Impulsive Choice in Spontaneously Hypertensive (SHR) and Lewis (LEW) Rats[1]

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Abstract

The Spontaneously Hypertensive rat (SHR), the most widely accepted rodent-model of Attention Deficit/Hyperactivity disorder (ADHD), usually is compared with its normotensive control, the Wistar Kyoto (WKY) rat, seeking differences in impulsivity between strains. The utilization of the WKY as a control strain for the SHR, however, has been questioned. Dopamine deficits in nucleus accumbens may cause low tolerance to delayed consequences in the SHR. Locomotion and dopamine activities in the Lewis (LEW) rat are comparable to those in the SHR, suggesting that both strains will develop similar levels of impulsivity. This possibility was examined with SHRs and LEWs responding to concurrent-chains procedures. Choice was measured in the initial link where two random interval schedules operating concurrently on two levers arranged entries to two terminal links, one delivering 1-food pellet immediately and the other 4-food pellets with several delays randomly presented during the session. Both strains learned to choose impulsively with training, but the SHRs developed faster changes in preference and more impulsive choices than the LEWs. The Hyperbolic-decay Model and the Generalized Matching Law described choice well. Positive correlations between estimates of discounting rate and sensitivity to the immediacy of reinforcement confirmed some consistencies between these models of choice.

Key words: Impulsivity, choice, ADHD, SHR, LEW, rats.

Resumen

La rata espontáneamente hipertensa (SHR), el modelo de roedor para el trastorno por déficit de atención e hiperactividad (ADHD) más ampliamente aceptado, usualmente se compara con la rata normotensa Wistar Kyoto (WKY) investigando diferencias en impulsividad entre las dos cepas. Sin embargo, se ha cuestionado el uso de la WKY como una cepa control para la SHR. Carencias de dopamina en el núcleo accumbens de la SHR pueden causar poca tolerancia a consecuencias demoradas. La locomoción y actividad de dopamina en la rata Lewis (LEW) son similares a las que muestra la SHR, sugiriendo que las

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dos cepas desarrollan niveles similares de impulsividad. Esta posibilidad se examinó con ratas SHR and LEW que trabajaron en programas concurrentes encadenados. La elección se midió en el eslabón inicial con programas de intervalo aleatorio operando concurrentemente en dos palancas que arreglaron las entradas a dos eslabones terminales, uno entregó 1-pella de comida prontamente y el otro 4-pellas de comida con demoras aleatoriamente presentadas en la sesión. Las dos cepas aprendieron a elegir impulsivamente. Pero la SHR mostró cambios en preferencia más rápidos y elecciones más impulsivas que la LEW. El modelo hiperbólico de caída y la ley de igualación generalizada explicaron la elección impulsiva. Correlaciones positivas entre tasas de descuento y sensibilidad a la inmediatez del reforzamiento, confirmaron consistencias entre los dos modelos de elección.

Palabras clave: Impulsividad, elección, ADHD, SHR, LEW, ratas.

Introduction

Impulsive behavior is studied in laboratory settings arranging a choice between a smaller amount of food obtained immediately and a larger amount of food obtained after a delay (Logan, 1965). Choosing the smaller-sooner amount of food (SSF) over the larger-later amount of food (LLF) is impulsive behavior (Ainslie, 1974; Rachlin & Green, 1972) that minimizes the overall amount of food (Mazur, 2000), and choosing the LLF is self-controlled behavior (Logue, 1988) that maximizes the overall amount of food. Delay discounting is the behavioral process describing how humans and non-human animals discount the value of the LLF (its efficacy) with increasing delay to obtain it (Vanderveldt et al., 2016). Mazur's (1987) hyperbolic-decay model effectively describes the effect that an increasing delay to obtain the LLF has on choice.

$$V = \frac{A}{(1+kD)}. \quad (1)$$

Where V is the value of the LLF, A its amount, D the delay to obtain it, and k a free parameter to calculate how quickly the LLF is discounted with increasing D. The precision of the hyperbolic-decay model in describing delay discounting data from humans and nonhuman animals, has been documented in several of studies using a variety of procedures (see Madden & Johnson, 2010). Choosing an optimal way to study impulsive choice is challenging because different procedures (e.g., discrete trials, adjusting-amount, and adjusting-delay titration techniques) could affect the results of the study (Aparicio et al., 2013). Some procedures produced mixed results with some organisms discounting the LLF at high rates and others discounting the LLF at low rates (for a review see, Madden & Bickel, 2010).

Recent research on delay discounting (Aparicio et al., 2019, 2020) shows that a modified version of Baum's (1974) Generalized Matching Law (GML) also defines impulsive choice well.

$$\log\left(\frac{BLL}{BSS}\right) = s * \log\left(\frac{DSS}{DLL}\right) + \log b. \quad (2)$$

Where BLL and BSS are behavior allocations, measured in time or responses, to the alternatives associated with the LLF and SSF, respectively; DSS and DLL are the delays to the SSF and LLF, respectively; *b* is a free parameter assessing bias toward one alternative or the other arising from factors other than DSS and DLL; and *s* is a free parameter estimating sensitivity of behavior ratio (BLL/BSS) to

the ratio of immediacies of reinforcement (i.e., DSS/DLL, the reciprocal of delay reinforcement). The steeper the slope of the regression line (i.e., the higher value of *s*), the higher the sensitivity of choice to the immediacy of reinforcement. Research comparing the hyperbolic decay model (Eq. 1) with the Generalized Matching Law (Eq. 2) fitting impulsive choices made by non-human animals, reported positive correlations between estimates of discounting rate (*k* in Eq. 1) and sensitivity to immediacy of reinforcement (*s* in Eq. 2) showing compatibility between these two models of choice (Aparicio et al., 2019).

A general result in studies of delay discounting using concurrent-chains procedures and rats as subjects is that impulsive choice increases with the organism's experience in the choice situation (Aparicio et al., 2013, 2015, 2019). This finding suggests that naïve Spontaneously Hypertensive (SHR) and Lewis (LEW) rats will choose less impulsively at the beginning of the study than at the end of it, regardless of their genetic and neurochemical differences. The present study examined this possibility with SHR and LEW rats choosing between a smaller amount of food (1-pellet) obtained immediately, and a larger amount of food (4-pellets) obtained after a 0.1, 5, 10, 20, 40, or 80 s delay presented in random order during the session. The aim is to show that impulsive choice in LEWs and SHRs follows a comparable learningprocess. Studying impulsive choice in the SHR and LEW is important because these strains of rats are potential models of the Attention Deficit/Hyperactivity Disorder (ADHD), supporting the idea that it is a developmental disorder (Russell, 2007) and theoretical approaches predicting ADHD (Sagvolden, 2000). Note that the goal of this study is to compare one potential model of ADHD (SHR) with another potential model of ADHD (LEW) rather than comparing two potential models of ADHD (SHR and LEW) with their source strains Wistar Kyoto (WKY) and Wistar (WIS) rats, respectively.

The SHR is an inbred strain derived from the Wistar Kyoto rat (WKY) and selected for its hypertensive phenotype (high systolic blood pressure) to produce a hypertensive strain of rats (Okamoto & Aoki, 1963). The WKY is the source strain and normotensive control for the SHR, and the Wistar rat (WIS) is the source strain for the WKY. The SHR is a validated animal model of ADHD (Sagvolden, 2000) and childhood hyperactivity (Sagvolden et al., 1992), displaying behaviors characterizing ADHD such as poor sustained attention (Diana, 2002), irregularities in memory (Meneses et al., 1996), learning insufficiencies (Meneses & Hong, 1998), resistance to extinction (Brackney, et al., 2012; Johansen & Sagvolden, 2004), hypersensitivity to delayed consequences (Johansen et al., 2005), hyperactivity (Knardahl & Sagvolden, 1979), and impulsivity (Fox et al., 2008; Paule, et. al., 2000). Studies on delay discounting show that the SHR chooses more impulsively than the WKY responding to discrete trial procedures (Adriani et al., 2003; Fox et al., 2008), multiple two-component concurrent-chains procedures (Orduña, 2015; Orduña & Mercado, 2017), and concurrent-chains procedures (Aparicio et al., 2019, 2020). The WKY qualifies as an appropriate control strain for the SHR to study impulsivity and cognitive deficits linked to ADHD (e.g., Adriani et al., 2003; Russell, 2007; Sagvolden, 2000); however, some research questions the validity of the WKY as a control strain for the SHR (e.g., Sagvolden et al., 2008, 2009; Sagvolden & Johansen, 2012).

Genetic differences between the SHR and WKY suggest that the WKY might not be an appropriate control for the SHR (e.g., Drolet et al., 2002; Johnson et al., 1995) because the WKY is hypoactive instead of being normotensive (Alsop, 2007; Robertson et al., 2008). Moreover, hypertension is not the only factor causing learning deficits in the SHR (Diana, 2002). The SHR tolerates irregular activity of dopamine in the striatum and mesolimbic system (Nakamura et al., 2001; Oades et al., 2005). Insufficiencies of norepinephrine and serotonin in the SHR (Heal et al., 2008) are comparable to those

characterizing individuals diagnosed with ADHD (Toot et al., 2004). For an organism to tolerate delayed consequences, the consistent activity of dopamine, norepinephrine, and serotonin is required (Cardinal et al., 2001). Inconsistent activity of these neurotransmitters can potentially affect the expression of genes involved in ADHD, causing genetic differences between the WKY and SHR (DasBanerjee et al., 2008). The SHR undergoes faster dopamine uptake in the ventral striatum and nucleus accumbens than the WKY which is linked to impulsivity (Miller et al., 2012). Also, the SHR tolerates lower dopamine release in the dorsal striatum than the WKY, affecting its motor activity (Miller et al., 2012). The study of the neurochemical systems of two groups of SHRs, one group displaying high impulsivity and the other displaying low impulsivity, revealed the same levels of serotonin (5-HT) in the medial frontal cortex (MFC) and cingulate cortex (CC). Yet, the group of low impulsive SHRs showed lower 5-HT turnover in the MFC and lower noradrenaline levels in the MFC and CC, and the same levels of dopamine in the MFC and CC than the group of high impulsive SHRs. These differences in neurochemical systems of low and high impulsive SHRs suggest two subtypes of ADHD, inattentive (ADHD-IA) and hyperactive-impulsive (ADHD-HI), respectively (Adriani et al., 2003). A combination of subtype ADHD-AI with subtype ADHD-HI will result in a subtype ADHD-C (Garcia & Kirkpatrick, 2013) suggesting that ADHD is a heterogeneous condition (Castellanos & Tannock, 2002; Nigg, 2006; Sonuga-Barke et al., 2010) caused by multiple potential pathways (Sonuga-Barke, 2002, 2003; Wählstedt et al., 2009).

The Lewis rat (LEW) is an inbred strain derived from the source strain Wistar (WIS) rat, and the Fischer 344 (F344) rat is the inbred control for the LEW. Studies on delay discounting show that the LEW chooses more impulsively producing steeper discounting functions than the F344 (e.g., Anderson & Diller, 2010; Anderson & Woolverton, 2005; Huskinson et al., 2012; Madden et al., 2008; Stein et al., 2012). This finding has been attributed to neurochemical differences between the LEW and F344 in dopamine (DA) and serotonin (5HT) systems (Cadoni & Di Chiara, 2007). The LEW endures lower levels of DA and 5HT in several areas of the brain (Burnet, et al., 1966), fewer D_2 receptors in the striatum and nucleus accumbens core, fewer D_3 receptors in the nucleus accumbens shell and olfactory tubercule, and less 5-HT binding sites in the hippocampus and frontal cortex than the F344 rat (Flores et al., 1998; Selim, & Bradberry, 1996). Compared to the F344, the LEW rat shows higher preference for ethanol (Suzuki et al., 1988), etonitazene (Suzuki et al., 1992), nicotine (Brower et al., 2002), cannabis (Gardener & Lowinson, 1991), cocaine (Kosten et al., 1997), and self-administration of morphine (Ambrosio et al., 1995; Martín et al., 2003). This type of drug seeking behavior characterizing the LEW is linked to impulsivity (i.e., Garcia-Lecumberri et al., 2011). Differences in impulsivity between the LEW and F344 decrease with extended training the choice situation (Aparicio, et al., 2013), indicating that impulsivity in animals is not a static property of behavior determined by genetic and neurochemical mechanisms (i.e., Aparicio et al., 2015). Studies analyzing impulsive choice in SHR, LEW, WKY, and WIS rats looking for potential models of impulse choice, conducted separated assessments of choice for the manipulations of magnitude of the LLF and delay to the SSF (Garcia & Kirkpatrick, 2013). Comparisons between the SHR and WKY revealed similar preferences for the LLF and no between strain differences in overall self-control, the WKY and SHR made comparable choices and developed equivalent adjustments to changes in magnitude of the LLF and delay to the SSF. Comparisons between the LEW and WIS indicated that the former made more impulsive choices than the latter strain of rats, suggesting deficits in the LEW to process the magnitude of the LLF and the delay to the SSF. Together, these findings failed to support the notion that the SHR strain is a rodent model of ADHD suggesting that the LEW is a more feasible model of at least some characteristics of ADHD (Garcia & Kirkpatrick, 2013).

Research on anxiety analyzing central serotonergic systems of LEW and SHR rats shows similar levels of locomotion activity and 5-HT1a receptors for both strains (Kulikov et al., 1997; Ramos et al., 1997). This is important because an appropriate control for the SHR (i.e., the LEW) should exhibit similar hyperactivity characterizing the SHR; the WKY, however, is hypoactive rather than normotensive (Alsop, 2007; Robertson et al., 2008). The aim of the present study is to show that impulsive choice in LEW and SHR rats follows a similar process, both strains learn to choose impulsively with extended training in the choice situation. It is expected that at the end of training, the SHR will choose more impulsively than the LEW due to poor sustained attention (Diana, 2002) and hypersensitivity to delayed consequences in the SHR (Johansen et al., 2005).

Method

Subjects

Two strains of inbred male rats, 8-SHR and 8-LEW (Charles River, Wilmington, MA), 218- and 187-days old, respectively, were the subjects. All rats had experience on auto-shaping procedures establishing the acquisition and maintenance of lever pressing (Aparicio et al., 2020). The rats were individually housed in plastic cages with water always available in a temperate controlled vivarium (ranging from 68 to 72 degrees F) maintaining a 12:12-h light dark cycle (lights on at 0700). Animals were maintained on a regimen of food restriction such that 20 minutes after the end of each experimental session the rats were weighed and fed with approximately 10 g (+/- 2 g) of Purina Chow (Mazuri®). At the beginning of the study, the weights of the SHRs ranged from 263 to 296 g (M = 280 g) and the weights of the LEWs from 327 to 345 g (M = 336 g); when the study ended, the weights of the SHRs ranged from 287 to 345 g (M = 315 g) and the weights of the LEWs from 375 to 394 g (M = 384g). The sessions were conducted daily at approximately the same time (12:00).

Apparatus

Eight Coulbourn Instruments® (Whitehall, PA) test cages for rats (E10-11R TC), each measuring 30 cm x 33 cm x 25 cm, were used. Two retractable levers (E23-17RA), 3.3 cm x 1.5 cm, were mounted on the front wall of each cage 6 cm above the floor; the edge of one lever (left-lever) was 2.3 cm from the left side wall of the cage and the edge of the other (right-lever) was 2.3 cm from the right wall of the cage. A third non-retractable back lever (H21-03R) was centered on the back wall of each cage 6 cm above the floor. All levers required a force of 0.2 N to be operated. One 24-V DC stimulus light (H11-03R) was placed 3.5 cm above each retractable lever. A 24-V DC house-light (H11-01R) was centered on the back wall of the cage 19 cm above the non-retractable lever which provided the illumination of the chamber. A dry-food dispenser (H14-23R), placed behind the front wall of each cage, delivered 45-mg grain-based pellets (BioServ®, F0165) into a 3 cm x 4 cm food cup (E14-01R) centered between the left and right retractable levers, 4.5 cm from the left lever and 4.5 cm from the right lever at 2 cm from the floor. A white noise generator (E12-08) was installed on the back wall of each cage at 20 cm from the floor, 1 cm from the left sidewall and 1 cm below the ceiling and connected to a 2.6 cm x 4.0 cm speaker (H12-01R) to deliver a continuous white noise of 20 kHz (+/- 3 dB). Two computers each linked to 4-cages using Habitest Lincs (H02-08), delivered the stimuli and recorded the responses executing Coulbourn Instruments® software (Graphic State Notation, V 3.03) at a 0.01-s resolution. All animals used and procedures implemented in this study were approved by Salem State University, Institutional Animal Care

and Use of Laboratory Animals (IACUC 011817-2), according to the guidelines of NIH (No. 8023). There is no conflict of interest that should be reported in this study.

Procedure

All rats were directly exposed to a novel concurrent-chains procedure developed in our laboratory (Aparicio et al., 2015, 2019). It consisted of six different delay components (0.1, 5, 10, 20, 40, 80 s) arranging 60-choice cycles for each session. Delay components were selected and presented in random order during the session to arrange 10-choice cycles each. The session started with the illumination of the house light signaling the beginning of the choice cycle. One response on the back lever extended the front left and right levers into the chamber, turning on the lights above them and turning off the house light. Choice was measured in the initial link of the concurrent-chains procedure by recording the number of responses that the rats emitted on the extended left and right levers. Two random interval schedules, averaging 11 s each and operating concurrently on the levers (con RI 11 s RI 11 s), arranged entries to two terminal links. One RI was associated with the left or SS lever and the other RI with the right or LL lever. When the SS lever was selected by one RI 11 s as the operative lever, the first response on the SS lever advanced the cycle to the terminal link causing the other non-operative LL lever to retract from the chamber. The next response on the operative SS lever produced the SSF (1-food pellet) after a 0.1 s delay. After the delivery of the SSF, the operative SS lever was retracted from the chamber and the light above it turned off signaling the end of the choice cycle. After that, the house light was turned on signaling the beginning of the next choice cycle, requiring the rat to move from the front wall to the back wall of the chamber and to press the back lever again to repeat the same sequence of actions completing the cycle. For choice cycles where the LL lever was selected as the operative lever by one RI 11 s, the first response on the LL lever caused the SS lever to retract from the chamber turning off the light above it. The next response on the LL lever started a fixed time (FT) of 0.1, 5, 10, 20, 40, or 80 s to deliver the LLF (4-food pellets). The responses on the LL lever during the FT (i.e., the delay to LLF) had no scheduled consequences. The LLF was delivered at the end of the delay, retracting the LL lever from the chamber, turning of the light above it, and signaling the end of the choice cycle. Thus, each delay component delivered ten foods followed by a 60-s blackout, after which a different delay component was randomly selected for another 10 cycles. To prevent a possible bias that the rats might have for one lever over the other, for four rats of each strain, the left lever produced the SSF and the right lever the LLF. These relations were reversed for the other four rats of each strain, the left lever produced the LLF and the right lever the SSF. With the rats responding to the concurrent-chains procedure, these conditions were studied for 180 consecutive days.

Data analysis

The data from all 180 consecutive sessions were used for data analysis. Global analyses organized the data in 12 blocks of 15 sessions each, and local analyses used the data from all 180 sessions sorted by delay component (0.1, 5, 10, 20, 40, or 80 s) examining choice food by food delivery. All calculations of choice used initial-link responses emitted on the LL and SS levers. For the global analyses block by block of sessions, the responses the rats emitted on the LL and SS levers were counted separately for each delay component and were aggregated across 15 sessions of the same block. Each delay component allowed computations of 6-proportions of LL choice ((LL responses / (LL responses + SS responses)), 6-ratios of responses (LL responses / SS responses) for each rat within a strain, and the average of the group. To calculate the number of responses that the rats emitted food by food delivery within a delay component,

the data were polled across all 180 sessions of the same delay component, counting responses on the LL and SS levers separately for each food delivery regardless of whether it was LLF (4-food pellets) or SSF (1-food pellet). Ten proportions of LL choice and ten ratios of responses were calculated for each delay component, resulting 60-proportions of LL choice and 60-response ratios for the six delay components. Because data in delay discounting are not normally distributed (Myerson & Green, 1995), and two main requirements of the analysis of variance normality and equal error variance were not fulfilled, nonparametric Wilcoxon signed ranks tests assessed differences in preference, discounting rate (k in Eq. 1), and sensitivity to immediacy of reinforcement (s in Eq. 2). Nonlinear curve fitting, linear fitting, and statistical tests at the alpha level of .05 were executed with Origin® software (version 2021). Equations 1 and 2 were entered into the Origin as a user defined equation, providing the nonlinear curve fitting to the proportions of LL choice and the linear fitting to response ratios, respectively. The parameter A was free to vary in Eq.1, A was not assumed to be 1.0 at the y-intercept. For linear fitting, the delay ratios (SS / LL) transformed into base-2 logarithms entered Eq. 2 as factors of the independent variable and $\log_2$ of response ratios (LL responses / SS responses) as the factors of the dependent variable.

Results

Preference

Preference for either the LLF or SSF was estimated with the proportion of LL choice. It was plotted against 12-blocks of sessions in Figure 1 (the global analysis) and 10-food deliveries in Figure 2 (the local analysis) regardless of whether each food was a SSF or LLF. From top to bottom, the graphs show proportions of LL choice computed for each delay component. Unfilled symbols stand for proportions of LL choice computed for the individuals and filled symbols with error bars stand for the mean proportions of LL choice computed for the groups of the SHRs (circles) and LEWs (squares). The left graphs display proportions of LL choice produced by the SHRs and the right graphs display those produced by the LEWs. The dotted line intercepting the y-axis at 0.5 is the indifference line indicating that a similar number of responses was emitted on the SS and LL levers. Proportions of LL choice greater than 0.5 indicate preference for the LLF (i.e., more responses were emitted on the LL lever than on the SS lever), and those smaller than 0.5 indicate preference for the SSF (i.e., more responses were emitted on the SS lever than on the LL lever).

Figure 1 shows that the SHRs and LEWs developed a clear preference for the LLF when it was obtained with a negligible delay (0.1 s). The proportions of LL choice that the group of the LEWs produced across blocks of sessions (M = .70) were comparable to the proportions of LL choice produced by the SHRs (M = .69). Two rats of each strain produced proportions of LL choice close to the indifference line, but most rats of both strains produced proportions of LL choice indicating a strong preference for the LLF. The proportions of LL choice produced by the individual LEWs, ranging from .44 to .94 (Mdn = .69), were greater (W = 3014, p = .012) than those produced by the individual SHRs, ranging from .35 to .94 (Mdn = .63). When the LLF was obtained with delays of 5 and 10 s, both strains showed a slight decrease in their preference for the LLF; proportions of LL choice decreased from .70 to about .60. Two rats of each strain produced proportions of LL choice indicating either indifference or small preference for the SSF. The proportions of LL choice that the individual LEWs produced with a 5 s delay to obtain the LLF, ranging from .30 to .93 (Mdn = .60), were comparable (W = 2398, p = .799) to proportions of LL choice produced by the individual SHRs, ranging from .27 to .91 (Mdn = .60). Equally, the proportions of LL choice that the individual LEWs produced with the 10 s delay to obtain the LLF,

ranging from .24 to .93 (*Mdn* = .58), were similar (*W* = 2618, p = .290) to proportions of LL choice produced by the individual SHRs, ranging from .25 to .91 (*Mdn* = .57). When the LLF was obtained with a 20 s delay, the rats' preference for the LLF moved to indifference.

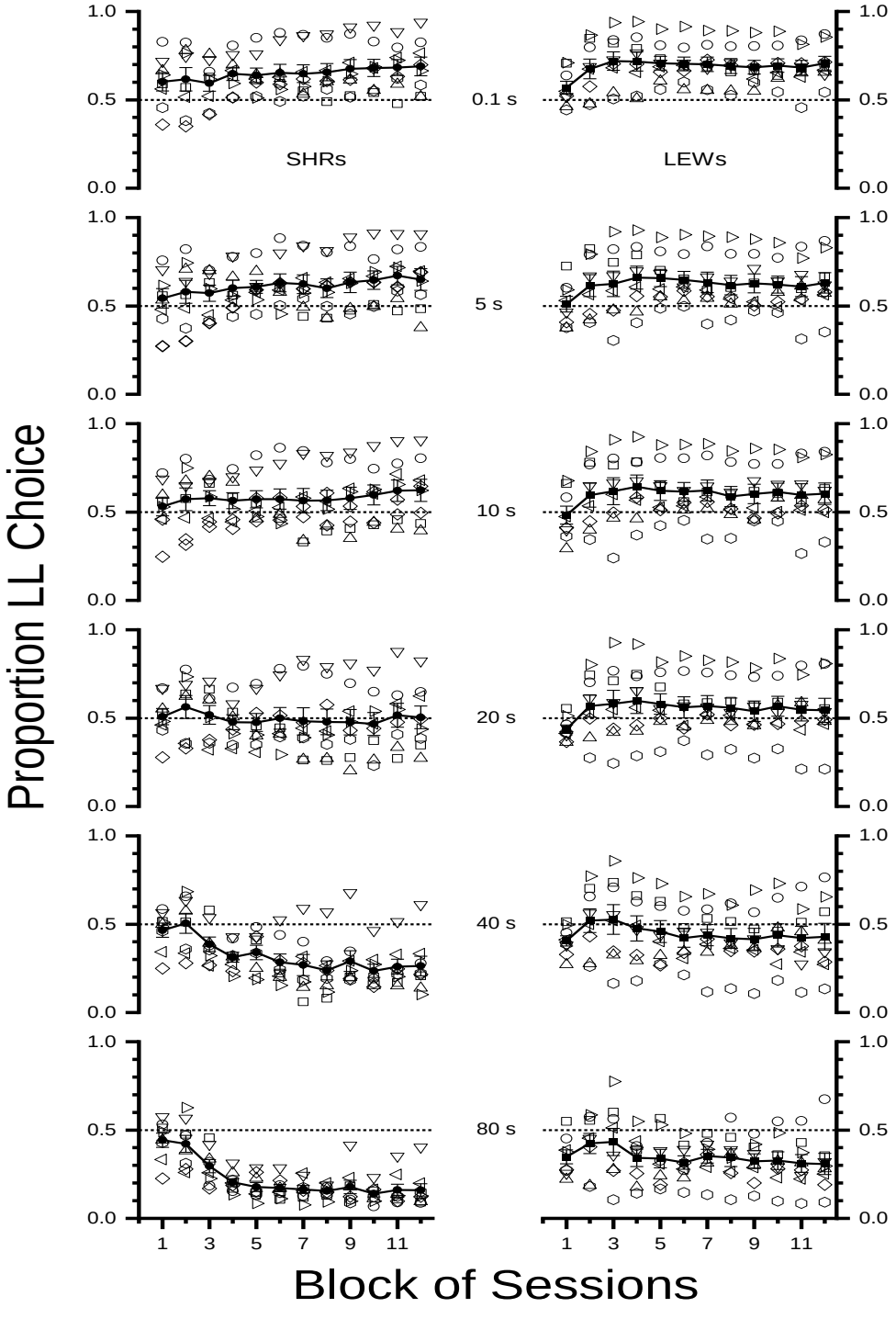

Figure 1. Proportion of LL choice ((LL/(LL+SS)) as a function of block of sessions. The left graphs show data produced by the SHRs and the right graphs data produced by the LEWs. From top to bottom the graphs are organized by delay component (0.1, 5, 10, 20, 40, and 80 s). The unfilled symbols represent data from individuals and filled symbols joined by the solid line data from the group. The dotted line intercepting the y-axis at .5 is the indifference line.

Proportions of LL choice produced by the group of the SHRs show stable indifference across blocks of sessions (*M* = .50) and those produced by the group of the LEWs show a slight preference for the LLF (*M* = .55). The exceptions were proportions of LL choice produced by the SHRs in block-2 showing a small preference for the LLF (*M* = .56) and proportions of LL choice made by the LEWs in block-1 displaying a small preference for the SSF (*M* = .45). Generally, the proportions of LL choice produced by the individual LEWs across blocks of sessions ranging from .21 to .93 (*Mdn* = .53), were greater (*W* = 3001, p = .013) than the proportions of LL choice produced the individual SHRs ranging from .20 to .88 (*Mdn* = .46). When the delays to obtain the LLF were 40 and 80 s, the SHRs and the LEWs emitted more responses on the SS lever than on the LL lever, producing mean proportions of LL choice indicating preference for the SSF that gradually increasing with increasing blocks of sessions. For the choices made by the group of the SHRs with the 40 s delay to the LLF, blocks 1 and 2 show mean proportions of LL choice close to indifference (*M* = .48) and blocks 3 to 12 mean proportions of LL choice indicating preference for the SSF (*M* = .29). With the 80 s delay to get the LLF, the SHRs produced mean proportions of LL choice (*M* = .18) indicating that their preference for the SSF was strengthened across blocks of sessions. For the choices that the group of the LEWs made responding to the 40 s delay component, block 1 shows proportions of LL choice indicating a small preference for the SSF (*M* = .40) and blocks 2 to 4 indifference (*M* = .51). Except for three LEWs showing preference for the LLF across blocks of sessions, the LEWs' preference for the SSF was recovered in block 5 and increased slightly from blocks 6 to 12 (*M* = .45). When the LLF was delayed 80 s, most LEWs produced proportions of LL choice indicating a preference for the SSF (*M* = .30). Two LEWs, however, showed indifference across blocks of sessions of the 80 s delay component. The proportions of LL choice produced by the individual LEWs with the 40 s delay to the LLF, ranging from .11 to .86 (*Mdn* = .42), were greater (*W* = 3639, p < .001) than those produced by the individual SHRs ranging from .06 to .68 (*Mdn* = .28). Also, the proportions of LL choice produced by the individual LEWs with the 80 s delay to the LLF, ranging from .08 to .77 (*Mdn* = .33), were greater (W = 3873, p < .001) than those produced by the individual SHRs ranging from .07 to .63 (*Mdn* = .18).

Figure 2 shows the proportions of LL choice that the SHRs and LEWs produced for each food obtained within a delay component. This local analysis counted responses on the LL and SS levers separately for each food regardless of whether it was a LLF or SSF, polling the data across all 180 sessions of the same delay component to compute ten proportions of LL choice for each delay component. All graphs show that choice changed food by food with the SHRs and LEWs tracking the lever producing the LLF. Both strains pressed the LL and SS levers with similar frequency to obtain the first food that each delay component delivered, producing proportions of LL choice indicating either indifference (*M* = .50) or a slight preference for the SSF (*M* = .48). This result was likely caused by delay components that occurred in random order and were preceded by a 1-min blackout, making it difficult for the rats to anticipate the up-coming delay component. Two or three consecutive foods obtained with the same component were required for the rats to detect the delay to the LLF. When the delay to obtain the LLF was 0.1 s, both strains pressed more on the LL lever than on the SS lever.

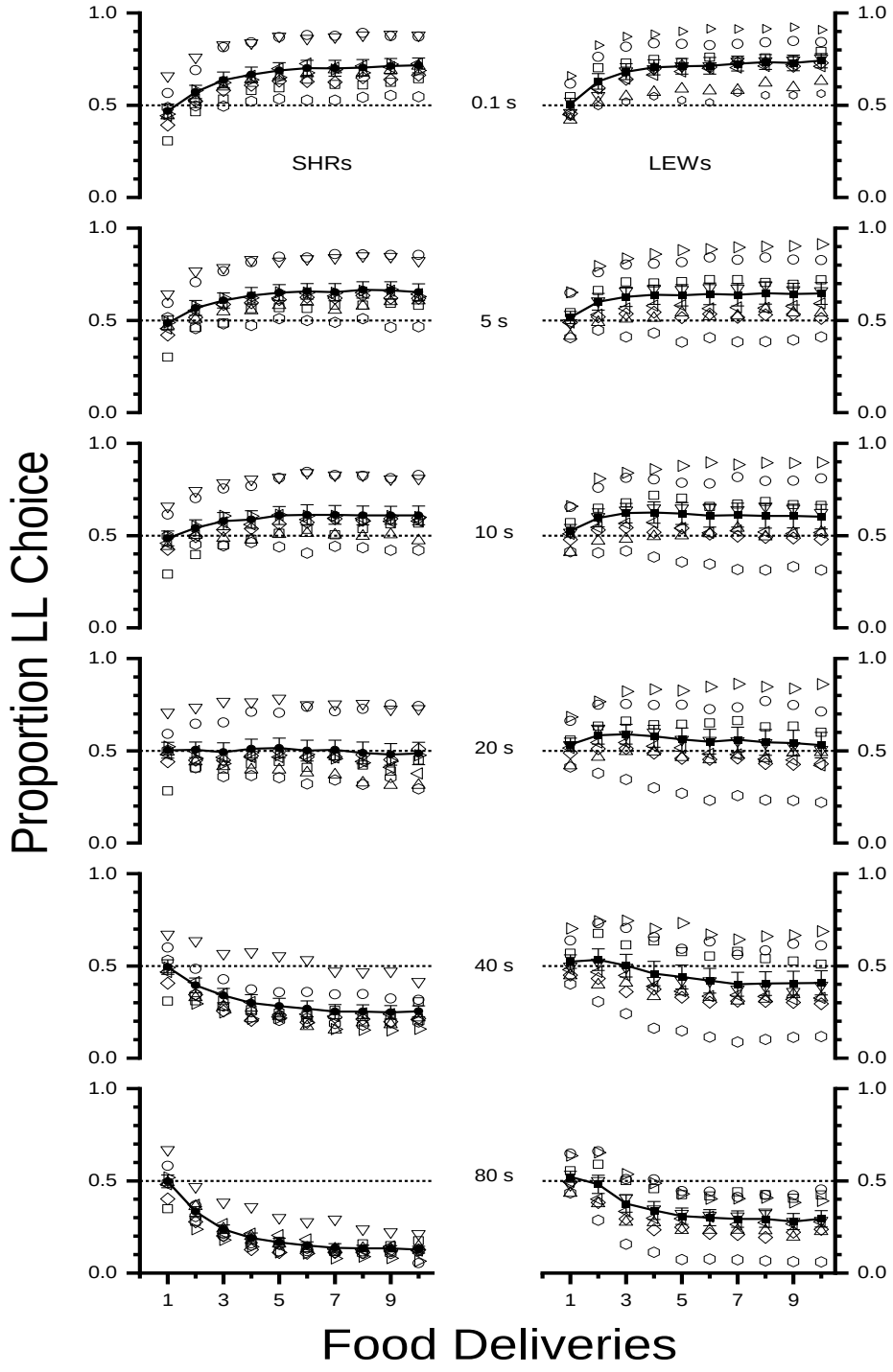

Figure 2. Proportion of LL choice as a function of foods delivered by each delay component. Other details as in Fig. 1.

The SHRs produced mean proportions of LL choice increasing from .47 (with the first food) to .70 (with the last five foods) within the 0.1 s delay component. For two SHRs, preference for the LLF increased from .55 (with the first food) to .80 (with the last five foods). One SHR shows proportions of

LL choice indicating indifference across food deliveries of the 0.1 s delay component. The LEWs show mean proportions of LL choice increasing from .51 (with the first food) to .75 (with the last five foods) within the 0.1 s delay component. Two LEWs show proportions of LL choice indicating a weak preference for the LLF (.54) across food deliveries, contrasting with two other LEWs showing proportions of LL choice increasing from .55 (with the first food) to about .90 (with the last five foods) within the 0.1 s delay component. Proportions of choice produced by the individual LEWs, ranging from .42 to .92 (*Mdn* = .71), were not significantly different (W = 2019, p = .055) from those produced by the individual SHRs, ranging from .31 to .89 (*Mdn* = .65). When the delay to obtain the LLF was 5 s, the SHRs and LEWs produced proportions of LL choice comparable to those produced when the delay to the LLF was 0.1 s. One LEW developed a weak preference for the SSF. Yet, the proportions of LL choice produced by the individual LEWs, ranging from .38 to .91 (*Mdn* = .58), were not different (W = 1458, p = .438) from those generated by the SHRs, ranging from .30 to .85 (*Mdn* = .61). Both strains show a slight decrease in preference for the LLF across foods of the 10 s delay component, with mean proportions of LL choice produced by the LEWs (M = .65) and SHRs (M = .61) indicating indifference. Two rats, one of each strain, produced proportions of LL choice indicating a slight preference for the SSF across foods of the 10 s delay component. The individual LEWs produced proportions of LL choice ranging from .31 to .90 (*Mdn* = .57), comparable (W = 1633, p = .952) to those produced by the individual SHRs ranging from .29 to .84 (*Mdn* = .57). The 20 s delay component shows mean proportions of LL choice produced by the SHRs (M = .50) and LEWs (M = .51) indicating indifference across foods. The exceptions were two rats of each strain maintaining a preference for the LLF (M = .70), and three rats, one LEW and two SHRs, developing a preference for the SSF with the second and subsequent foods obtained within the 20 s delay component. The proportions of LL choice produced by the individual LEWs, ranging from .22 to .86 (*Mdn* = .53), were greater (W = 2181, p = .006) than the proportions of LL choice produced by the individual SHRs, ranging from .28 to .78 (*Mdn* = .46). A preference for the SSF emerged with the foods delivered by the 40 s delay component and was strengthened by foods delivered by the 80 s delay component. Regarding choices made by the group of SHRs, Figure 2 shows proportions of LL choice decreasing from .49 to .25 across food deliveries of the 40 s delay component and from .49 to .12 across food deliveries of the 80 s delay component. One SHR shows a slight preference for the SSF, with proportions of LL choice decreasing from .67 to .41 across food deliveries of the 40 s delay component. With the first two foods delivered by the 40 s delay component, the choices made by the LEWs moved slowly from indifference (M = .50) to a weak preference for the SSF (M = .40) with the last five foods. Two LEWs maintained their preference for the LLF with the consecutive foods delivered by the 40 s delay component, contrasting with another LEW showing an increasing preference for the SSF. With consecutive foods delivered by the 80 s delay component, all LEWs gradually developed a clear preference for SSF producing proportions of LL choice decreasing from about .51 with the first food to .30 with the last five foods. One LEW developed a strong preference for the SSF, producing proportions of LL choice with values close to zero for the last six foods delivered by the 80 s delay component. The proportions of LL choice that the individual LEWs produced with the 40 s delay to obtain the LLF, ranging from .09 to .74 (*Mdn* = .42), were greater (W = 2760, $p < .001$) than the proportions of LL choice produced by the individual SHRs, ranging from .15 to .67 (*Mdn* = .26). Similarly, the proportions of LL choice that the individual LEWs produced with the 80 s delay to obtain the LLF ranging from .06 to .66 (*Mdn* = .36), were greater (W = 3005, $p < .001$) than the proportions of LL choice produced by the individual SHRs ranging from .05 to .67 (*Mdn* = .16).

Discounting Rate

Mean proportions of LL choice produced by the group of the SHRs (circles) and the group of the LEWs (squares) are plotted in Figure 3 as a function of the delay to the LLF. The graphs organized by blocks of sessions from block-1 upper left-corner to block-12 lower right-corner, show the discounting functions that the SHRs and LEWs generated choosing between the LLF and SSF. The lines are best fits of Eq. 1 to mean proportions of LL choice produced by the SHRs (solid lines) and LEWs (dashed lines). Estimates of the discounting rate (*k* in Eq. 1) for mean proportions of LL choice produced by the SHRs (k_{SHR}) and LEW (k_{LEW}), appear in the upper right corner of each graph. Table 1 summarizes empirical parameters from Eq. 1 fitting mean proportions of LL choice produced by the group of the SHRs and the group of LEWs.

Table 1. Hyperbolic-decay model, resulting parameters (Eq. 1).

	A		*k*		R^2	
Block	SHR	LEW	SHR	LEW	SHR	LEW
1	0.564	0.535	0.004	0.008	0.819	0.872
2	0.609	0.654	0.005	0.007	0.983	0.966
3	0.619	0.692	0.013	0.008	0.962	0.915
4	0.673	0.720	0.027	0.013	0.984	0.990
5	0.679	0.708	0.028	0.013	0.968	0.995
6	0.703	0.705	0.034	0.015	0.966	0.995
7	0.693	0.695	0.036	0.013	0.971	0.989
8	0.700	0.680	0.041	0.013	0.972	0.977
9	0.709	0.683	0.032	0.014	0.976	0.996
10	0.742	0.689	0.046	0.014	0.956	0.984
11	0.737	0.678	0.036	0.015	0.938	0.990
12	0.737	0.702	0.035	0.016	0.942	0.994
Mean	**0.680**	**0.678**	**0.028**	**0.012**	**0.953**	**0.972**

All graphs show that the hyperbolic-decay model (Eq. 1) fitted the choices made by the SHRs and LEWs, accounting for changes in mean proportions of LL choice that occurred as a function of the increasing delay to the LLF. Table 1 shows R^2 ranging from .819 to .983 (*M* = .953) for the discounting functions produced by the SHRs and from .872 to .995 (*M* = .972) for the discounting produced by the LEWs. Estimates of *A* (y-intercept) ranged from .56 to .74 (*M* = .68) for the discounting functions produced by the SHRs and from .54 to .72 (*M* = .68) for the discounting functions produced by the LEWs (see Table 1). All discounting functions show that the SHRs and LEWs discounted the LLF with the increasing delay to obtain it. The slopes of the discounting functions indicate that the SHRs and LEWs produced discounting rates (*k* in Eq. 1) that increased with increasing blocks of sessions (i.e., extended training in the choice situation).

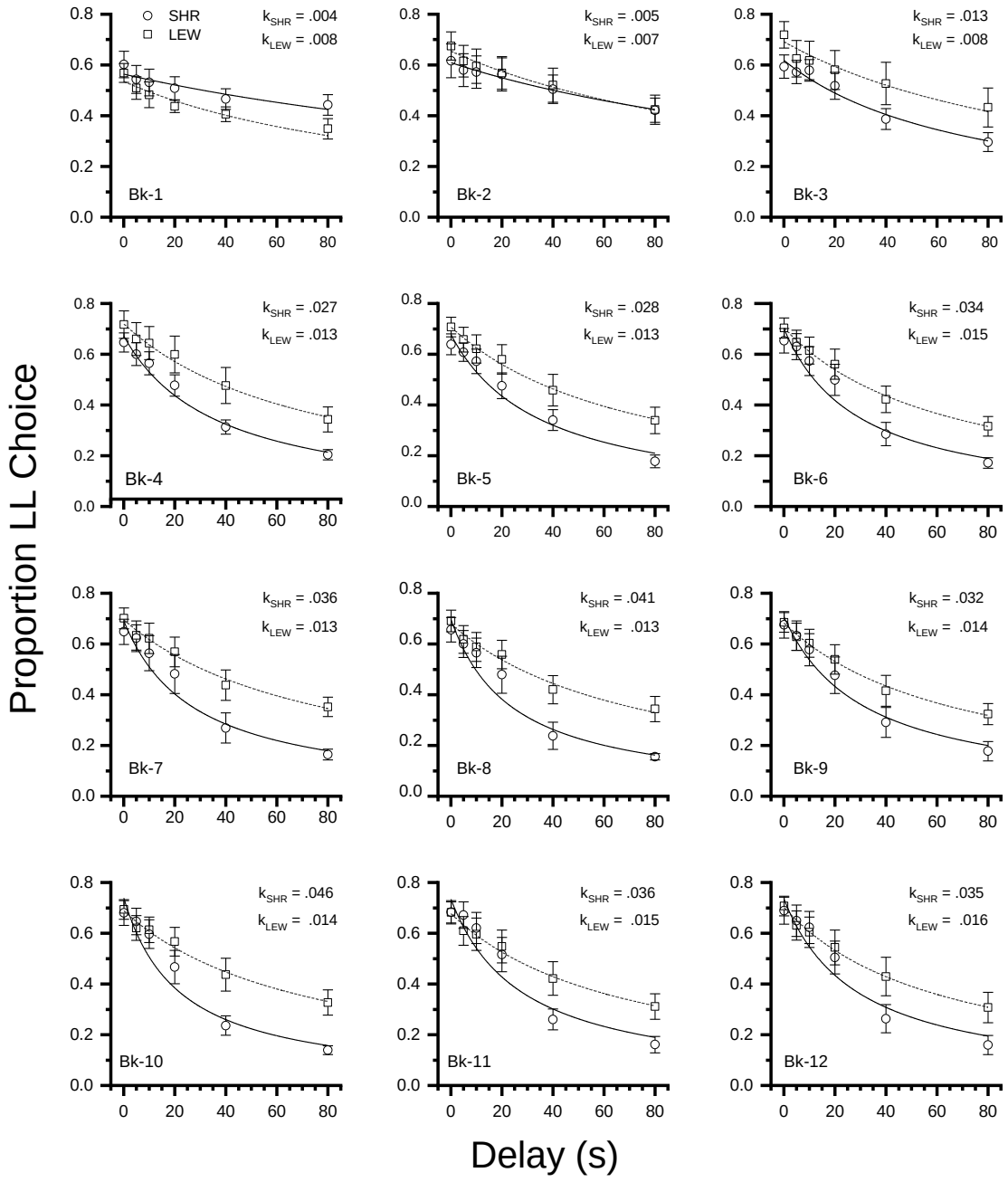

Figure 3. Proportion of LL choice as a function of the delay (s) to deliver the LLF. From left to right and top to bottom, the graphs show discounting functions produced in 12 blocks of 15 sessions each. The unfilled circles represent mean proportions LL choice computed for the group of SHRs and unfilled squares mean proportions of LLL choice computed for the group of LEWs. Estimates of discounting rate for the data produced by the SHRs (k_{SHR}) and LEWs (k_{LEW}) appear on the upper right corner of each graph. The line is the best fits of Eq. 1 to the data produced by the group.

Block 1 shows that the slope of the discounting function produced by the group of the LEWs is steeper (k = .008) than the slope (k = .004) of the discounting functions produced by the group of the SHRs, suggesting that early in training, the LEWs chose more impulsively than the SHRs. The proportions of LL choice that the individual LEWs produced across delays to the LLF ranging from .22

to .73 (*Mdn* = .45), were greater (*W* = 351, *p* = .014) than the proportions of LL choice produced by the SHRs ranging from .23 to .83 (*Mdn* = .52). Yet, the discounting rates produced by the individual LEWs ranging from .005 to .013 (*Mdn* = .008), were greater (*W* = 33, *p* = .042) than the discounting rates produced by the individual SHRs ranging from .000 to .009 (*Mdn* = .005). Block 2 shows discounting functions of similar shapes, but the slope of the discounting function produced by the group of the LEWs is slightly steeper (*k* = .007) than the slope (*k* = .005) of the discounting function produced by the group of the SHRs. The individual LEWs produced discounting rates ranging from .004 to .023 (*Mdn* = .006), that were comparable (*W* = 24, *p* = .437) to discounting rates produced by the SHRs ranging from .002 to .014 (*Mdn* = .003). Correspondingly, the proportions of LL choice produced by the individual LEWs ranging from .18 to .87 (*Mdn* = .56) were equivalent (*W* = 721, p = .175) to the proportions of LL choice produced by the individual SHRs ranging from .26 to .82 (*Mdn* = .57). Block 3 shows that the discounting function produced by the group of the SHRs has a slope steeper (*k* = .013) than the slope (*k* = .008) of the discounting function produced by group of the LEWs, indicating that the SHRs made more impulsive choices than the LEWs. The proportions of choice generated by the individual LEWs ranging from .11 to .94 (*Mdn* = .59), were greater (*W* = 862, *p* = .004) than the proportions of choice generated by the individual SHRs ranging from .17 to .76 (*Mdn* = .46). Nonetheless, the discounting rates produced by the individual LEWs ranging from .003 to .065 (*Mdn* = .009) were similar (*W* = 14, *p* = .624) to the discounting rates produced by the individual SHRs ranging from .004 to .021 (*Mdn* = .017). In blocks 4 and 5, the SHRs' impulsive choices increased substantially, contrasting with the LEWs' impulsive choices showing small changes; note that the slopes of the discounting functions produced by the group of the SHRs (*k* = .027 and .028, respectively), are steeper than the slopes (*k* = .013) of the discounting functions produced by the group of the LEWs. The individual LEWs produced proportions of LL choice ranging from .14 to .94 (*Mdn* = .56), that were greater (*W* = 3629, *p* < .001) than the proportions of LL choice produced by the SHRs ranging from .08 to .85 (*Mdn* = .48). Correspondingly, the discounting rates produced by individual SHRs ranging from .013 to .046 (*Mdn* = .023), were greater (*W* = 109, *p* = .036) than the discounting rates produced by the individual LEWs ranging from .003 to .041 (*Mdn* = .013). In blocks 6 to 12, the group of the LEWs produced discounting functions showing slopes ranging from .013 to .016 (*M* = .014) indicating a slight increase in their impulsive choices. In contrast, the discounting functions produced by group of the SHRs show slopes ranging from .032 to .046 (*M* = .037) showing that their impulsive choices increased considerably with increasing blocks of sessions. So, discounting rates produced by the individual SHRs ranging from .012 to .072 (*Mdn* = .035), were greater (*W* = 1330, *p* < .001) than discounting rates produced by the individual LEWs ranging from .004 to .075 (*Mdn* = .014). Congruently, the proportions of LL choice produced by the individual SHRs ranging from .06 to .94 (*Mdn* = .48) were significantly different (*W* = 17706, *p* < .001) from the proportions of LL choice produced by the individual LEWs ranging from .08 to .91 (*Mdn* = .55).

Sensitivity of Choice to Immediacy of Reinforcement

The next analysis extended the generality of findings showing that the GML (Eq. 2) fits delay discounting data produced by nonhuman animals (Aparicio, 2015; Aparicio et al., 2019). Initial-link responses that the rats emitted on the LL and SS levers were counted separately for each delay component and were aggregated across 15-sessions of the same block. Six response ratios (LL responses / SS responses) were computed for each rat and the mean of the group. Response ratios were transformed into base-2 logarithms and plotted in Figure 4, SHRs (circles) and LEWs (squares), as a function of delay ratios (SS/LL) transformed into base-2 logarithms. The 0 on the x-axis is the $\log_2$ of the 0.1 / 0.1 s delay ratio

and - 9.6 (close to the origin) is the $\log_2$ of the 0.1 / 80 s delay ratio. The dotted line intercepting the y-axis at 0 is the indifference line, indicating that the response ratio was equal to 1 and the $\log_2$ of it equal to 0. On the y-axis, values greater than 0 indicate preference for the LLF (i.e., $\log_2$ of response ratios > 1) and values smaller than 0 preference for the SSF (i.e., $\log_2$ of response ratios < 1). Graphs show response ratios computed for 12 blocks of sessions. The lines are best fits from Eq. 2 to $\log_2$ of response ratios produced by the SHRs (solid line) and LEWs (dashed line). Eq. 2 is expressed as a power law and appears in the bottom of each graph showing empirical parameters for bias (*b*) and sensitivity of choice to the immediacy of reinforcement (*s*). Table 2 shows resulting parameters from Eq. 2 fitting response ratios produced by the group of SHRs and the group of LEWs.

Table 2. Generalized matching law, resulting parameters (Eq. 2).

	b		*s*		R^2	
Block	SHR	LEW	SHR	LEW	SHR	LEW
1	0.591	0.536	0.190	0.125	0.990	0.840
2	1.035	1.390	0.124	0.152	0.597	0.708
3	1.020	1.711	0.173	0.176	0.433	0.788
4	1.506	2.054	0.299	0.257	0.623	0.617
5	1.632	1.700	0.298	0.209	0.510	0.608
6	1.939	1.796	0.381	0.252	0.607	0.656
7	1.837	1.627	0.380	0.218	0.619	0.679
8	2.052	1.529	0.436	0.205	0.698	0.670
9	2.028	1.513	0.366	0.214	0.596	0.644
10	2.381	1.558	0.463	0.198	0.629	0.593
11	1.914	1.388	0.368	0.198	0.557	0.644
12	2.319	1.599	0.409	0.215	0.548	0.664
Mean	**1.688**	**1.533**	**0.324**	**0.202**	**0.617**	**0.676**

Figure 4 shows that the GML (Eq. 2) fitted response ratios produced by the SHRs and LEWs accounting for changes in response ratios that occurred as a function of dynamic changes in the delay ratio. For the response ratios produced by the SHRs, goodness of fit (R^2) ranged from .433 to .990 (M = .617) and from .593 to .840 (M = .676) for the response ratios produced by the LEWs (see Table 2). Both strains developed a bias for pressing on the LL lever, with bias (*b*) ranging from 0.59 to 2.38 (M = 1.69) for the response ratios produced by the SHRs and from 0.54 to 2.05 (M = 1.53) for the response ratios produced by the LEWs. The rats' bias for pressing on the LL lever caused choice to deviate from matching to undermatching as changes in response ratios were slower than those predicted by the GML (Eq. 2) changing the delay ratio.

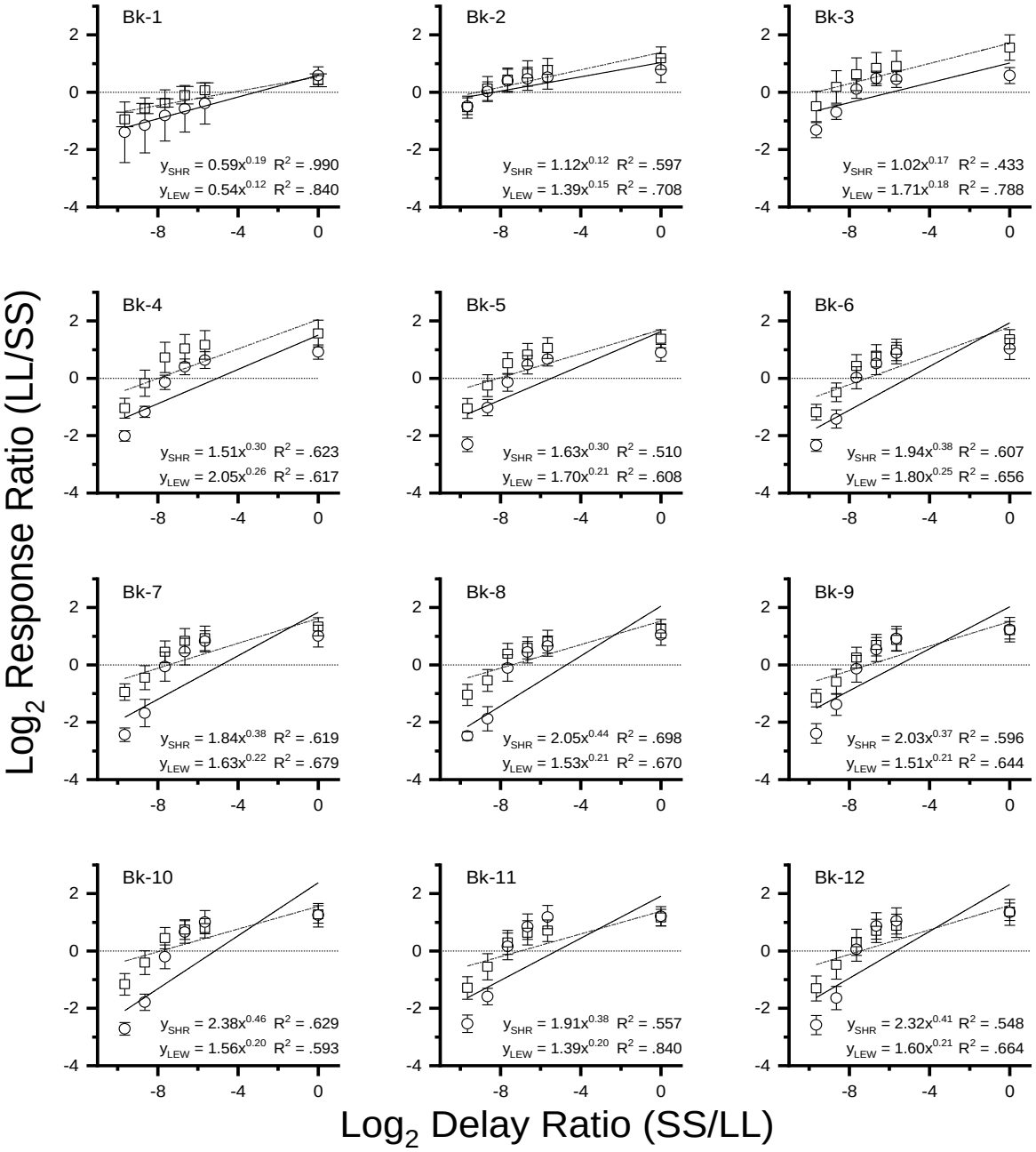

Figure 4. Log_2 of response ratio (LL/SS) as a function of the Log_2 of the delay ratio (SS/LL). The dotted line intercepting the y-axis at zero is the indifference line and the solid line the best fit of Eq. 2 to the mean data produced by the groups of SHRs and LEWs. Other details as in Fig. 3.

The choices that the group of the LEWs made early in training (blocks of sessions 1 to 3) were comparable to the choices made by the group of the SHRs. Sensitivity to the immediacy of reinforcement (s in Eq. 2) for the choices made by the group of the LEWs (s = 0.12, 0.15, and 0.18, respectively, M = 0.15) was comparable to sensitivity for the choices made by the group of the SHRs (s = 0.19, 0.12, and 0.17, respectively, M = 0.16). The response ratios produced by the individual LEWs ranging from – 3.09 to 3.88 (Mdn = 0.11) were similar (W = 5827, p = .226) to the response ratios produced by the individual

SHRs ranging from – 2.30 to 2.27 (*Mdn* = 0.10). Correspondingly, sensitivity to the immediacy of reinforcement for the choices made by the individual LEWs, *s* ranging from .07 to .30 (*Mdn* = .15), was comparable ($W = 200$, $p = .157$) to sensitivity for the choices made by the individual SHRs, *s* ranging from .01 to .25 (*Mdn* = .11).

In blocks of sessions 4 to 6, the SHRs made more impulsive choices than the LEWs. Sensitivity to the immediacy of reinforcement for the choices made by the group of the SHRs (*s* = 0.30, 0.30, and 0.38, respectively, *M* = 0.33) was higher than sensitivity for the choices made by the group of the LEWs (*s* = 0.26, 0.21, and 0.25, respectively, *M* = 0.24). Response ratios produced by the individual LEWs ranging from – 2.59 to 4.02 (*Mdn* = 0.34) were greater ($W = 7844$, $p < .001$) than response ratios produced by the individual SHRs ranging from – 3.43 to 2.91 (*Mdn* = - 0.12). Sensitivity to the immediacy of reinforcement for the choices made by the individual SHRs, *s* ranging from .16 to .43 (*Mdn* = .29), was higher ($W = 241$, $p = .009$) than sensitivity for the choices made by the individual LEWs, *s* ranging from .10 to .31 (*Mdn* = .23). In blocks of sessions 7 to 9, the SHRs' sensitivity of choice to the immediacy of reinforcement increased (*s* = 0.38, 0.44, and 0.37, respectively, *M* = 0.39) which contrasted with the LEWs' sensitivity of choice to the immediacy of reinforcement that decreased (*s* = 0.22, 0.21, and 0.21, respectively, M = 0.21). Accordingly, response ratios produced by the individual SHRs ranging from – 3.94 to 3.37 (*Mdn* = - 0.16) were significantly different ($W = 3058$, $p < .001$) from response ratios produced by the individual LEWs ranging from – 3.08 to 3.08 (*Mdn* = 0.20). Thus, sensitivity to the immediacy of reinforcement for the choices made by the individual SHRs, s ranging from .24 to .50 (*Mdn* = .32), was greater ($W = 276$, $p < .001$) than sensitivity for the choices made by the individual LEWs, s ranging from .11 to .37 (*Mdn* = .21). While the choices made by the group of the LEWs show a slight decrease in sensitivity to reinforcement in blocks 10 to 12 (*s* = 0.20, 0.20, and 0.21, respectively, *M* = 0.20), the choices made by the group of the SHRs show the highest sensitivity to the immediacy of reinforcement (*s* = 0.46, 0.37, and 0.41, respectively, *M* = 0.41). Response ratios made by the individual SHRs ranging from – 3.77 to 3.94 (*Mdn* = - 0.03) were different ($W = 3665$, $p < .001$) from response ratios made by the individual LEWs ranging from – 3.44 to 2.98 (*Mdn* = 0.20). Thus, sensitivity for the choices made by the individual SHRs, s ranging from .26 to .53 (*Mdn* = .33), was greater (W = 293, $p < .001$) than sensitivity for the choices made by the individual LEWs, s ranging from .14 to .35 (*Mdn* = .23).

Discounting Rate *and Sensitivity of Choice to the Immediacy of Reinforcement*

Both strains show that their impulsive choices increased with extended training in the choice situation (180 sessions). In block-12 of sessions; however, the group of the SHRs made more impulsive choices generating higher discounting rates (*k* = .035) and greater sensitivity to the immediacy of reinforcement (*s* = 0.41) than the group of the LEWs (*k* = .016, *s* = 0.21, respectively). These results were verified with discounting rates and estimates of sensitivity of choice to the immediacy of reinforcement computed with choices made by the individual SHRs and LEWs. These computations are plotted in Figure 5 as a function of blocks of sessions. The top graphs show discounting rates produced by the individual SHRs (left graph) and LEWs (right graph) and the bottom graphs show estimates of sensitivity to the immediacy of reinforcement. The unfilled symbols stand for estimates for the choices made by the individuals and the filled symbols stand for estimates averaged for the group of the SHRs (circles) and LEWs (squares). Lines are best fit generated by a 4-parameters logistic (4PL) nonlinear regression model formally expressed as follows.

$$y = \frac{A_1 - A_2}{1+(x/x_0)^p} + A_2, \quad (3)$$

where A_1 is the lowest or initial value estimated for either *k* or *s*, p is the slope of the curve, x_0 its inflection, and A_2 serving as the highest or final value estimated for either *k* or *s*.

The top graphs of Figure 5 show that the discounting rates produced by the SHRs and LEWs increased with increasing block of sessions. Eq. 3 fitted mean discounting rates produced by the SHRs (R^2 = .989) and LEWs (R^2 = .939). Discounting rates produced by individual SHRs ranging from 0 to .072 (*Mdn* = .026) are significantly higher (W = 3575.5, p < .001) than discounting rates produced by the individual LEWs ranging from .003 to .075 (*Mdn* = .013). The parameters A_1 and A_2 revealed that the discounting rates produced by the SHRs increased from .004 to .036 as the discounting rates produced by the LEWs increased from .008 to .018, respectively. The slope of the curve fitting discounting rates produced by the LEWs is steeper (p = 4.99) than the slope of the curve fitting discounting rates produced by the SHRs (p = 4.35), indicating that discounting rates produced by the LEWs increased faster than discounting rates produced by the SHRs. Estimates of the inflections of the curves show that the discounting rates produced by the LEW reached asymptotical level sooner (x_0 = 3.02) than the discounting rates produced by the SHRs (x_0 = 3.62).

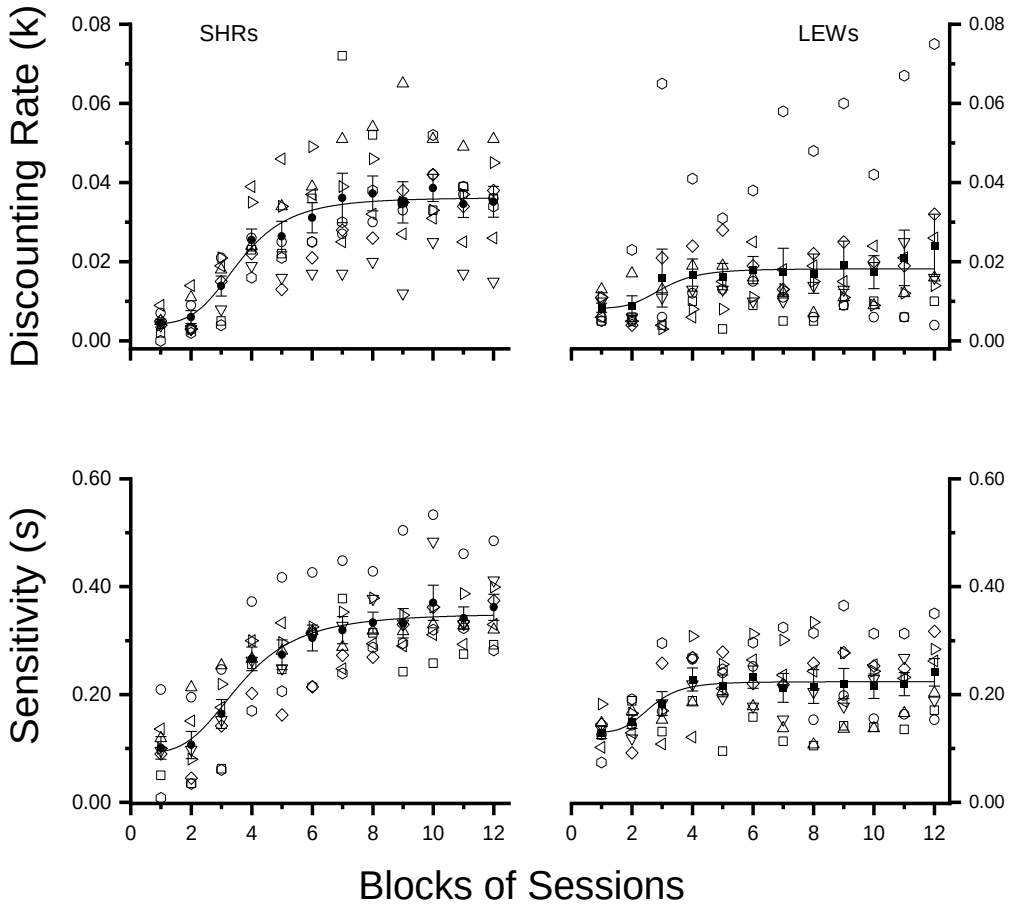

Figure 5. For the data produced by the individual SHRs (left graphs) and LEWs (right graphs), estimates of discounting rate (top) and sensitivity of choice to the immediacy of reinforcement (bottom) as a function of blocks of sessions. Unfilled symbols are the data from the individuals and filled symbols with error bars the mean of the group.

The bottom graphs show that sensitivity of choice to the immediacy of reinforcement increased as a function of extended training in the choice situation. Eq. 3 suitably fit the mean estimates of sensitivity to the immediacy of reinforcement computed for the choices made by the SHRs (R^2 = .974) and LEWs (R^2 = .957). Sensitivities to the immediacy of reinforcement estimated for the choices made by the individual SHRs ranging from .008 to .533 (*Mdn* = .292) are significantly greater (W = 3694.5, p < .001) than sensitivities estimated for choices made by the individual LEWs ranging from .074 to .365 (*Mdn* = .192). For the choices made by the SHRs the parameters A_1 and A_2 estimated that sensitivity to the immediacy of reinforcement increased from 0.09 to 0.35 as the choices made by the LEWs regarding sensitivity to the immediacy of the reinforcement increased from 0.13 to 0.22, respectively. The slope of the curve fitting estimates of sensitivity for the choices made by SHRs (p = 3.65) is steeper than the slope of the curve fitting estimates of sensitivity for the choices made by the LEWs (p = 2.62); thus, changes in sensitivity to the immediacy of reinforcement occurred faster for the SHRs than for the LEWs. The inflections of the curves fitting estimates of sensitivity indicate that the choices made by the LEWs reached maximum level earlier in training (x_0 = 2.62) than the choices made by the SHRs (x_0 = 3.65).

The last analysis extended the generality of findings showing some regularity between the Hyperbolic-decay Model (Eq. 1) and the Generalized Matching Law (Eq. 2). Discounting rates produced by the individual SHRs and LEWs were plotted in Figure 6 against estimates of sensitivity of choice to the immediacy of reinforcement. The left graph shows computations for the SHRs and the right graph computations for the LEWs. Unfilled symbols represent estimates for the individual SHRs and LEWs and filled symbols estimates averaged for the group of SHRs (circles) and LEWs (squares). Results from linear regression and Pearson's r appear on the left-upper corner of each graph. The graphs show positive correlations between discounting rates and estimates of sensitivity of choice to the immediacy of reinforcement. The slopes of the regression lines fitting mean estimates of k and s for the group of the SHRs (s = 1.58) and LEWs (s = 1.56), are comparable. Distinctly, the positive correlation between mean estimates of k and s for the group of the SHRs (r = .991) is higher than the positive correlation between mean estimates of k and s for the group of the LEWs (r = .942). Linear regression accounted for changes in mean estimates of k and s for the group of SHRs (R^2 = .980) and LEWs (R^2 = .876). The slopes of the lines fitting estimates of k and s for the choices made the individual SHRs ranging from 0.05 to 0.27 (*Mdn* = 0.13) were similar (W = 27, p = .233) to the slopes of the lines fitting estimates of k and s for the choices made by the individual LEWs ranging from 0.04 to 0.22 (*Mdn* = 0.11). Positive correlations between k and s for the choices made by the individual SHRs, *Pearson's r* ranging from .856 to .987 (*Mdn* = .924), were similar (W = 23, p = .529) to positive correlations between k and s for the choices made by the individual LEWs, Pearson's ranging from .684 to .975 (*Mdn* = .905). Linear regression fitted estimates of k and s, R^2s ranging from .706 to .971 (*Mdn* = .839) for the choices made by the individual SHRs were comparable (W = 23, p = .529) to R^2s ranging from .415 to .946 (*Mdn* = .801) for the choices made by the individual LEWs.

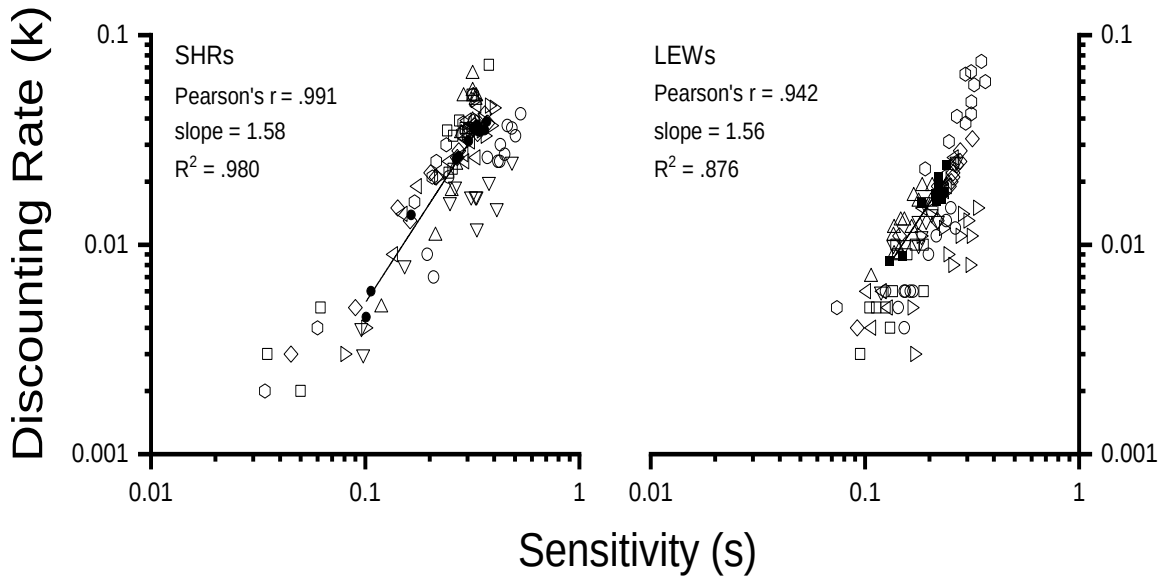

Figure 6. Estimates of *k* as a function of estimates of *s*. The left graph shows the data from the SHRs, and the right graph shows the data from the LEWs. The unfilled symbols represent the estimates for the data of the individual SHR and WKYs and filled symbols with regressions lines the mean for the group data. Regression results and Pearson's r appear on the left-upper corner of each graph. Note the $\log_{10}$ base scales on the x- and y-axis.

Discussion

Preference

The analyses of choice revealed that the LEWs developed a stronger preference for the LLF than the SHRs across blocks of sessions (Fig. 1) and food deliveries (Fig. 2). The analysis of the proportion of LL choice block by block of sessions allowed the scrutiny of global changes in preference, supporting the notion that naïve non-human animals learn to choose impulsively with their experience in the choice situation regardless of their genetic or neurophysiological conditions at the beginning of training (Aparicio et al., 2019). When the LLF was obtained with a slight delay (0.1 s), both strains pressed the LL lever more than the SS lever developing a strong preference for the LLF. The LEWs and SHRs showed a small decrease in their preference for the LLF when it was obtained with delays of 5 and 10 s. The LEWs' preference for the LLF continued when it was delayed 20 s, but the SHRs pressed both levers with similar frequency showing indifference to produce either the LLF or SSF. Both strains pressed the SS lever more than the LL lever when the LLF was delayed 40 or 80 s, producing proportions of LL choice indicating that the LEWs' and SHRs' preference for the SSF increased across blocks. These findings are consistent with those showing that preference for the LLF gradually changes to preference for the SSF when the delay to LLF changes dynamically within sessions (Aparicio et al., 2019), and the present study extends the generality of these findings to SHR and LEW rats.

The local analysis of choice food by food delivery remarkable demonstrated that LEW and SHR rats track with their responses the lever producing the LLF (Fig. 2). It was shown that the LEWs and SHRs pressed both the SS and LL levers to produce the first food within a delay component, which indicated an indifference in choosing the SSF or LLF, respectively. This result occurred because the delays to the LLF were presented in random order during the session, making it difficult for the rats to anticipate the first amount of food (1-pellet or 4-plellets) to be delivered with the actual delay component. It has

been shown that two or more foods produced with the same lever are required for the rats to detect the amount of food and the delay to obtain it (Aparicio et al., 2020). In the present study, the LEWs and SHRs pressed the LL lever more than the SS lever to produce the LLF with delays of 0.1 and 5 s. Both strains showed a slight decrease in their preference for the LLF when it was obtained with a 10 s delay while showing an indifference to obtain either the LLF or SSF when the LLF was delayed 20 s. The LEWs' and SHRs' preference for the SSF emerged when the LLF was delayed 40 s, and it was confirmed when they obtained the LLF with an 80 s delay. These findings support the notion that impulsive choice in non-human animals is controlled food by food with their responses tracking the amount of food and the delay to obtain it (Aparicio, et al., 2019, 2020).

Discounting Rate

In regards to choosing between the SSF and the LLF, the SHRs and LEWs produced discounting functions indicating that the LLF was discounted as a function of the delay to obtain it (Fig. 3). Mazur's (1987) hyperbolic-decay model fitted the data produced by the SHRs and LEWs well, accounting for most of the variability in the proportion of LL choice that occurred as a function of rapid changes in the delay to the LLF. The discounting functions produced by the SHRs and LEWs showed y-intercepts (A) with values that increased across blocks of sessions, indicating that their sensitivity to the magnitude of the LLF increased with increased training to obtain the LLF with a .01 s delay. Also, the slopes of the discounting functions produced by the SHRs and LEWs indicated that discounting rate (k) increased across blocks of sessions (Fig. 5). In the first block of sessions, the discounting functions produced by the LEWs had slopes steeper than the slopes of the discounting functions produced by the SHRs, indicating that the LEWs made more impulsive choices at the beginning of the study than the SHRs. In the second block of sessions, the slopes of the discounting functions produced by SHRs were equivalent to the slopes of the discounting functions produced by the LEWs, suggesting no differences in discounting rates. Impulsive choice in the SHRs increased notoriously with increasing blocks of sessions, producing discounting functions with slopes steeper than the slopes of the discounting functions produced by LEWs. These findings add to the cumulative body of empirical evidence showing that impulsive choice increases with the organism's experience in the choice situation (Aparicio, 2015; Aparicio et al, 2013, 2020), supporting the notion that impulsivity in non-human animals is not a static property of behavior solely determined by genetic and neurochemical mechanisms (Aparicio et al., 2019).

Sensitivity of Choice to Immediacy of Reinforcement

A modified version of Baum's (1974) Generalized Matching Law (GML) was used to estimate sensitivity of choice to the immediacy of reinforcement (s) and a bias (b) for pressing one lever more times than the other. The GML (Eq. 2) fitted discounting data produced by the SHRs and LEWs (Fig. 4), accounting for changes in response ratios that occurred as a function of dynamic changes in delay ratios. The SHRs and LEWs developed a bias for pressing the LL lever more times than the SS lever causing choice to deviate from matching to undermatching (Baum, 1974), with changes in their response ratios that were slower than changes in delay ratios. Consistent with the discounting rates (k in Eq. 1) that the SHRs and LEWs produced in blocks of sessions 1 to 3, estimates of sensitivity to the immediacy of reinforcement (s in Eq. 2) showed no differences between strains in impulsive choice early in training. In blocks of sessions 4 to 6, however, the choices made by the SHRs indicated higher sensitivity to the immediacy of reinforcement than the choices made by the LEWs. Whereas in blocks 7 to 12 the choices made by LEWs showed minor changes sensitivity to the immediacy of reinforcement; comparably, the

choices made by the SHRs indicated their highest sensitivity to the immediacy of reinforcement. These results extend the generality of findings showing that Baum's GML fits discounting data produced by non-human animals well (Aparicio, 2015; Aparicio et al., 2019), detecting factors causing undermatching such as asymmetrical pausing, inconsistency in preference through time, patterns of changeover, and brief bouts of responding (Baum, 1979).

Hyperbolic decay model and the generalized matching law

At the beginning of training (blocks of sessions 1 and 2) the group of LEW rats made more impulsive choices than the group of SHR rats. For both groups impulsive choice increased as a function of increasing blocks of sessions. At the end of training (blocks of sessions 9 to 12), however, the SHRs produced higher discounting rates (Fig. 3) and developed more sensitivity to the immediacy of reinforcement (Fig. 4) than the LEWs. More evidence supporting the finding that SHRs chosen more impulsively than LEWs, came from the analyses of the choices made by the individual SHRs showing greater discounting rates (k in Eq. 1) and higher sensitivity to the immediacy of reinforcement (s in Eq. 2) than the individual LEWs (Fig. 5); confirming that the SHRs behave more impulsively than the LEWs, perhaps due to poor sustained attention (Diana, 2002) and hypersensitivity to delayed consequences in the SHR (Johansen et al., 2005).

A 4 -parameters logistic (4PL) nonlinear regression model (Eq. 3) fitted discounting rates and estimates of sensitivity to the immediacy of reinforcement well, accounting for changes in values of k and s that occurred as a function of increasing the number of blocks of sessions. The slope of the curve (p) fitting the discounting rates (k values) produced by the LEWs was steeper than the slope of the curve fitting the discounting rates produced by the SHRs, indicating that the discounting rates produced by the LEWs changed faster than discounting rates produced by the SHRs. However, the slope of the curve (p) fitting estimates of sensitivity to the immediacy of reinforcement (s values) for the choices made by the SHRs, was steeper than the slope of the line fitting estimates of sensitivity to the immediacy of reinforcement for the choices made by the LEWs, indicating that the choices made by SHRs developed faster changes in sensitivity to the immediacy of reinforcement than the choices made by the LEWs. The inflection points of the curves (x_0) fitting estimates of k and s for the choices made by the LEWs showed values lower than those of the inflection points fitting estimates of k and s for the choices made by the SHRs, indicating that the choices made by the LEWs reached to asymptotical level faster than choices made by the SHRs. For the choices made by individual LEWs, estimates of the initial values (A_1) of k and s were higher than those corresponding to the choices made by individual the SHRs, confirming the LEWs made more impulsive choices at the beginning of the training than the SHRs. The claim that the SHRs developed more impulsivity across blocks of sessions than the LEWs was nicely supported by estimates of final values (A_2) of k and s, indicating that at the end of training the SHRs produced greater discounting rates and developed higher sensitivity to the immediacy of reinforcement than the LEWs. The current 4-parameters logistic (4PL) nonlinear regression model has been successfully used to estimate the inhibitory control of responses in non-human animals (Elcoro, et al., 2016), as well as, to analyze the acquisition, behavioral inhibition, and restoration of responses in SHRs and LEWs (Aparicio et al., 2020). The present study extends the efficacy and generality of Eq. 3 to estimate changes in discounting rate and sensitivity to the immediacy of reinforcement. Future research analyzing impulsivity in inbred strains of SHR and LEW rats, may find the current 4-parameters logistic nonlinear regression model (4PL) useful to estimate the effect of neuropharmacological variables on their impulsive choices.

Lastly, the present study looked for evidence supporting some compatibility between the hyperbolic-decay model (Eq. 1) and the generalized matching law (Eq. 2). Discounting rates (*k*) produced by the SHRs and LEWs were plotted as a function of estimates of sensitivity of choice (*s*) to the immediacy of reinforcement (Fig. 6). We found positive correlations between *k* and *s*. The line fitting estimates of *k* and *s* for the choices made by the SHRs showed a slightly steeper slope (1.58) and higher *Pearson' r* (.991) than the slope of the line fitting estimates of *k* and *s* for the choices made by LEWs (*s* = 1.56 and Pearson's *r* = .942, respectively). These results confirm compatibility between the hyperbolic-decay model and the generalized matching law (Aparicio et al., 2015, 2019, 2020).

Conclusions

Both strains learned to choose impulsively with their experience in the choice situation regardless of their genetic or neurophysiological conditions at the beginning of the study. Early in training the LEWs made more impulsive choices than the SHRs, but late in training the SHRs developed more impulsive choice than the LEWs.

The analysis of the proportion of LL choice, block by block of sessions, provided a global view of gradual changes in preference across delay components, and the analysis of the proportion of LL choice food by food delivery a local view of changes in preference within delay components indicating that the SHRs and LEWs tracked their responses with the lever producing the largest amount of food (LLF). Both strains produced discounting functions indicating that the LLF was discounted with the increasing delay to obtain it.

Mazur's (1987) hyperbolic-decay model fitted the discounting data produced by the SHRs and LEWs suitably. Both the y-intercept (*A*) and the slope (*s*) of the discounting functions produced by the SHRs and LEWs increased as a function of training in the choice situation, indicating that sensitivity to the magnitude of the LLF and discounting rate, respectively, increase with learning. Impulsive choice increased notoriously in the SHRs producing discounting functions with slopes steeper than the slopes of the discounting functions produced by LEWs.

A modified version of Baum's GML (1974) fitted discounting data produced by the SHRs and LEWs well. Both strains developed a bias for pressing the LL lever more than the SS lever with their choices indicating strong undermatching. Early in training estimates of sensitivity of choice to the immediacy of reinforcement (s) indicated no differences between strains regarding impulsive choice. Late in training, however, the SHRs showed higher sensitivity to the immediacy of reinforcement than the LEWs. Concerning the choices made by individual SHR and LEW rats, a 4-parameters logistic (4PL) nonlinear regression model (Eq. 3) fitted estimates of *k* and *s* well, showing that both discounting rate and sensitivity of choice to the immediacy of reinforcement increased as a function of the increasing blocks of sessions. Positive correlations between *k* and *s* suggested some regularities between the hyperbolic-decay model and the generalized matching law fitting discounting data.

Overall, the present study supports the possibility that the LEW strain might be a feasible control for the SHR strain, both are inbred strains learning to choose impulsively on delay discounting tasks. Future research analyzing impulsivity in inbred strains SHR and LEW rats, might find a 4-parameters logistic (4PL) nonlinear regression model useful to estimate the effects of environmental factors and neuropharmacological variables on impulsive choice.

The connection between ADHD and impulsive choice requests the creation of preclinical models for the prevention and treatment of ADHD, identifying potential neural factors controlling impulsive choice. Studies evaluating rodent models of ADHD suggest that the SHR is not a valid model of impulsive choice, the SHR possesses an endophenotype causing inter-individual differences in impulsive choice and no differences with its control strain the WKY, suggesting that the LEW is a more appropriate model of impulsive choice displaying more characteristics of ADHD than the SHR (Garcia & Kirkpatrick, 2013). A suitable preclinical animal model of ADHD requires both internal and external validity to make extrapolations from animals to humans (Pound & Ritskes-Hoitinga, 2018). While some aspects of animal models of ADHD can be improved to a limited extent, the existing differences between animals and humans prevent the possibility to achieve a fully external validity; thus, the following question posed by Pound and Ritskes-Hoitinga: Is it possible to overcome issues of external validity in preclinical animal models? which remains unanswered.

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