolerate delays and inhibit responses. The *DSM-IV TR* provides a clinical definition of the characteristics of ADHD including impulsivity, which is useful for diagnoses, but researchers investigating it in laboratory settings (Ainslie, 1975; Green, Myerson, & McFadden, 1997; Rachlin & Raineri, 1992) have defined impulsive behavior in a more precise, behavior analytic way .

In an examination of the similarities and differences among the definitions of impulsive behavior proposed by multiple disciplines (e.g., social psychology, economics), Ainslie (1975) reviewed several key behavioral characteristics of impulsivity from a behavior-analytic perspective. Unlike other approaches, the behavior-analytic approach does not attribute the cause of behavior to mental states or other hypothetical constructs. Rather, according to the behavior-analytic view, behavior is a function of the interaction of an individual's ontogenetic and phylogenetic history with current environmental circumstances (Skinner, 1981). Consistent with this, Ainslie suggested that an individual's behavior is impulsive when he or she engages in behaviors resulting

in smaller reinforcers delivered sooner (SS) rather than behaviors that result in larger reinforcers delivered later (LL).

A recent extension of Ainslie's (1975) definition of impulsive behavior suggests that individuals with impulse disorders such as ADHD may be more sensitive to delayed consequences than are individuals without such disorders (Green et al., 1997; Rachlin & Raineri, 1992). For example, when presented concurrently with a smaller reinforcer and a larger reinforcer delivered at the same time, individuals will generally select the larger reinforcer. As the delay to the larger reinforcer increases, most individuals will change preference from the larger reinforcer to the smaller reinforcer because the subjective value of the larger reinforcer decreases as the delay increases. That is, the subjective value of the larger reinforcer is discounted as the delay increases. When the subjective value of the larger reinforcer is so low that it is below the subjective value of the smaller reinforcer, the individual will choose the SS reinforcer. If individuals with ADHD are more sensitive to such delays, they will discount delayed reinforcers more steeply. That is, given a choice between a LL reinforcer and a SS reinforcer, the subjective value of the LL reinforcer is more likely to be smaller than the subjective value of the SS reinforcer for the individuals who are more sensitive to the delayed consequences. Thus, individuals with ADHD may show preference for the SS reinforcer even when the delay to the LL reinforcer is relatively short (Green et al., 1997).

In an experiment involving children diagnosed with ADHD, Tripp and Alsop (2001) assessed whether children would behave impulsively when presented with a choice between a secondary reinforcer delivered immediately and a secondary reinforcer delivered after some delay. Thirty-six children diagnosed with ADHD and 36 children

who were developmentally normal served as participants for the study. Using a discrete-trial procedure, the children responded by selecting one of two keys with pictures of faces that corresponded with faces that were presented on a computer monitor. Responses on the key that matched the displayed face resulted in the consequence particular to that face. Matching one of the faces correctly always resulted in delivery of a token immediately and matching the other face correctly always resulted in delivery of a token after a 3.5-s delay. Incorrect responses did not result in token delivery and resulted in the monitor going blank for 50 s. Children with ADHD made more responses on the key that resulted in the immediate reinforcer relative to typically developed children, regardless of the face presented on the monitor. That is, children with ADHD made more incorrect responses on the key associated with immediate reinforcement (when shown the face associated with delayed reinforcement) than incorrect responses on the key associated with delayed reinforcement (when shown the face associated with immediate reinforcement). These data are consistent with the notion that children diagnosed with ADHD are less able to tolerate delays than their typically developing peers are when the reinforcer amount is constant. However, these data do not address whether children with ADHD demonstrate a preference for a smaller, immediate reinforcer over a larger, more delayed reinforcer more than normally developing peers.

Binder, Dixon, and Ghezzi (2000) examined this question using delay-to-reinforcement procedures in an effort to teach self-control to children with ADHD. Each procedure consisted of four conditions: a natural baseline, a choice baseline, a second choice baseline, and self-control training. During the natural baseline, Binder et al. (2000) assessed the maximum delay each child could tolerate before obtaining a

reinforcer and used that duration to calculate the delay to reinforcement for the larger reinforcer during the choice baseline conditions. During the first choice baseline, the children allocated behavior between two response alternatives: one that resulted in a smaller, edible reinforcer delivered immediately and another that resulted in larger, edible reinforcer delivered after a delay that was three times the maximum delay tolerated during natural baseline. During the second choice baseline, both the small and large reinforcers were available immediately. In the self-control condition, the response options were the same as during the first choice baseline condition, but the researchers provided verbal activities and games for each child to attend to during the delay when the child selected the larger, delayed reinforcer. During the first choice baseline condition, the children reliably chose the SS reinforcer when the delay to the LL was in effect. During the second choice baseline, when both the large and small reinforcer were immediate, children reliably chose the larger, immediate reinforcer In the self-control condition, children chose the larger, delayed reinforcer approximately 75% of the time. In fact, that the children with ADHD allocated more responding for SS reinforcers than the LL reinforcers supports Ainslie's (1975) definition of impulsive behavior.

The results from Tripp and Alsop (2001) and Binder et al. (2000) demonstrated that the examined children with ADHD preferred the SS reinforcers to the LL reinforcers. Studies like these that directly investigate the behaviors of interest in clinical populations are important for adding to our understanding of those behaviors. However, differences in the individual history of each child in those studies may have influenced their choices between the alternatives, which highlight the advantages to studying animal models of clinical disorders (Ferguson, 2001). Non-human animal models allow researchers to

investigate variables related to the etiology and treatment of clinical disorders with fewer differences in genetic and behavioral histories that potentially affect the behaviors of interest. Additionally, the use on non-human subjects in experiments allows for greater control over prevailing conditions such as motivating operations that are advisable to hold constant during experimentation (Sagvolden, Russell, Aase, Johansen, & Farshbaf, 2005).

With regard to the study of ADHD, one of the most frequently used non-human animal models is the spontaneously hypertensive rat (SHR) (Sagvolden, 2000). Numerous studies have demonstrated that SHRs display behavioral characteristics analogous to the behaviors of individuals diagnosed with ADHD. Research assessing the validity of the SHR across measures of sustained attention (Berger & Sagvolden, 1998; Aase & Sagvolden, 2006), increased motor activity and behavioral variability (Wultz & Sagvolden, 1992; Mook, Jeffrey, & Neuringer, 1993; Saldana & Neuringer, 1998), and impulsiveness (Sonuga-Barke, Taylor, Sembi, & Smith, 1992; Fox, Hand, & Reilly, 2008; Hand, Fox, & Reilly, 2009) has shown that SHRs demonstrate behavior analogous to that of individuals with ADHD.

To evaluate impulsivity in SHRs, Hand et al. (2006) examined the manner in which delayed reinforcement affected the acquisition of lever pressing. Seven SHR and seven Wistar Kyoto rats (WKY), a progenitor strain for the SHRs and the strain most often used as a control for purposes of comparison, responded under a tandem fixed ratio (FR 1), differential reinforcement of other behavior (DRO 15-s) schedule. During the FR component, each lever press triggered the DRO component. The DRO was a 15-s unsignaled interval that reset if the rat made another response prior to the completion of

the interval. If no response occurred during the 15-s interval, the rat received a food pellet. The average rate of lever pressing throughout the 30 experimental sessions was significantly lower for the SHRs than the WKYs. In addition, relative to the WKYs, the SHRs were slower to acquire lever pressing under the tandem schedule. SHRs were also more likely to continue responding once the DRO had begun and therefore they earned fewer reinforcers per session than the WKYs. As a non-human animal model of ADHD, the SHRs demonstrated a response rate with respect to delayed reinforcement similar to individuals with ADHD (Saldana & Neuringer, 1998; Hand et al., 2006).

To determine differences among SHR, WKY, and Long Evans (LE) rats' toleration of delayed consequences, Sanabria and Killeen (2008) conducted two separate experiments using two measures: a lever hold task (LHT) and a schedule of differential reinforcement of low rates of behavior (DRL). In the LHT, delivery of food reinforcers resulted if the rat held down and subsequently released a lever between a minimum and an adjusting maximum duration. The rats completed eight initial minimum duration conditions: 0.25, 0.5, 0.75, 1, 1.5, 2.25, 3.38, and 5 s. The initial minimum duration increased in the following session after a rat met the duration criterion for at least two sessions. The initial maximum duration was set at 2 s, and both the minimum and the maximum response duration adjusted according to within-trial responses. Responses that exceeded the maximum duration increased the maximum time by 0.02 s and responses met the duration criterion increased the minimum time by 0.01 s until the minimum duration equaled the maximum time. The results showed that both the SHR and WKY rats exhibited shorter mean response durations than the LEs. The shorter mean response durations emitted by the SHRs are consistent with their use as an animal model of

ADHD. The similarity in response durations of the SHRs and the WKYs was unexpected given that WKYs are the most commonly used control strain for the SHRs and as such, their behavior should differ from SHRs along dimensions that define the disorder. That is, to the extent that WKYs are an appropriate control for SHRs, the response duration of the WKYs should have been longer than the SHRs. One possible reason for the behavioral similarity of the SHRs and WKYs is the similarity of potential influential physical characteristics, such as weight. The SHRs and WKYs had similar weights with rats in both strains weighing considerably less than the LEs, which might have rendered the SHRs and WKYs physically unable to depress the lever for extended lengths of time.

To address concerns that such physical differences among the strains may have affected the outcome of the first experiment, Sanabria and Killeen (2008) performed a second experiment to assess impulsive behavior in these three strains using three different variations of a DRL procedure. The DRL 5-s procedure required each rat to make successive lever presses no quicker than the specified interresponse time of 5 s. During the DRL-LH 5-s condition, considered analogous to the maximum duration in the LHT in the first experiment, responses made after LH, which started at a value of 10 s, increased the LH time to increase by 0.03 s and reinforced responses decreased the LH time by 0.01 s. In the final procedure, there was no LH and each reinforced response increased the DRL time requirement by 0.75%, from the starting interresponse time requirement of 5-s to a maximum interresponse time of 60 s. In the DRL 5-s condition, the SHRs were least efficient at producing reinforcement (they emitted more responses per reinforcer), the WKYs were more efficient than the SHRs, and the LEs were more efficient than the WKYs. With the addition of the LH to the DRL 5-s schedule, the efficiency of the LEs

decreased and there was no effect on WKY and SHR efficiency. During the increasing DRL procedure, the mean number of sessions for the rats in each strain to reach the 60 s criterion was 51.8 (*SD* = 8.0) for the SHRs, 27.7 (*SD* = 12.1) for the LEs, and 24.3 (*SD* = 4.4) for the WKYs. Taken together, these data support the idea that SHRs are more sensitive to delayed consequences than the other strains; however, they may be more similar to the WKYs than to other strains on certain behavioral tasks. Accordingly, the WKY's behavioral inconsistency calls into question whether they are an appropriate control strain for the SHR in behavioral work.

Research has demonstrated the extent to which SHRs prefer smaller magnitude reinforcers delivered immediately to larger reinforcers delivered after a delay. Consistent with Ainslie's (1975) suggestion, it is a well-established finding that, all else being equal, the subjective value of a reinforcer at any given point in time is directly related to its size, or amount, and inversely related to the delay until its delivery (Mazur, 1987). To describe this delay-discounting relation mathematically, Mazur (1987) proposed the hyperbolic-decay model described by the following equation:

$$V = A/(1+kD)$$

where *V* represents the current subjective value of the delayed reinforcer, *D* represents the delay until its delivery, *A* represents the reinforcer amount, and *k* reflects the steepness of the resulting curve, which is associated with individual sensitivity to the delay values and the extent to which an organism discounts the value of delayed reinforcer. The more impulsive the behavior, the steeper the discounting curve and the higher the resulting *k* values will be. In studies that parametrically manipulate reinforcer magnitudes and delays over a range of values, curves resulting from *k* values can be

determined for individual rats and their values compared to assess differences in impulsivity

Using the hyperbolic decay model (Mazur, 1987) to examine the rate of discounting exhibited by SHRs, Johansen, Sagvolden, and Kvande (2005) investigated whether SHRs demonstrated more impulsive behavior than WKYs by comparing *k* values obtained from delay-discounting data. In the first experiment, SHRs and WKYs responded on a random interval (RI) 30-s schedule of reinforcement until response rates stabilized. After each rat's responding achieved stability, a tandem RI 30-s non-signaled resetting delay schedule (RI 30-s RD *x*-s) began. The non-signaled resetting delay component required that the lever not be pressed for a specified time. Delay testing occurred in ascending order and included 0, 0.33, 1.0, and 3.0-s. Progression from one delay to the next occurred after the data were stable. For analysis, each 15-min RI 30-s RD *x*-s session was divided into three 5-min segments. At a delay of 0 s, the SHRs responded more frequently and produced shorter IRTs than the WKYs. As the delay time increased, response rates decreased for both strains, but the SHRs continued to emit bursts of responses with short IRTs. Results revealed a significant interaction between type of strain and length of delay; SHRs were more sensitive to increases in delay length than the WKYs. To describe the differences in response rate across delay condition mathematically, Johansen et al. (2005) also analyzed the results using the hyperbolic decay in order to determine the sensitivity to the delay (*k*). When applied to the data, the hyperbolic decay model explained between .90 to .99 of the variance in the first segment and .49 to.99 of the variance in the third segment. Although the SHRs had a higher mean *k* values (M = 1.83) than the WKYs (M = .90), the difference was not statistically

significant. Overall, the SHRs and WKYs demonstrated similar sensitivity to the delay conditions on the RI 30 s RD *x* s schedule. However, the role of the short IRTs emitted by the SHRs could not be determined from the current experiment.

To explore the role of the short IRTs, Johansen et al. (2005) conducted a second experiment in which short IRTs were required for reinforcement by combining a schedule of differential reinforcement of high rates of behavior (DRH) with a VI schedule. During the experiment, the VI schedule initially began at VI 1 s and gradually increased to a VI 60 s. Each lever press that satisfied the conditions of the VI initiated the DRH requirement, and to complete the DRH, the rat had to press the lever again within 1 s in order to earn the reinforcer, which occurred after a non-signaled random delay as in the earlier experiment. Responses made prior to the end of the delay reset the delay instead of returning the schedule back to the VI component. Delivery of a reinforcer occurred if the rat satisfied the delay conditions of the RD. Eight delay-to-reinforcement conditions for the RD were tested: 0.0, 0.5, 1.0, 2.0, 4.0, 8.0, and 16.0 s. In order to analyze the data, each session was divided into three 10-min segments. Results from the second experiment showed that both SHRs and WKYs demonstrated higher IRTs as compared to the first experiment. In the second experiment, however, rate of SHR lever pressing was significantly higher (shorter IRTs) than the WKYs. To assess the IRT difference across the eight RD conditions, the hyperbolic decay model was fit to the data. Overall, the hyperbolic decay model explained .94 to .99 of the variance in the rats' responses across the delay conditions. In the first segment of the sessions, the *k* parameter was not significantly different between the SHRs ($k = 1.06$) and the WKYs ($k = 0.87$). However, during the final segment of the sessions, a significant difference in *k* parameter value was

found between the SHRs (k = 1.11) and WKYs (k = .64). The difference in k parameters suggests that SHRs were more sensitive to the delay-to-reinforcement changes as compared to the WKYs. When the delay was at or near 0 s, SHRs demonstrated a high rate of lever pressing; increases in the delay to reinforcement resulted in decreased rates of lever pressing emitted by the SHRs. There was a substantial difference in the rate of responding across delay conditions when contrasting the IRTs of the SHRs to those of the WKYs.

SHR's and WKY's sensitivity to delay of reinforcement has been compared using discrete-trial choice procedures analogous to those in the human research (Binder et al., 2000; Fox et al., 2008). Fox et al. (2008) conducted two experiments in which rats chose between one pellet delivered immediately and three pellets delivered after some delay. In the first experiment, the delay for the LL increased from 1 s to 24 s and then decreased from 24 s back to 1 s across sessions. During the ascending series of sessions, both SHRs and WKYs showed a higher proportion of choices for the LL reinforcer until the delay increased beyond 6 s. This effect was much more pronounced for the SHRs (k = 0.015) than the WKYs (k = 0.001). During the descending series of sessions, SHRs always chose the LL reinforcer (k = 0.52) less often than did WKYs (k = 0.02) and the SHRs were slower to reverse preference from the SS reinforcer back to the LL reinforcer. In the second experiment, Fox and colleagues (2008) used the same procedure except the length of the delay varied randomly over successive sessions. The results indicated a trend in data similar to those from the ascending series of the first experiment. Although these results provided some support for the idea that SHRs are more sensitive to delay than WKYs, the fact that the results depended on how delays varied across sessions

suggests that procedural variables exerted some control. To examine this further, the current experiment will use a procedure developed by Mazur (1987), and adapted by Green and Richards (Green & Estle, 2003; Green, Myerson, Holt, Slevin, & Estle, 2004; Richards, Mitchell, De Wit, & Seiden, 1997).

The present study adopted a procedure that was similar to Fox et al. (2008) except that the amount of a SS reinforcer was manipulated within sessions across multiple conditions with different amounts of the LL reinforcer. The advantage of using a within-session adjusting amount is that the point where rats value the associated reinforcers amounts, while being indifferent to the delays imposed on the levers, can be determined. Given concerns about the suitability of WKYs as an appropriate control strain when investigating the impulsive behavior of SHRs (Sanabria & Killeen, 2008), Wister rats (WIs), the progenitor strain of the WKYs, were used as an additional control strain. To examine discounting, I compared the *k* parameters that resulted from determining the best fit functions using Mazur's hyperbolic decay function and a modified hyperbola-like decay function (Green, Fry, & Myerson, 1994; Myerson & Green, 1995) described by the following equation:

$$V = A/(1+kD)^s$$

where the exponent *s* in the denominator is a scaling parameter that reflects sensitivity to the delay conditions. Numerous investigations have shown that the modified, hyperbola-like discounting function describes human and nonhuman animal discounting better than Mazur's (1987) hyperbolic decay function (Green et al., 1994; Green et al., 2004; Myerson & Green, 1995). As in Mazur's (1987) equation, higher *k* values indicate steeper. When the *s* parameter equals a value of '1.0', this equation produces the same

result as Mazur's simple hyperbolic function. Values of *s* that are closer to 0.0 indicate more sensitivity to changes in delay when the delay duration is short whereas higher values of *s* that are greater than 1.0 indicate more sensitivity to changes in the delay when the delay duration is long.

In addition to examining the *k* parameter of the hyperbola-like discounting function, the area-under-the-curve (AUC) provides an additional measure of delay discounting to compare across strains (Myerson, Green, & Warusawitharana, 2001). The AUC is calculated based on the data points, independent of the curve modeled by the hyperbolic decay model or hyperbola-like function. It is determined by normalizing the data and dividing the graph into a series of trapezoid whose area is calculated by the following equation:

$$(x_2 - x_1)/[(y_1 + y_2)/2]$$

where x_1 and x_2 are the data points of successive delays and y_1 and y_2 are the vertical distance from the x-axis to the data points x_1 and x_2, respectively. The sum of the individual trapezoids is the AUC and these values range from '0' to '1'. Smaller AUCs indicate greater discounting and can corroborate a high *k* parameter obtained from the best fit hyperbolic or hyperbolic-like function. An advantage of the AUC measure is that it is derived from the actual data as opposed to a function that best fits the data. Because it is not based on a best-fit function, a second, related advantage is that is free from any theoretical assumptions that would be made in deciding the nature of the mathematical equation used to determine the function. A final advantage of the AUC measure is that unlike distributions of discounting parameter estimates distributions of the area measure typically are not skewed significantly. Thus, it might possible to compare area measures

from individuals in different groups using parametric statistical tests, which is not the case for the discounting parameter estimates (Myerson et al., 2001).

Using both the *k* parameter and the AUC, I examined the validity of the SHRs as an animal model of ADHD to the extent that the SHRs have smaller AUC and greater discounting (i.e., higher *k* values) than the WKYs and the WIs. Additionally, I hypothesized that, given the issues associated with the WKYs' behavior on certain tasks, the WKYs would have smaller AUC and higher *k* values than the WIs.

Method

Subjects

Four SHRs, 4 WKYs, and 4 WIs served as subjects. At the beginning of the study, all rats were approximately 150 days old. Each rat was housed individually in standard plastic laboratory cages (23cm X 20.5cm) with wire bar lids in the Miller Hall Animal Research Facility at James Madison University. The colony room was maintained at approximately 24 degrees Celsius on a 12:12-hr light: dark cycle. Water was available in the home cage at all times, and each rat received 12 - 15 g of food per day, which included .045 mg pellets (Bio-Serv, Frenchtown, NJ; TestDiet, Richmond, IN) earned during experimental sessions. If a rat did not earn the maximum daily food allotment during a session, it received Harlan (Madison, WI) rodent diet (8604) in the home cage 3 hrs after the experimental session.

Apparatus

Experimental sessions occurred in Med-Associates (Georgia, VT) rodent operant chambers (ENV-008CT) housed in ventilated, sound and light attenuated cubicles (ENV-018MD). The operant chambers contained two retractable response levers (ENV-122CM) located on the front wall, on either side of an opening through which pellet delivery occurred. A third retractable lever was located on the back wall across from the feeder opening. Above each lever were three colored LED cue lights (red, yellow, and green, left to right). A house light was located at the top of the back wall of the operant chamber above the lever and a 4.0 KHz (80 db) speaker, controlled by a Med Associates Audio Stimulus Generator (ANL-926), was located above the pellet dispenser. A

computer using Med-state MED-PC IV programming language controlled the operant chambers.

Procedure

Pretraining**.** During pretraining sessions, the houselight remained illuminated throughout the session. For the first habituation session, before placing each rat in its chamber the food receptacle was baited with 25 food pellets. No levers extended, and there were no pellets delivered from the hopper during this session. For the second habituation session, the food receptacles again were baited with 25 pellets prior to the session, and pellets were delivered on a random time (RT) 30-s schedule with a probability of delivery of .3 every 10-s. An audible 500-ms 2000 Hz tone accompanied each pellet delivery throughout pretraining. Each habituation session ended when the rat received 100 pellets or 110 min elapsed.

Following habituation, autotraining began. One of the front levers (counterbalanced across rats) extended into the chamber according to a RT 30-s schedule with a probability of delivery of .3 every 10-s. During the lever extension, all three LED lights above the lever illuminated. If the rat made a response on the extended lever, the lever retracted, the LED lights terminated, and a pellet delivery occurred immediately. If the rat failed to make a response on the extended lever within 10 s, the lever retracted and a pellet was delivered. Once the rat made 10 responses on the extended lever, lever pressing was placed under an operant contingency such that the lever remained extended and the LED lights remained illuminated until the rat responded. A response on the extended lever resulted in the lever retracting, termination of the LED lights, and pellet delivery. Once lever pressing was established, the extended lever varied systematically

across days; each rat received seven sessions with left lever extension, eight sessions with right lever extension, and two sessions with rear lever extension.

Adjusting Amount Procedure. The experimental conditions of the adjusting amount procedure were similar to Green et al. (2004). Each session included 40 trials arranged in 10 four-trial blocks and terminated once all 40 trials were completed, 100 min had elapsed, or 300 pellets (13.5 g) were delivered, whichever came first. Each block included one larger, later (LL) sample trial and one smaller, sooner (SS) sample trial in random order, followed by two choice trials. Each trial began with the illumination of the house light and the yellow center light above the rear lever accompanied by extension of the rear-wall lever. When the rat pressed the lever, it retracted and the yellow light terminated. Table 1 shows the assignment of front levers and LED lights for the SS and LL alternatives for the rats that completed all delay conditions. SS lever assignment was counterbalanced across rats and it remained constant throughout the experiment.

During sample trials, one of the two levers on the front wall extended into the chamber accompanied by illumination of a LED light. Once the rat pressed the lever, it retracted and the house light terminated, beginning the reinforcer delay. The LED light remained illuminated during the delay but was extinguished once food delivery began. Food delivery was signaled by a 10-s 2000 Hz tone. Each intertrial interval (ITI) began with the illumination of the house light. The duration of each ITI varied in order to keep the time between trials at 70 s.

During choice trials, both front-wall levers extended into the chamber and the LED lights associated with each alternative illuminated. When the rat pressed one of the

levers, both levers retracted and only the chosen alternative's LED light remained illuminated. Following the delay associated with the chosen alternative, the reinforcer associated with that alternative was delivered, and the ITI followed in the same manner as during sample trials.

Similar to Green et al. (2004), the larger reinforcer was five pellets and there were five longer delay conditions: 2, 4, 8, 16, and 32 s. Table 1 lists the delay order, pseudo-randomized across the rats. The shorter delay remained at .5 s throughout the study and each rat's behavior during the choice trials determined the number of reinforcers associated with the SS alternative throughout each session. Selection of the LL alternative on both choice trials resulted in the SS alternative increasing by one pellet for the next block of trials. Selection of the SS alternative on both choice trials resulted in the SS alternative decreasing by one pellet for the next block of trials (to a minimum of one pellet). Selection of the SS alternative on one choice trial and the LL alternative on the other choice trial, regardless of the order of the choices, resulted in no change in the SS amount for the next block of trials. For the first session of each LL delay condition, the amount of the SS reinforcer began at one pellet and for all subsequent sessions in the condition, the choices made in the last block of trials of the preceding session determined the amount of the SS reinforcer at the beginning of the session.

To determine stability, the last five sessions were divided into half-sessions, and the mean number of pellets earned from the SS alternative during each half was compared to the overall mean number of SS reinforcers earned across the full sessions. Each LL delay condition terminated when the mean number of reinforcers earned from

the SS alternative during each half-session was within two pellets of the overall mean number of reinforcers earned form the SS alternative.

Results

Of the 12 rats, 8 (2 SHRs, 3 WKYs, and 3 WIs) finished all five delay conditions. Four were unable to achieve stable responding in all five delay conditions in the time available to complete the study. One SHR completed only 2 delay conditions and a second SHR completed only 4 conditions. The fourth WKY completed only 2 delay conditions, and the fourth WI completed only 3 conditions.

The major data of interest are the points of indifference for each rat during each delay condition. The point of indifference is the point at which a subject allocates responding equally between the smaller, sooner (SS) and larger, later (LL) alternatives, indicating that they are of equal subjective value. In this procedure, the mean number of pellets earned from the SS alternative during the last five sessions of the condition was designated the point of indifference (Green et al., 2004). Table 1 shows the mean number of sessions required for each rat to achieve stable responding in each delay condition, thus allowing the points of indifference to be determined.

The subjective value of the LL amount was determined by expressing the mean number of pellets delivered by the SS lever during the last five sessions as a proportion of the LL pellet amount. Thus, a value of '1' indicates that the LL alternative of five pellets delivered after the delay in question had the same subjective value as five pellets delivered immediately. Values lower than '1' indicate that the LL alternative of five pellets delivered after the delay in question had the same subjective values as fewer than five pellets delivered immediately. For example, if the point of indifference was three pellets, it would be expressed as 3/5, or 0.6. The hyperbolic decay (Mazur, 1987) and hyperbola-like (Green et al., 1994) functions were determined, and I evaluated the data

by comparing the *k* parameters from those functions as well as comparing the AUC values for the actual data points for the rats in each strain. Of the eight rats that completed all of the delay conditions, one WKY (Q-3-4) provided data that met Johnson and Bickel's (2008) criteria for nonsystematic discounting data. Although this rat's individual data are presented for illustrative purposes, they are not included in group data analyses.

Figures 1 and 2 show the indifference points along with the best-fit curve based the hyperbolic decay model (Mazur, 1987) for individual rats and the median subjective values of the LL for the rats in each group. Generally, the subjective value of the LL reinforcer decreased as the duration of the delay increased, regardless of rat strain. The fit of the hyperbolic decay curve ranged from inadequate to adequate; individual R^2 values ranged from .05 to .91 and the R^2 values for SHRs, WKYs, and WIs, as calculated from the median subjective values of the LL reinforcer for each strain, were .32, .58, and .79, respectively. Given the extremely poor fit of the hyperbolic function in numerous cases (specifically, Q-1-1, and Q-2-1), I applied the hyperbola-like discount function suggested by Green et al. (1994) to the data to determine if the additional free parameter described the data better than Mazur's hyperbolic function.

Figures 3 and 4 shows the indifference points along with the best-fit curve based on the hyperbola-like discounting function (Green et al., 1994) for individual rats and the median values for the rats in each group. The fit of the hyperbola-like discounting curve varied across individual rats, with R^2 values ranging from .79 to .97; the R^2 values calculated from the median subjective value of the LL reinforcer for the SHRs, WKYs, and WIs were .90, .98, and .90, respectively. Adding the second free parameter to the

hyperbolic decay model resulted in a better fit, as evidenced by the higher R^2 values at both the individual and group level. Every R^2 value for the hyperbola-like model was higher than the corresponding R^2 value for the hyperbolic decay model. In some cases, the R^2 value increased dramatically (Q-1-1, Q-2-1, and Q-2-4). However, an increase in R^2 alone is not sufficient for declaring the more complicated model a better fit as increasing the number of free parameters generally improves model fit. In this case, the fact that the value of the additional free parameter *s* deviated from 1 (the expected value for *s* if the simple hyperbolic and the hyperbolic-like functions provide equal fits) for all three strains (see Figure 4), provides additional support for this view. Together the R^2 and *s* values obtained from the best-fit hyperbolic-like function indicate that it describes the rats' data better than Mazur's (1987) hyperbolic decay function. Accordingly, I used the results from the hyperbola-like model for subsequent analyses.

Hyperbola-like curve fitting using the median subjective value of the LL reinforcer for each strain at each delay yielded results indicating that the rate of discounting was steeper for the SHRs, (k = 3.484, s = .3504) than both the WKYs (k = 1.884, s = .3783) and the WIs (k = 0.6225, s = .4934) indicating that the SHRs were more sensitive to increases in the delay to the LL reinforcer than both control strains. In addition, the scaling parameter *s* was less than one for all three strains (Figure 4), thus demonstrating that all three strains were more sensitive to changes in the LL delay length when the delay was short.

As an additional measure of discounting, I calculated the AUC for each rat based on the LL subjective value obtained at each delay (Myerson et al., 2001). The left panel of Figure 5 shows the AUC for each animal as a function of strain, and the right panel of

Fig 5 shows the *k* values from the hyperbola-like discounting function graphed in a similar manner in order to facilitate comparison between the two measures. Consistent with the *k* parameter estimates, the AUC calculated from the median subjective values of the LL reinforcer for each strain demonstrated that SHRs (AUC = .2511) discounted slightly more steeply than the WKYs (AUC = .2821) and more steeply than the WIs (AUC = .3209).

Discussion

The findings from the current experiment are consistent with the current literature supporting SHRs as an animal model for ADHD (Fox et al., 2008; Hand et al., 2006; Johansen et al., 2005; Johansen et al., 2008; Sagvolden, 2000; Sagvolden et al., 2008; Wultz & Sagvolden, 1992). As the delay to the LL reinforcer increased, the subjective value of the LL reinforcer decreased substantially for the SHRs. Although the subjective value of the LL reinforcer also decreased across delays for the WKYs and WIs, compared to the SHRs, the subjective values of the LL reinforcer for both the WKY and WI control strains remained higher at each delay condition. The *k* parameters estimated from both the hyperbolic decay model and the hyperbola-like discounting model indicated that SHRs discount more steeply than the WKY and WI control animals do. Similarly, the AUC values indicated that the SHRs discounted similarly to the WKYs and both strains discounted more steeply than the WIs. Overall, the hyperbola-like discounting function described the data better than the simple hyperbolic function.

Numerous studies have compared the *k* parameter values from different species, including pigeons, rats, and humans, in order to determine if there are species differences in rate of discounting (Green et al., 1997; Green et al., 2004; Mazur, 2000; Richards et al., 1997). According to both the *k* parameter and AUC measures, compared with other rat strains, specifically Sprague-Dawleys (Green et al., 2004; Richards et al.), the SHRs in the current study yielded a steeper discounting function. Interestingly, the WKYs and WIs in the current study also yielded steeper discounting functions than had been reported previously for Sprague-Dawleys (Green et al., 2004); in fact, the rate of discounting for all three strains in the current study was more similar to that of pigeons

(Green et al., 2004; Mazur, 2000). Compared to reports on humans' discounting rates (Green, et al., 1997), SHRs, WKYs, and WIs all discounted more steeply. Noteworthy in the current context is that previous investigations of species differences in discounting rates all indicated that the simple hyperbolic decay model provided an adequate description of the data for species other than humans (Green et al., 2004); this was not the case in the current experiment. The fact that the *s* parameter for all strains was considerably less than a value of one indicates that all three strains were more sensitive to changes in the delay when the delay length was short and contributes to why the hyperbola-like discounting function demonstrated a better fit to the data than the hyperbolic decay model (Green et al., 1994). The extent to which this finding has any theoretical meaning warrants further exploration.

The differences in the steepness of each strain's discounting function in the current study suggest differences between these strains in sensitivity to delay conditions. Using a task that included delayed reinforcers, Binder et al. (2002) showed that individuals diagnosed with ADHD were more sensitive to delay than typically developing peers. Similarly, the measures of discounting obtained in the current experiment suggest that SHRs are more sensitive to delay than either WKYs or WIs. These data complement the data reported by Fox et al., (2008) showing that, within given a choice between a SS reinforcer and a LL reinforcer, SHRs were more likely to select the SS reinforcer, even when the delay to the LL reinforcer is short. Moreover, they are consistent with behavior analytic definitions of impulsivity (Green et al., 1997; Rachlin & Raineri, 1992) and thus, support the use of SHRs as a nonhuman animal model of ADHD.

In addition to answering the primary research question, the current data speak to whether WKYs provide an appropriate control strain in studies employing SHRs as a nonhuman animal model of ADHD (Sanabria & Killeen, 2008). Using the LHT and DRL tasks, Sanabria and Killeen found that SHRs and WKYs responded similarly in that both strains were unable to hold (LHT) or withhold (DRL) responses for the specified interval. In the current study, rats made a single response for one of two alternatives and then awaited reinforcement according to the delay associated with their choice. Using choice as the basis for investigating impulsive behavior, the current data reveal and overall discounting rate for the WKYs was less steep than the discounting rate of the SHRs but steeper than the discounting rate of the WIs. However, inspection of the individual data showed that the *k* parameters and AUC values for two of the WKYs fell within the range of the SHRs' *k* parameters and AUC values. In contrast, both of the WIs who provided systematic data had *k* parameters and AUC values outside the range of the SHRs. Thus, the individual data of the WKYs demonstrate that some of the WKYs discount similarly to the SHRs whereas WIs generally do not. This finding is consistent with the Sanabria and Killeen data showing more similarity than difference between SHRs and WKYs and support the assertion that the WKYs' might not be appropriate as a control strain for the SHRs. In contrast, the systematic differentiation between the discounting functions for the WIs and the SHRs suggest that the WIs may provide a better control strain in for the SHRs in future studies.

A number of features of the current experiment limit the conclusions one can draw from these data. There were only 4 rats from each strain and only 8 of those 12

rats– 3 WI, 3 WKY, and 2 SHRs – completed all of the planned delay conditions within the time available for data collection. Future work of this type should include a larger number of rats per strain, which would permit the use of inferential statistical tests appropriate for between-subject comparisons that the small number of subjects in the current study precluded. The fact that some rats did not finish all of the conditions exacerbated the limitation imposed by the initially small number of rats in each strain and future work of this type should plan a longer timeframe for data collection. A final suggestion for future work of this type is the inclusion of more than one LL amount condition. The current study was unable to determine whether the strains demonstrated systematic variations in delay discounting rate as a function of the magnitude of the LL reinforcer. Green et al., 1997 showed a negatively accelerated reduction in delay discounting rate of college students choosing between hypothetical monetary rewards as the LL reward amount increased. Although Green et al. (2004) failed to find any magnitude effect for either pigeons or Sprague-Dawley rats, because magnitude effects have been shown in the human literature, demonstrating a magnitude effect for the SHRs, WKYs, and/or WIs would provide further validation toward their use as a nonhuman model of human behavior.

As a non-human animal model of ADHD, the SHRs show patterns of behavior analogous to individuals diagnosed with ADHD as outlined by the *DSM-IV-TR*, including inattentiveness, hyperactivity, and impulsivity (American Psychiatric Association, 2000). In the current study, which used an adjusting amount procedure, the subjective value of the LL reinforcer decreased more steeply for the SHRs' relative to the control strains. Continued research similar to the current study will provide further evidence toward

validation of the SHRs as a nonhuman animal model of ADHD and will help to identify the behavioral limits of this nonhuman model. Additionally, continuing research using the adjusting amount procedure with SHRs, other rat strains and other species, including humans, will provide information about the conditions in which the adjusting amount procedure is sensitive to detecting impulsive behavior. If validated as a measure to assess impulsive behavior of clinical populations, the adjusting amount procedure may be used for diagnostic purposes. Used in conjunction with currently validated clinical measures of ADHD and impulsive behavior such as the Disruptive Behaviors Disorders Rating Scale (DBD; Pelham, Gnagy, Greenslade, & Milich, 1992), the adjusting amount procedure can provide objective behavioral, data to corroborate the subjective self-report data of the DBD thereby improving the diagnostic process.

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Table 1.

Assignment of the adjusting lever, session order, and mean number of sessions required for stable responding on each delay

Strain/Rat ID	Adjusting Lever Assignment	Order of LL Delay Conditions	Number of Sessions to reach criterion
SHR			
Q-1-1	Right	2-s,	5
		8-s,	11
		16-s	5
		4-s	5
		32-s	5
Q-1-2	Left	2-s	22
		8-s	5
		16-s	5
		4-s	5
		32-s	5
WKY			
Q-2-1	Right	2-s	7
		8-s	11
		16-s	6
		4-s	5
		32-s	5
Q-2-3	Right	4-s	13
		16-s	5
		2-s	6
		8-s	5
		32-s	5
Q-2-4	Left	4-s	8
		16-s	10
		2-s	16
		8-s	8
		32-s	5
WI			
Q-3-2	Left	2-s	6
		8-s	10
		16-s	5
		4-s	6
		32-s	5
Q-3-3	Right	2-s	10
		8-s	6
		16-s	5
		4-s	5
		32-s	5

Figure Captions

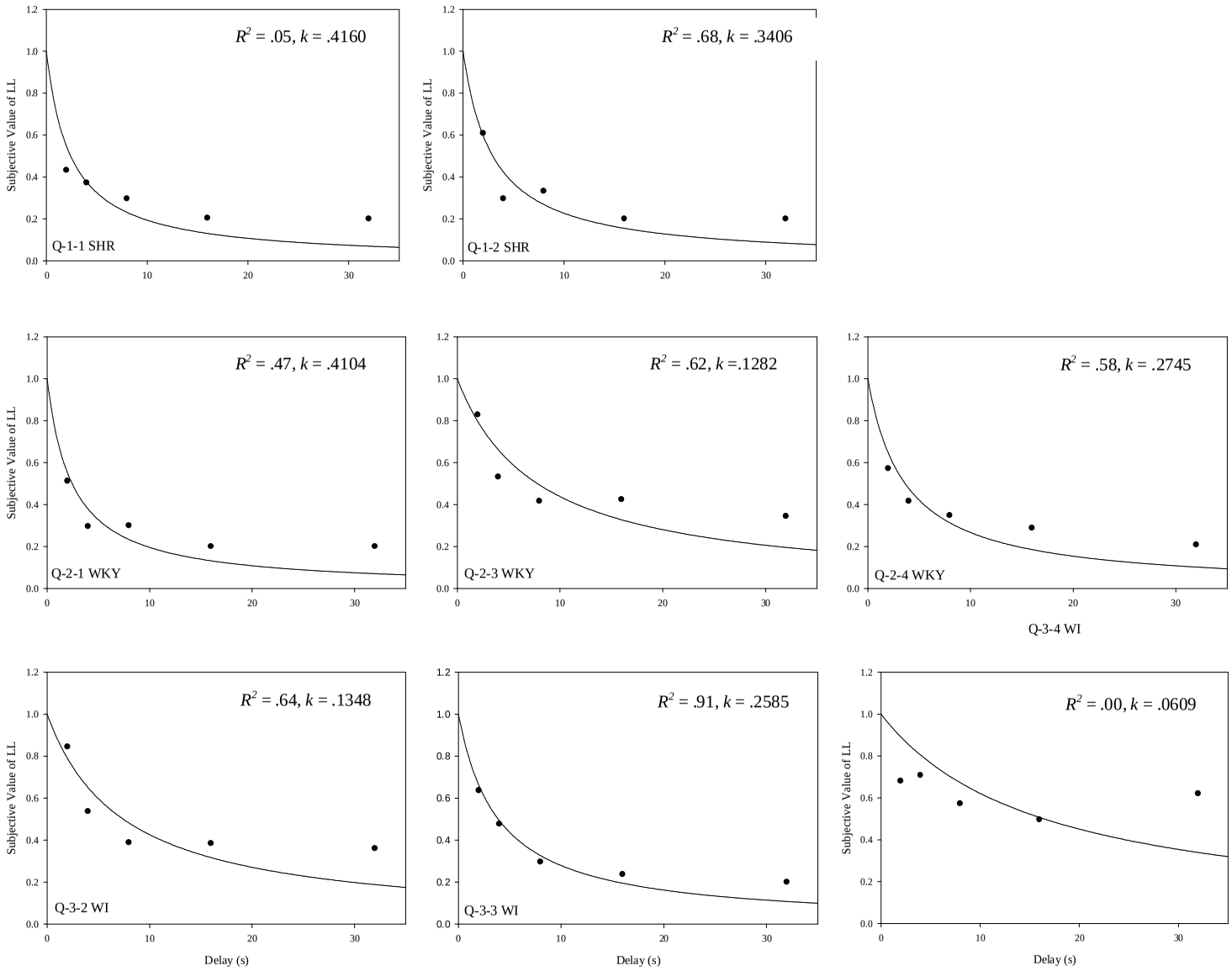
Figure 1. *Individual discounting data using Mazur's (1987) formula*

Figure 2. *Mean group data for Mazur's (1987) discounting curves*

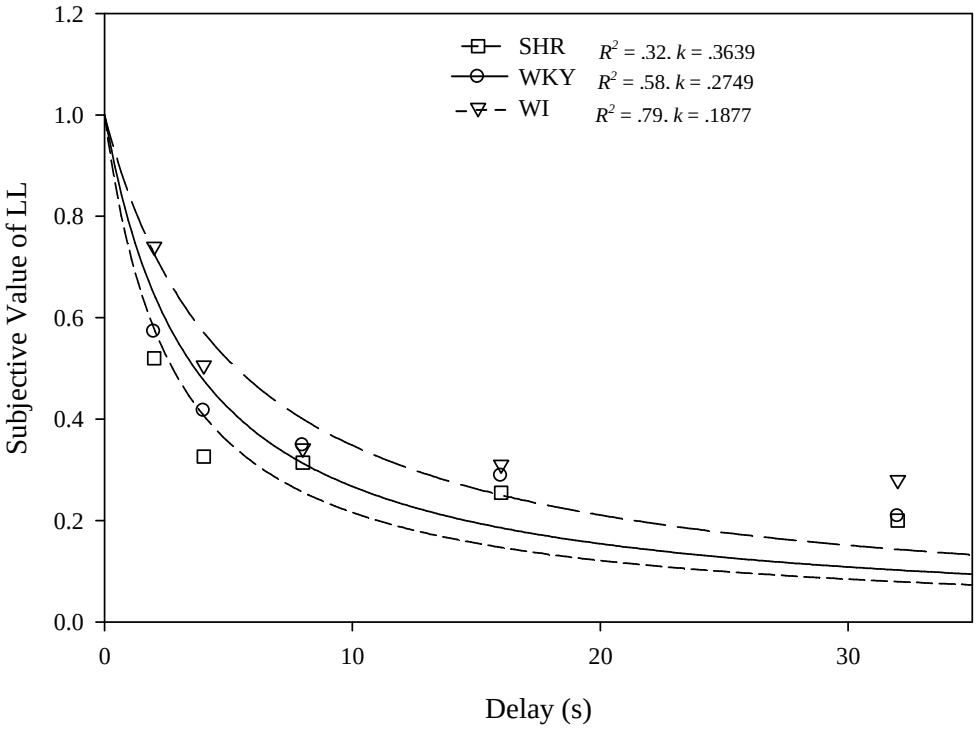
Figure 3. *Individual discounting data using Green and colleagues' (1994) formula*

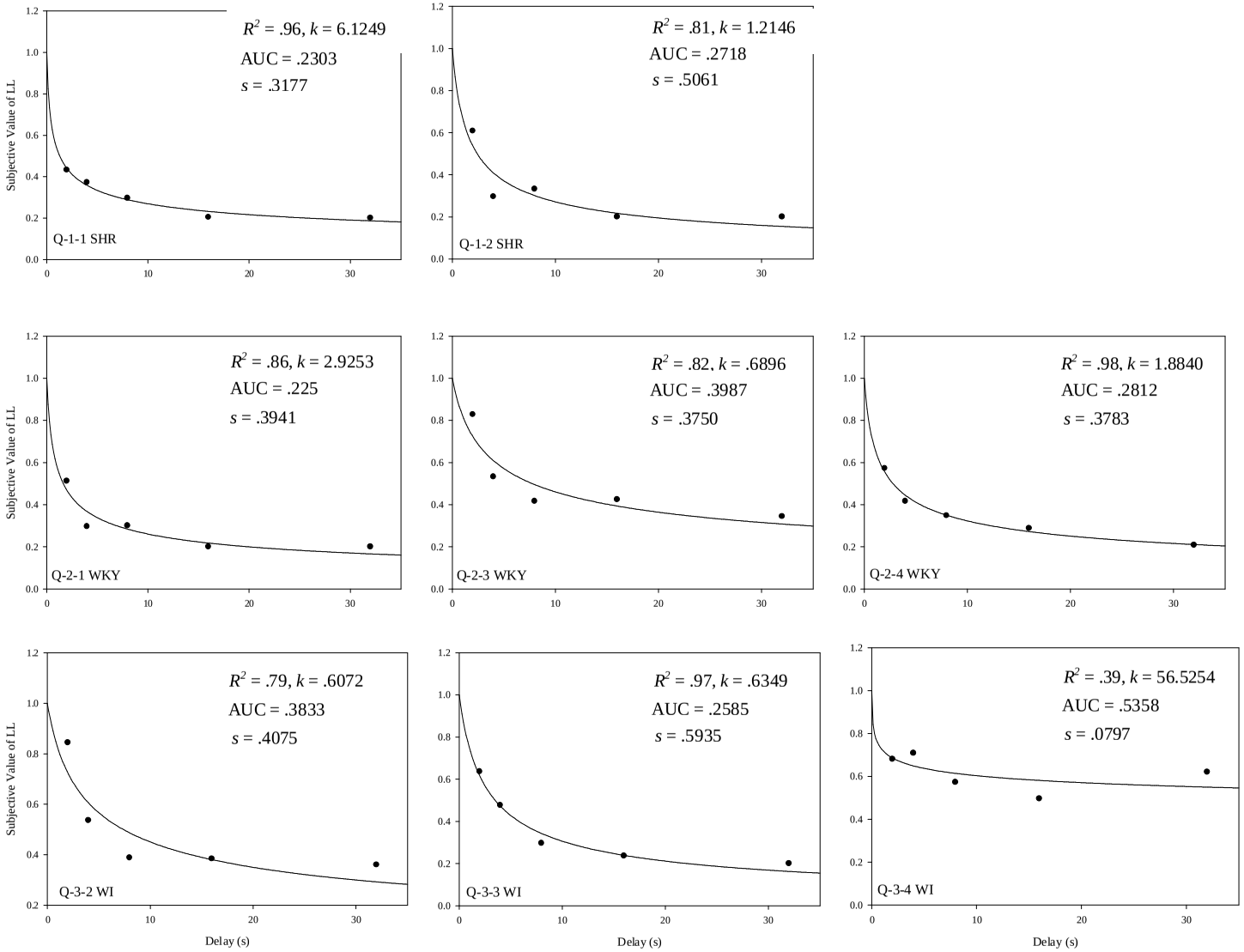
Figure 4. *Mean Group data for the Green and colleagues' (1994) discounting curves*

Figure 5. *AUC values (left panel) and estimated k-parameter values (right panel)*

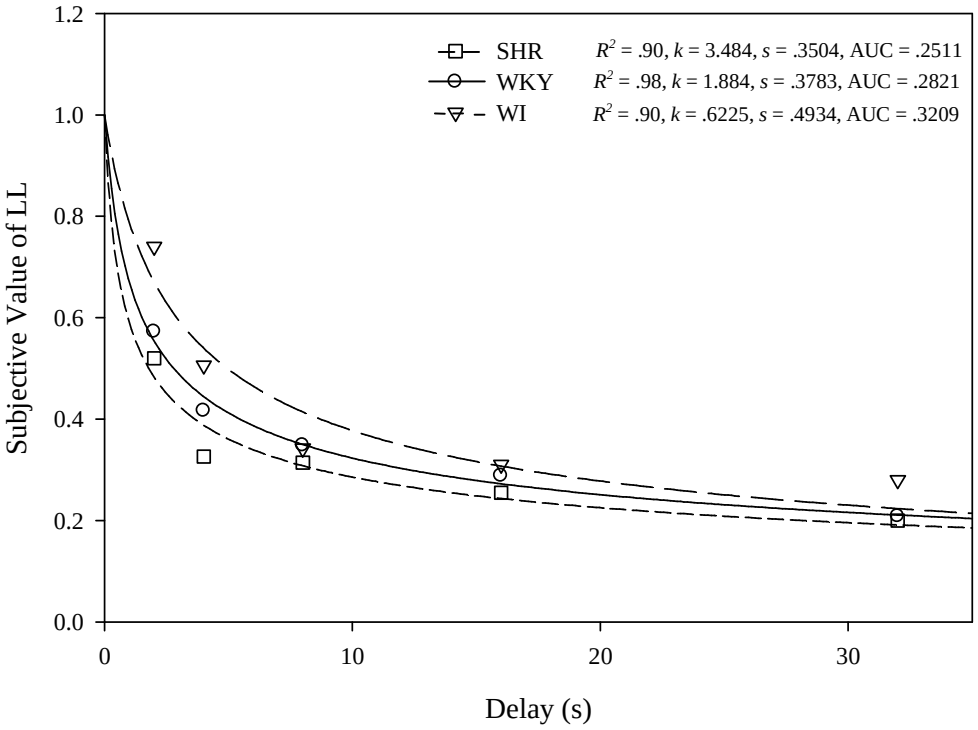

R^2 = .05, k = .4160
Q-1-1 SHR
R^2 = .68, k = .3406
Q-1-2 SHR
R^2 = .47, k = .4104
Q-2-1 WKY
R^2 = .62, k =.1282
Q-2-3 WKY
R^2 = .58, k = .2745
Q-2-4 WKY
Q-3-4 WI
R^2 = .64, k = .1348
Q-3-2 WI
R^2 = .91, k = .2585
Q-3-3 WI
R^2 = .00, k = .0609
Subjective Value of LL
Delay (s)

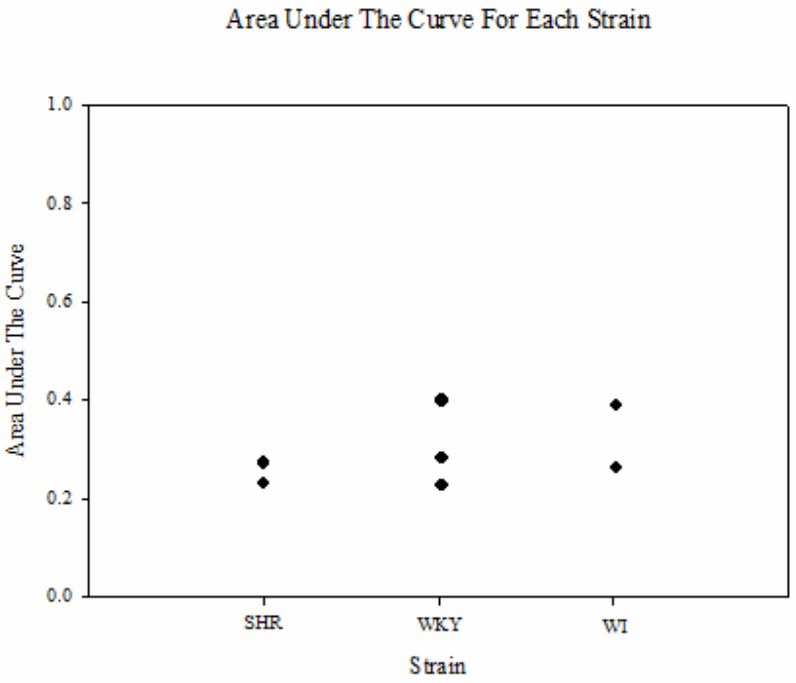
Median Subjective Value of LL (Hyperbolic)

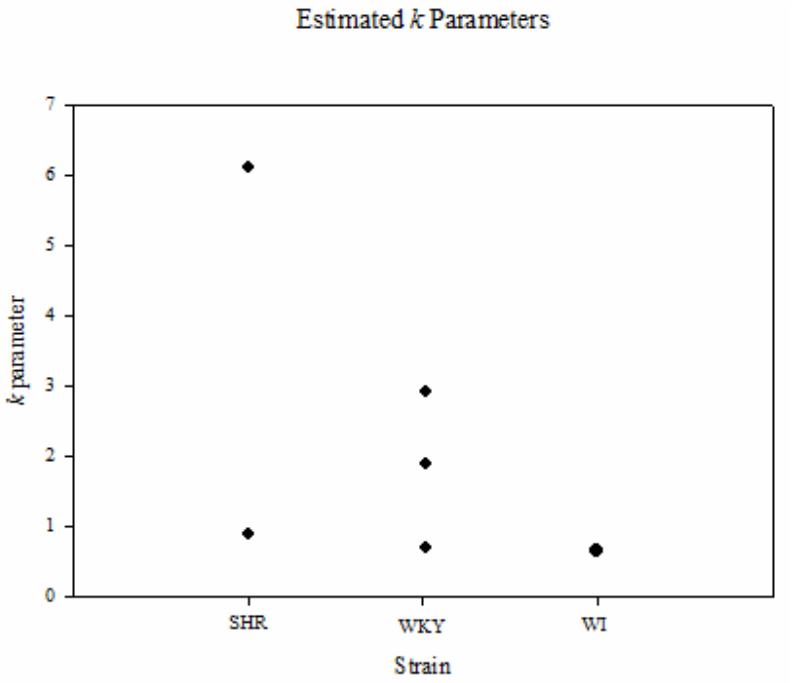



R^2 = .96, k = 6.1249
AUC = .2303
s = .3177
Q-1-1 SHR
R^2 = .81, k = 1.2146
AUC = .2718
s = .5061
Q-1-2 SHR
R^2 = .86, k = 2.9253
AUC = .225
s = .3941
Q-2-1 WKY
R^2 = .82, k = .6896
AUC = .3987
s = .3750
Q-2-3 WKY
R^2 = .98, k = 1.8840
AUC = .2812
s = .3783
Q-2-4 WKY
R^2 = .79, k = .6072
AUC = .3833
s = .4075
Q-3-2 WI
R^2 = .97, k = .6349
AUC = .2585
s = .5935
Q-3-3 WI
R^2 = .39, k = 56.5254
AUC = .5358
s = .0797
Q-3-4 WI
Subjective Value of LL
Delay (s)

Median Subjective Value of LL (Hyperbola-like)




Area Under The Curve For Each Strain
Area Under The Curve
1.0
0.8
0.6
0.4
0.2
0.0
SHR
WKY
WI
Strain


Estimated k Parameters
k parameter
7
6
5
4
3
2
1
0
SHR
WKY
WI
Strain