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Differential effects of social and novelty enrichment on individual differences in impulsivity and behavioral flexibility

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Abstract

Early life experience profoundly impacts behavior and cognitive functions in rats. The present study investigated how the presence of conspecifics and/or novel objects, could independently influence individual differences in impulsivity and behavioral flexibility. Twenty-four rats were reared in an isolated condition, an isolated condition with a novel object, a pair-housed social condition, or a pair-housed social condition with a novel object. The rats were then tested on an impulsive choice task, a behavioral flexibility task, and an impulsive action task. Novelty enrichment produced an overall increase in impulsive choice, while social enrichment decreased impulsive choice in the absence of novelty enrichment and also produced an overall increase in impulsive action. In the behavioral flexibility task, social enrichment increased regressive errors, whereas both social and novelty enrichment reduced never reinforced errors. Individual differences analyses indicated a significant relationship between performance in the behavioral flexibility and impulsive action tasks, which may reflect a common psychological correlate of action inhibition. Moreover, there was a relationship between delay sensitivity in the impulsive choice task and performance on the DRL and behavioral flexibility tasks, suggesting a dual role for timing and inhibitory processes in driving the interrelationship between these tasks. Overall, these results indicate that social and novelty enrichment produce distinct effects on impulsivity and adaptability, suggesting the need to parse out the different elements of enrichment in future studies. Further research is warranted to better understand how individual differences in sensitivity to enrichment affect individuals' interactions with and the resulting consequences of the rearing environment.

Keywords

Impulsive choice; behavioral flexibility; impulsive action; differential rearing; individual differences; rats

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1. Introduction

The environment that individuals experience during their early lives has been shown to exert a critical impact on their development [e.g., 1, 2]. The early rearing environment has been suggested to influence brain development and behaviors in adulthood, and may contribute to the development of psychiatric disorders, such as substance abuse, schizophrenia, and depression [see 1, 3, 4–6]. Animal models provide opportunities for well-controlled rearing environment manipulations, so efforts have been underway to study the effects of differential rearing on development and behavioral manifestations in adulthood in animal models [e.g., rodent models; 7]. In the classic environmental enrichment paradigm, socially-isolated rats are singly housed in a small wire-mesh cage, while environmentally-enriched rats are housed in a larger cage with conspecifics and novel objects that are changed and/or rearranged periodically [7–9]. Compared to environmentally-enriched rats, socially-isolated rats exhibit hyper-reactivity to novel environments, greater responding to rewarding stimuli, cognitive deficits in novel object discrimination and rule learning, and more aggressive social interactions with conspecifics [e.g., 7, 8]. Accordingly, differential rearing has a considerable effect on various phenomena.

Some of the consistent effects of differential rearing, such as differences in responding to rewarding stimuli and cognitive differences in rule learning, have led to the inference that early-life exposure to different environments may influence individuals' impulsivity and adaptability (behavioral flexibility). Indeed, behavior in these tasks may be differentially sensitive to different aspects of the enrichment paradigm [see 10 for relevant evidence]. Impulsivity and adaptability have been suggested as two contributing factors to maladaptive behaviors, such as substance abuse and pathological gambling [3]. However, previous research has yet to reach a consensus in terms of the effects of the early rearing environment on impulsivity and adaptability. Impulsivity is a multi-faceted construct that is often broadly sub-divided into impulsive choice and impulsive action [11–14], with impulsive choice referring to impulsivity within decision making situations and impulsive action referring to the inability to inhibit or stop a single response. Regarding impulsive choice, previous enrichment studies have indicated that environmentally-enriched rats are less impulsive (thus more willing to choose to wait for a larger reward) than their isolated counterparts [15–17], while other research has reported the opposite result [5]. Furthermore, while past research has indicated that socially-isolated rats exhibit higher levels of impulsive action in a differential-reinforcement-of-low-rates (DRL) task which requires inhibiting responses for periods of time [18, 19], other reports have demonstrated that socially-isolated rats are less impulsive in terms of response inhibitory capacities compared to environmentally-enriched [15] and socially-housed rats [20].

Adaptability can be operationalized in terms of behavioral flexibility, or the ability to override a previously learned action and produce a new response given a change in the environment [21, 22]. Adaptability may be related to impulsivity, in that the inhibition of previously learned patterns is often critical for successful behavioral change. Previous analyses of behavioral flexibility using reversal learning tasks, in which individuals now have to select a previously unreinforced option while inhibiting choices of the previously reinforced option, have suggested that socially-isolated rats exhibit slower behavioral shifts

after reversal relative to socially-housed rats [23–25] and environmentally-enriched rats [26, 27]. Moreover, isolated rats perseverated more on the previously rewarded lever in a two-lever DRL task [19], suggesting deficits in switching responses [see also 28 for evidence of perservation of response tendencies]. However, other reports have indicated that socially-isolated rats exhibit more flexible performance than socially-housed rats [29], or that there are no effects on behavioral flexibility as a function of rearing environment [30]. Moreover, Schrijver and Würbel [31] reported that socially-isolated rats, compared to socially-housed rats, did not exhibit deficits in simple reversal learning, but did exhibit deficits when they had to shift their attention from focusing on spatial cues to visual cues or vice versa [also see 32], thus indicating potential deficits in set shifting. Therefore, it is critical to further elucidate how the rearing environment can affect individual differences in different forms of impulsivity and behavioral flexibility.

While the classic environmental enrichment paradigm has provided key insight into the effects of differential rearing on brain development and behavioral phenomena, the social and novelty aspects of enrichment are inherently confounded. Moreover, there are many variations on the classic paradigm that involve greater or lesser focus on the different dimensions of enrichment [7]. The combination of confounding variables and paradigmatic variations can create challenges in interpreting discordant results. Furthermore, social and novelty (physical) enrichment may differentially affect the behavioral and neurobiological mechanisms underlying impulsivity and behavioral flexibility. For example, one consequence of environmental enrichment is increased hippocampal neurogenesis [33], but these effects may be predominantly due to novelty enrichment, rather than social enrichment [34]. Additionally, novelty, rather than social, enrichment has been shown to result in learning and memory improvements [34], although the opposite result has also been reported [35]. Schrijver, Pallier [36] showed that social isolation selectively impaired reversal learning relative to social enrichment, while the absence of novelty enrichment selectively impaired spatial learning in comparison to novelty enrichment [also see 37]. Thus, some of the discrepant results regarding the effects of environmental enrichment on impulsive choice, impulsive action, and behavioral flexibility described above may be ultimately accounted for in terms of the nature of the enrichment employed.

Another common confounding factor in the traditional enrichment paradigm is the difference in rearing cage size [e.g., 7]. The traditional enrichment paradigm involves a large cage while the isolation paradigm involves minimal living space. Increased living space could potentially affect impulsivity and/or adaptability through the effects of exercise on cognitive and neuronal function [e.g., 38]. However, the potential dissociation between social and novelty enrichment and the potential confound of cage size on impulsivity and behavioral flexibility have yet to be addressed, which is one of the goals of the present study.

Finally, differential rearing could contribute to impulsivity and adaptability through an interaction with individual differences. Kirkpatrick, Marshall [16] examined the interaction of differential rearing in the classic enrichment paradigm with impulsive and risky choice behaviors. The authors reported that isolated rats made more impulsive choices in general, and that individuals from both enriched and isolated rearing groups that were more impulsive tended to be more risk-seeking. They also found that individuals that were more

adaptable in changing their choice behavior in the impulsive choice task tended to be more adaptable in the risky choice task as well. Rearing environment did not interact with the individual differences correlations, but instead only exerted group-level effects on impulsive choice alone. However, to our knowledge, there has yet to be a comprehensive evaluation of how rearing environment may interact with individual differences correlations across impulsive choice, impulsive action, and behavioral flexibility tasks. Thus, given the potential interaction between rearing environments and individual differences, it is critical to focus on group-level effects of enrichment as well as enrichment effects on individual differences, another aim of the present study.

The overarching goal of the present experiment was to parse out the contribution of social and novelty enrichment in an attempt to address the previously reported discrepancies in the effects on impulsivity and adaptability, while controlling for potential confounds. Here, we specifically focused on impulsive choice within a delay discounting procedure [see 39], impulsive action within a DRL procedure [see 40], and behavioral flexibility within a set-shifting task [41] as the behaviors in these procedures are known to be affected by differential rearing. The current study set out to explore (1) the relationship between differential rearing and individual differences and (2) its effect on moderating impulsivity and adaptability. The effects of these differential enrichment conditions were disentangled via alteration of the classic enrichment paradigm. Social and novelty enrichment were tested in a 2×2 design (i.e., presence and absence of social and novelty enrichment, respectively). Cage size was controlled for by housing all of the rats in standard shoebox cages. It was hypothesized that social and novelty environment would potentially produce different effects within impulsive choice, impulsive action, and behavioral flexibility paradigms.

2. Materials and Methods

2.1. Animals

Twenty-four experimentally-naïve male Sprague-Dawley rats, obtained from Charles River (Kingston, NY, USA), arrived to the colony at Kansas State University (Manhattan, KS, USA) at post-natal day (PND) 21. Their housing conditions varied based on rearing manipulation (see 2.3.1. *Environmental rearing*). Prior to the onset of behavioral testing, the rats were placed on a restricted diet to maintain their weights at approximately 85% of their projected ad libitum weight based on growth charts obtained from the supplier. When supplementary feeding was required following an experimental session, the rats were fed in their home cages directly after testing (together for pair-housed rats and individually for singly-housed rats). The rats had free access to water at all times in both the home cages and experimental chambers. The colony room was maintained on a 12:12 hr reversed light:dark cycle with lights off at approximately 7 a.m. Several red lamps provided illumination throughout the dark cycle. All experimentation occurred during the dark cycle.

2.2. Apparatus

Behavioral testing was conducted in a set of 24 identical operant chambers (Med Associates; St. Albans, VT, USA). Each chamber measured $25 \times 30 \times 30$ cm and was housed inside of a ventilated, noise-attenuating box measuring $74 \times 38 \times 60$ cm. The chambers were located in

two separate rooms, with 12 chambers in each room. Two levers (ENV-122CM) were situated on either side of the food cup at approximately one third of the total height of the chamber and presses were recorded by a micro-switch. Nosepoke keys with cue lights (ENV-119M-1) were located directly above each lever. A magazine pellet dispenser (ENV-203) delivered 45-mg food pellets (Bio-Serv; Flemington, NJ, USA) into the food cup. Water was available through a metal tube that protruded through a hole in the lower-center of the back wall. MED-PC IV controlled experimental events and recorded the time of events with a 2-ms resolution [42].

2.3. Procedure

2.3.1. Environmental rearing—After arrival, the rats were separated into four groups ($n = 6$ in each) and subjected to differential rearing, in which they were maintained for the duration of the experiment. Group names indicate the combination of differential social enrichment (isolated condition, IC; social condition, SC) and differential novelty enrichment (non-novelty-enriched, −; novelty-enriched, +). Individual IC rats and pair-housed SC rats were housed in identically-sized home cages ($20 \times 43 \times 20$ cm) with Aspen chip bedding. The IC− group was singly housed in an opaque plastic cage and did not have exposure to novel objects. The IC+ group was singly housed in an opaque plastic cage and had 24 hr of daily exposure to one of seven small enrichment objects (designed for small animal enrichment and obtained from pet stores), which were pseudo-randomly rotated over the course of seven days. The SC− group was pair-housed in transparent plastic cages and did not have exposure to novel objects. The SC+ group was pair-housed in transparent plastic cages and had 24 hr of daily exposure to one of seven enrichment objects, which were pseudo-randomly rotated over the course of seven days. The rats were not handled during the rearing period (PND 21–51) except during a brief cage change/cleaning session that occurred every two weeks. After the rearing period, all rats were handled daily.

2.3.2. Magazine and lever press training—Rats first went through one session of magazine training, in which food pellets were delivered to the food magazine on a random time (RT) 60-s schedule of reinforcement. The rats were then trained to press both the left and right levers. The first phase of lever press training involved the delivery of food pellets on fixed ratio (FR) 1, random ratio (RR) 3, and RR 5 schedules of reinforcement, in which each schedule took up one block with 20 reinforcers on each lever. The second phase contained three blocks of the RR 5 schedule of reinforcement with 20 reinforcers on each lever per block. A 5-min inter-block interval (IBI) was implemented within both phases. The first phase of lever press training lasted for two sessions for all but two rats, who required three sessions for this training. The second phase of lever press training lasted for one session.

2.3.3. Task order—All rats were initially subjected to the impulsive choice task, followed by a buffer task, behavioral flexibility task, another buffer task, and an impulsive action task. This particular order and the use of the buffer tasks were designed to minimize carryover effects that have been previously reported in similar behavioral tasks [43].

2.3.4. Impulsive choice task—The impulsive choice task was designed to measure rats' preferences for a smaller-sooner (SS) reward versus a larger-later (LL) reward [e.g., 16]. Rats received a mixture of free choice and forced choice trials. One lever was designated as the SS lever; the other, the LL lever. Lever assignments were counterbalanced across rats. In forced choice trials, one lever was inserted into the chamber. The first lever press initiated the SS or LL delay and the first response following the delay resulted in reward delivery, lever retraction, and the start of a 60-s intertrial interval (ITI). On free choice trials, both levers were inserted into the chamber. A response on one of the levers resulted in the immediate retraction of the other lever. The trial progressed as in forced choice trials. There were 80 trials delivered in two 40-trial blocks with a 5-min IBI. Each block contained 16 forced trials (8 SS and 8 LL) and 24 free choice trials that were randomly intermixed. Each session lasted for approximately 2 hr.

The manipulated variable in the impulsive choice task was LL magnitude. The SS magnitude was always 1 pellet and the SS and LL delays were maintained at 10 and 30 s, respectively. In Phases 1–3, the LL reward magnitude was 1, 2, and 3 pellets, respectively. Each phase lasted for 10 sessions.

2.3.5. Lever buffer task—A lever buffer task was delivered to reduce carryover between tasks, and to measure side biases for the behavioral flexibility task. The first session of the buffer task employed FR 1, RR 3, and RR 5 schedules of reinforcement, and the second session of the buffer task employed an RR 5 schedule of reinforcement only.

2.3.6. Behavioral flexibility: visual discrimination phase—The behavioral flexibility task was adapted from Floresco, Block [21]. The visual discrimination task began in darkness with the levers retracted. The first trial was preceded by a 60-s interval. Each trial started with a 3-s illumination of one of the cue lights. In every pair of trials, the left or right cue light was illuminated once; the order within the pair of trials was random. Both levers were then inserted into the chamber. A lever press on either lever resulted in the retraction of both levers and termination of the cue light. A correct response was defined as a response on the lever below the illuminated cue light. An incorrect response was defined as a response on the lever below the non-illuminated cue light. Following the termination of the cue light, correct responses also resulted in the delivery of one food pellet and the onset of the 60-s ITI; incorrect responses proceeded as correct responses without reinforcer delivery. Each session lasted for 80 trials or for approximately 2 hr. This phase of the behavioral flexibility task lasted for eight sessions.

2.3.7. Behavioral flexibility: response discrimination phase—This procedure was identical to the visual discrimination procedure except that the correct response was defined as pressing the lever on the opposite side of the individual rat's side bias, regardless of the location of the illuminated cue light. The buffer task (see 2.3.5. *Lever buffer task*) was used to determine each rat's side bias, which was operationally defined as the lever corresponding with the shortest mean time to complete the RR 5 schedules of reinforcement during the second session of the buffer task. The response discrimination phase of the behavioral flexibility task lasted for two sessions.

2.3.8. Nose poke buffer task—For the nose poke buffer task, the rats were required to nose poke the cue lights, instead of pressing levers. The change in response modality was designed to minimize carryover effects from the previous tasks, and to train rats with a new response that was adopted in the subsequent impulsive action task. The rats received two sessions of training that were identical to the lever buffer task, apart from the change in response modality.

2.3.9. Impulsive action task—A differential reinforcement of low rates (DRL) 30 s procedure was delivered. After a 70-s initial interval to start the session, the left cue light was illuminated. The first response (nose poke) on the cue light initiated the task. Reinforcement on the current DRL was contingent on the rats' spacing their consecutive responses by at least 30 s. If the rat responded before 30 s had elapsed, then the interval was reset and the rat was required to wait at least another 30 s before a response could result in reinforcement (i.e., one food pellet). Each session lasted until a total of 80 reinforcers were delivered or for approximately 2 hr. Session termination was accompanied by termination of the left cue light. This task lasted for 10 sessions.

2.4. Data Analysis

All summary measures were obtained from the raw data using MATLAB 8.6 (The MathWorks; Natick, MA, USA). Analyses involved fitting generalized linear mixed-effects models with a binomial response distribution and a logit link function to the data [44]. These models are comparable to repeated-measures logistic regression analyses, allowing for parameter estimation as a function of the condition (fixed effects) and individual (random effects) [44–47]. Accordingly, mixed-effects models account for natural hierarchies in the data (i.e., grouping observations by individual and individual/condition assignments) [47]. The use of mixed-effects models has become the recommended analytical framework in psychology and neuroscience research [48], allowing for greater generalization to the population [48, 49], as random effects are calculated with reference to population means [47]. Accordingly, within-groups variation may be viewed as information of interest rather than error [see 45]. For example, in regards to the present experiment, mixed-effects modeling permits the estimation of differential biases (random intercepts) and sensitivities to changes in reward magnitude (random slopes) across subjects. Similarly, mixed-effects regression models, in contrast to ANOVAs, allow for the simultaneous inclusion of both categorical and continuous predictors in the same model [50], thus providing evaluation of between-group differences in changes across conditions (e.g., SC vs. IC differences in LL choice across different magnitude conditions).

Model fitting occurred in two stages: Analyses first determined the model with the best fitting random-effects structure, and then determined the model with the best fitting fixed-effects structure that incorporated the aforementioned best fitting random-effects structure. Given the current design, all potential random effects were also potential fixed effects; thus, the factor(s) within the best-fitting random effects structure were automatically included as fixed-effects [51]. In addition, group-level factors (social and novelty enrichment) that did not vary as a function of subject were entered into the model in this second stage. The model that minimized the Akaike information criterion (AIC), in which the doubled negative log

likelihood of the model is penalized by twice the number of estimated parameters, was selected for reporting. The model with the lowest AIC is the best approximating model of the data, incorporating a penalty for the expected improvement in fit due to added parameters [see 52]. Continuous predictors (e.g., session, LL magnitude) were mean-centered. The categorical predictors of social enrichment (SC, IC) and novelty enrichment (–, +) were effect coded with IC/SC as –1/+1 and –/+ as –1/+1, respectively. The fixed- and random-effects structures of the models for each of the task analyses are described in the corresponding results sections below and in the Supplementary Materials.

The dependent measures for each of the tasks were as follows: individual choices for the impulsive choice task (SS=0, LL=1), individual choices for the behavioral flexibility task (incorrect=0, correct=1), and individual inter-response times (IRTs) for the impulsive action task (unrewarded IRT=0, rewarded IRT=1). With the following exceptions, all responses from all sessions across all subjects were included in analyses, thus adding considerable power to the analyses. There were some sessions that were excluded from the analysis due to experimentation issues. For the impulsive choice task, one session from Phase 1 for 12 rats, one session from Phase 2 for 12 rats, and one session from Phase 3 for 2 rats were missing from the analysis. For the visual-cue discrimination phase of the behavioral flexibility task, one session was removed from analysis for 2 rats. For the impulsive action task, one session was removed for 3 rats. There were a total of 32,975 observations that were entered into the impulsive choice model. The behavioral flexibility analysis involved responses in both the visual and response task, resulting in 19,040 total observations. The impulsive action analysis included IRTs of 1000 s or less, resulting in 120,462 total observations.

3. Results

3.1. Impulsive choice

The best-fitting model included the overall intercept, social enrichment, novelty enrichment, LL magnitude, and session as main effects. The interaction terms of Social Enrichment $\times$ Novelty Enrichment, and LL Magnitude $\times$ Session were also included as fixed effects. The random-effects structure included intercept, LL magnitude, session, and LL Magnitude $\times$ Session. The Supplementary Materials include the full model output (Table S1), the graphical representation of the LL Magnitude $\times$ Session interaction (Figure S1), and the model fits to the individual differences in choice behavior as a function of LL magnitude and session (Figure S2); here, we focus on reporting the effects of the enrichment manipulations.

Figure 1A shows the mean proportion of choices for the LL outcome as a function of LL magnitude, as well as the rats' social enrichment and novelty enrichment conditions. Each group showed an increase in LL choice behavior as LL magnitude increased. The best model did not include interactions between LL magnitude and the enrichment conditions, indicating that the slope of the choice functions was not moderated by social or novelty enrichment. Figure 1B shows the mean proportion of LL choices for each group collapsed across LL magnitude. Novelty-enriched (+) rats were significantly less likely to make LL choices compared to non-novelty-enriched (–) rats, $t(32968) = -3.84$, $p < .001$, $b = -0.54$, 95% CI $[-0.81, -0.26]$, but there was no main effect of social enrichment, $t(32968) = 1.16$, $p = .247$, $b = 0.16$, 95% CI $[-0.11, 0.44]$. However, there was a significant Social $\times$ Novelty

Enrichment interaction, $t(32968) = -2.18$, $p = .029$, $b = -0.31$, 95% CI $[-0.58, -0.03]$. Specifically, post-hoc tests indicated that the SC- group made significantly more LL choices than the other three groups, $ps = .016$, while the other groups did not significantly differ from one another, $ps = .060$, suggesting that social enrichment in the absence of novelty enrichment increased LL choice (decreased impulsive choice).

3.2. Behavioral flexibility

The best-fitting model included the overall intercept, phase (Visual, Response), session, and Phase $\times$ Session as fixed effects. Intercept, phase, session, and Phase $\times$ Session also served as random effects. The full model (Table S2), the fixed effects figure of Phase $\times$ Session (Figure S3), and the random effects figure (Figure S4) are provided in the Supplementary Materials. Figure 2A shows the proportion of correct responses in the visual (V) and response (R) discrimination phases of the behavioral flexibility task for IC-, IC+, SC-, and SC+ rats. The mean proportion of correct responses increased from the visual to the response discrimination phases, $t(19036) = 12.09$, $p < .001$, $b = 2.40$, 95% CI $[2.01, 2.79]$, which was primarily due to the rats showing more correct responses at the onset of the response-discrimination phase than at the onset of the visual-discrimination phase (Figure S3). As seen in Figure 2A, all groups behaved relatively similarly across phases in regards to overall correct choices; accordingly, the best-fitting model did not include social or novelty enrichment as fixed effects. Indeed, there also was no main effect of social enrichment ($p = .615$) or novelty enrichment ($p = .663$) on trials to criterion in the response discrimination phase (i.e., 10 consecutive correct responses), nor any interaction between the two enrichment manipulations on this measure ($p = .080$).

A second analysis was conducted to more specifically evaluate the types of incorrect choices the rats made in the first session of the response discrimination phase. There were three possible types of incorrect choices in this phase (errors) [21]. *Perseverative* errors were those in which the rats responded on the lever below the cue light (i.e., correct choices in the visual discrimination phase) when the correct response was to respond on the opposite lever. These types of responses were recorded as perseverative errors so long as there were at least six of these types of errors in each eight-trial block. After an eight-trial block had passed in which there were five or fewer perseverative errors, these types of errors were recorded as *regressive* errors. The third type of error was a *never-reinforced* error, in which the rat responded on the lever that was neither below the illuminated cue light or on the correct side in the response discrimination phase (i.e., such a response was *not* reinforced in the visual or response discrimination phases). Perseverative errors are indicative of the extent to which individuals can adapt to a new reinforcement contingency. Regressive errors reflect the extent to which individuals continue responding in accordance with the new reinforcement contingency once it has been learned. Never-reinforced errors reflect exploration of other possible reinforcement contingencies.

For each error type, a generalized linear regression model with a Poisson distribution was conducted. Social enrichment was effect coded with IC/SC as $-1/+1$; novelty enrichment was effect coded with $-/+$ as $-1/+1$. Due to the small number of data points in these analyses, the best model for each error type was that which had the minimum AICc [i.e.,

AIC with a correction for small sample sizes; see 53]. Figure 2B shows the total perseverative, regressive, and never-reinforced errors in the first session of the response discrimination phase of the behavioral flexibility task for IC–, IC+, SC–, and SC+ rats. The best model of perseverative errors was an intercept-only model, suggesting that neither novelty nor social enrichment moderated perseverative error rate. Relative to IC rats, SC rats made significantly more regressive errors, $t(22) = 1.98$, $p = .047$, and significantly fewer never-reinforced errors, $t(21) = -2.38$, $p = .017$. Novelty-enriched (+) rats also made significantly fewer never-reinforced errors compared to non-novelty-enriched (–) rats, $t(21) = -2.90$, $p = .004$.

3.3. Impulsive action

The best-fitting model included the overall intercept, social enrichment, novelty enrichment, and session. The intercept and session also served as random effects. The full model (Table S3) and the random effects figure (Figure S5) are provided in the Supplementary Materials. Figure 3A shows the probability distribution of IRTs as a function of social and novelty enrichment conditions. The bimodal distribution in Figure 3A is consistent with the behavior traditionally observed in DRL tasks, in which there are frequent within-bout IRTs that are short in duration (IRTs < 1 s) and frequent between-bout IRTs of longer duration (IRTs 30 s). Overall, the groups exhibited IRT distributions indicating that they learned the IRT criterion, but there were some differences in the shapes of their distributions. The IC– group showed the highest incidence of very short (bout) IRTs, but their second peak was shifted to the right indicating better production of longer IRTs. Both SC groups showed a broader distribution of short IRTs and their peak of their longer IRTs fell short of the criterion suggesting poorer DRL efficiency. The IC+ group showed a more intermediate pattern between the two extremes. To provide a more direct measure of DRL efficiency, Figure 3B shows the proportion of IRTs that were rewarded (> 30 s) as a function of social and novelty enrichment. SC rats were significantly less likely to exhibit rewarded IRTs relative to IC rats, $t(120458) = -3.54$, $p < .001$, $b = -0.30$, 95% CI [–0.47, –0.14]. In addition, there was a trend for novelty enrichment to result in fewer rewarded IRTs compared to non-novelty enrichment, $t(120458) = -1.71$, $p = .087$, $b = -0.15$, 95% CI [–0.31, 0.02]. Although the effect of novelty enrichment was not significant, including this factor did improve the model fit indicating a nontrivial influence on the prediction of the rewarded IRTs.

3.4. Inter-task relationships

A final set of analyses was performed to evaluate the relationship between individual differences in the impulsive choice, behavioral flexibility, and impulsive action tasks. The correlational analyses focused on relationships at asymptotic levels of performance where there were no major interactions between enrichment conditions and session in the mixed-effects analyses. For the impulsive choice task, the final five sessions were used in the analyses. For the behavioral flexibility task, the last session of the visual discrimination phase and the first session of the response discrimination phase were used in analyses. Lastly, the final five sessions of the impulsive action task were used in the analyses.

For each rat, two measures of LL choice behavior were computed. The first was an overall self-control index, which was computed as the mean proportion of LL choices when the LL

magnitude was 2 and 3 pellets. Here, greater values reflect greater preference for LL over SS rewards when the outcomes differed in both reward magnitude and delay. These values were exponentially transformed to correct for negative skewness. The second was the delay sensitivity index, which was computed as the mean proportion of LL choices in Phase 1 of the impulsive choice task (i.e., when both SS and LL magnitudes were 1 pellet). For this measure, greater values reflect more choices for a delayed 1-pellet reward (LL) versus a more immediate 1-pellet reward (SS), and therefore less sensitivity to the delay. Specifically, rats who were more sensitive to the differences in SS and LL delays would be predicted to make more SS choices (i.e., fewer LL choices). These values were logit-transformed to correct for positive skewness. For the behavioral flexibility task, the mean proportion of correct responses in the last session of the visual discrimination phase was subtracted from the mean proportion of correct responses in the first session of the response discrimination phase. This difference score was operationally defined as a behavioral flexibility index when shifting from the visual discrimination phase to the response discrimination phase, such that larger values reflected smaller performance decrements (i.e., greater adaptability) given this shift. Lastly, the dependent measure from the impulsive action task was the mean proportion of rewarded IRTs. Here, higher values reflected a greater proportion of IRTs that were rewarded (i.e., IRTs < 30 s).

The first analysis of inter-task relationships involved correlational analyses between the summary measures from each task. Figure 4 shows the relationships and best-fitting line for each of these analyses. The correlational data are collapsed across groups in Figures 4A–E to look for general patterns in the individual differences; analyses of group moderation of these effects are presented subsequently. There was a significant positive relationship between rewarded IRTs and the behavioral flexibility index, $r = .69$, $p < .001$ (Figure 4A). Here, the rats that exhibited greater adaptability of their behavior in response to new reinforcement contingencies (visual discrimination phase → response discrimination phase of the behavioral flexibility task) were also those individuals that were more likely to perform rewarded IRTs in the impulsive action (DRL) task. However, there was no significant correlation between the overall self-control index (LL choice) and the behavioral flexibility index, $r = .07$, $p = .752$ (Figure 4B), or between the overall self-control index and rewarded IRTs, $r = .18$, $p = .411$ (Figure 4C). There was also a significant positive relationship between the delay sensitivity index and both rewarded IRTs, $r = .44$, $p = .030$ (Figure 4D), and the behavioral flexibility index, $r = .46$, $p = .024$ (Figure 4E).

A second analysis of the inter-task relationships was performed to determine whether the cross-task behavioral relationships were moderated by social and/or novelty enrichment conditions. This analysis employed a multiple regression approach rather than group-by-group correlations to evaluate moderation of the strength of the correlations [see 54]. For each regression analysis, the summary measure from one task (e.g., behavioral flexibility index) was regressed on the summary measure from one of the other tasks (e.g., rewarded IRTs from the impulsive action task). In these analyses, the continuous predictor of the analysis was mean-centered, and the categorical predictors of social and novelty enrichment were effects coded as in previous analyses. In each of the multiple regression analysis, all main effects and interactions were entered simultaneously into the model. As shown in Figure 4F, there was a significant Social Enrichment × Behavioral Flexibility Index

interaction on the delay sensitivity index, $t(16) = 2.47$, $p = .025$, such that SC rats showed a steeper positive relationship between the delay sensitivity and behavioral flexibility indices compared to IC rats. There were no other significant interactions between social and/or novelty enrichment condition and behavior in one task on behavior in a different task, $p > .200$.

4. Discussion

The goal of this experiment was to determine how social and novelty enrichment affect impulsivity and adaptability, classes of behaviors critically related to drug abuse, as well as other maladaptive behaviors and neurological disorders [55–62]. The small number of studies in this area have yielded disparate results, warranting further research to understand the complex effects of enrichment on behavior. One key factor is that the typical enrichment paradigm involves covarying social and novelty enrichment, as well as cage size. In the present study, cage size was a constant factor; social and novelty enrichment were manipulated separately. The results indicated a clear and distinct pattern of social and novelty enrichment effects on impulsivity.

The presence of novelty enrichment alone produced a significant increase in impulsive choice behavior. Enrichment has been proposed to exert a protective effect against drugs of abuse (e.g., psychomotor stimulants), and these effects have been proposed to stem from the novelty aspect of enrichment [e.g., 63]. Lower levels of impulsive choice are also associated with decreased susceptibility to drug abuse [13, 62, 64], and enrichment has been reported to reduce impulsive choice [16, 17]. Exposure to novelty enrichment following heroin self-administration has been shown to reduce the enriched rats' cue-induced reinstatement of drug-seeking behavior [65]. Given that novelty enrichment alone *increased* impulsive choice behavior (i.e., lower self-control), this suggests the possibility of distinct mechanisms of choice behavior and those involved in drug-taking. Therefore, future research should examine whether novelty enrichment does indeed have distinct effects on impulsive choice and the effects on responses to psychomotor stimulants, which thereby has potential implications for interpreting the effects of enrichment on drug-taking behaviors.

The results also indicated that when social enrichment alone was present (SC– condition in Figure 1B), the greatest levels of LL choice (self-control) were observed. Interestingly, previous research dissociating the effects of social and novelty enrichment has suggested that novelty (physical) enrichment improves learning and memory, but that social enrichment only promotes these improvements if paired with novelty enrichment [see 34]. Accordingly, social housing and novelty stimulation appear to be distinct yet interacting mechanisms of enrichment. Future research may, for example, consider directly assessing the rats' interactions with novel objects in IC and SC rats to further explore this possibility.

The impulsive action task revealed a different pattern of results, in that social enrichment exerted the primary effects on DRL performance. Specifically, IC rats made more rewarded IRTs relative to SC rats (Figure 3B), suggesting that IC rats exhibited relatively lower levels of impulsive action. Previous research has reported that socially- and novelty-enriched rats were more impulsive (in terms of impulsive action) compared to socially-isolated rats [15,

but see 18], which is consistent with the current findings. While these past studies have confounded social and novelty enrichment, the results of the current experiment suggest that higher levels of impulsive action in environmentally-enriched rats may be driven primarily by exposure to social rather than novelty enrichment.

The independent effects of social and novelty enrichment on impulsive choice and impulsive action are not surprising given the proposed multidimensionality of impulsivity [e.g., 14]. Relatedly, while the present study did not reveal any correlation between impulsive action and the overall self-control index of the impulsive choice task (Figure 4C), there was a significant relationship between impulsive action and the delay sensitivity index of the impulsive choice task. Decisions between a 1-pellet reward in 10 s (SS) and a 1-pellet reward in 30 s (LL) should result in fewer LL choices, such that greater values of the delay sensitivity index indicate greater suboptimal (LL) choice behavior. We found that rats that were more willing to wait for the same amount of reward (SS = LL = 1 pellet) also exhibited longer IRTs. In other words, rats that acted seemingly more suboptimal in one task (impulsive choice) were more optimal in another (impulsive action). Interestingly, some have argued that, in certain contexts, such behavior in the impulsive choice task may actually be somewhat rational [see 66, 67]. In regards to the present results, greater willingness to choose a delayed reward (impulsive choice) or to wait long enough to respond to receive reward (impulsive action) may reflect greater delay tolerance [i.e., reduced delay aversion; 68], or alternatively a “choose-long” bias, such that more reward could be earned at a lower response cost over a longer estimated period of time. Accordingly, given the inherent involvement of interval timing in impulsive choice and impulsive action tasks [69], shared mechanisms of interval timing may ultimately account for such a seemingly counterintuitive relationship [70–72]. However, as impulsive choice tasks critically evaluate the tradeoff between reward delay *and* reward magnitude, it is likely that impulsive choice and impulsive action are at least partially under the control of different mechanisms [see 11, 13, 14], even though both may predict susceptibility to drug abuse [62]. Thus, the current enrichment paradigm may provide a unique avenue for understanding these different types of impulsivity given that social and novelty enrichment could be used to manipulate impulsive action and impulsive choice, respectively, thereby reducing subsequent addictive behaviors. By separately manipulating impulsive choice and impulsive action within the same general paradigm, as well as the individual components of such tasks (e.g., delay vs. magnitude), it may be possible to parse out the shared versus unique mechanisms of these different forms of impulsivity.

In contrast to the results of the impulsive choice and impulsive action tasks, there were no effects of social and/or novelty enrichment on overall behavioral flexibility performance (Figure 3A). Previous research has shown that socially-isolated rats show improved reversal learning relative to socially-housed rats in a water maze task [29], while other studies have reported set-shifting deficits in socially-isolated versus socially-housed rats [31, also see 32]. Interestingly, in the current experiment, SC rats exhibited more regressive errors and fewer never-reinforced errors compared to IC rats, suggesting that IC rats exhibited better retention of the new rule (i.e., reinforcement contingency) than SC rats in the response discrimination phase of the task. Additionally, novelty-enriched (+) rats exhibited fewer never-reinforced errors compared to non-novelty-enriched (–) rats, potentially suggesting that non-novelty-

enriched (–) rats exhibited greater exploration of possible reinforcement contingencies during the acquisition of the actual new rule. Given individual differences in types of errors made (Figure 2B), the discrepancies in previous research may be driven by subject-specific proneness to making particular errors, thus leading to elevated or impaired behavioral flexibility. Moreover, Schrijver and Würbel [31] used a radial maze apparatus and reared the socially-housed animals in groups of three in larger cages than the socially-isolated rats were housed, suggesting that the discrepancy between the current results and their results may be explained by differential husbandry conditions and/or paradigmatic factors in the measurement of behavioral flexibility. In the current experiment, both IC and SC rats were housed in identically-sized cages, SC rats were pair-housed, and a two-lever operant chamber was used in testing. These differences in rearing environment or task structure may involve different processes. Indeed, inactivation of the medial prefrontal cortex differentially affected set-shifting performance in maze-based and operant-based tasks in rats [see 21], suggesting that different tasks may tap into distinct underlying mechanisms. Accordingly, future research should continue to elucidate the specific factors that influence behavioral flexibility in differentially reared rats in different paradigms.

The analysis of individual differences revealed a correlation between behavioral flexibility and impulsive action (Figure 4A). Specifically, the rats that performed better in set-shifting, which involves inhibiting previous response tendencies, were also better at inhibiting responding in the impulsive action task. This suggests that there may be a common factor in executive processes elicited in these two tasks. However, enrichment did not interact with this individual-differences relationship suggesting that these individual differences were driven by separate factors from the enrichment effects [see also 16 for related evidence]. One possible candidate that may account for the individual differences in both tasks is general adaptability, which has been previously proposed as a broad coping style that affects a range of behaviors including impulse control/behavioral inhibition [see 73].

Similarly, analysis of individual differences revealed a correlation between behavioral flexibility and the delay sensitivity index of the impulsive choice task (Figure 4E). Here, higher adaptability in the behavioral flexibility task was correlated with higher delay sensitivity and therefore more suboptimal behavior in the impulsive choice task (i.e., greater values of the delay sensitivity index reflect more LL choices when an SS choice would have delivered the same number of pellets sooner). This relationship was significantly moderated by social enrichment, such that SC rats showed a relatively steeper relationship between these two indices (Figure 4F).

Thus, impulsive action, behavioral flexibility, and impulsive choice in terms of delay sensitivity were all interrelated. Overall, the impulsive action – impulsive choice (delay sensitivity) relationship may likely be explained by shared timing mechanisms (described above), and the impulsive action – behavioral flexibility relationship is likely explained by overlapping inhibitory/executive processing mechanisms. Accordingly, rats that were better “timers” (i.e., more “patient” timers) may exhibit relative improvements in executive processing, thereby producing the three-pronged relationship between impulsive choice, impulsive action, and behavioral flexibility. In addition, there was a general pattern in that individuals that were more suboptimal in one task were also more suboptimal in other tasks,

which could simply be due to more variance in their behavior. For example, the SC rats made more errors on the DRL and behavioral flexibility task, suggesting that social enrichment could lead to more errors in behavior. In other words, individual differences in trait behavioral optimality may ultimately account for such cross-task correlations [also see 71, 74].

While the present results shed some light on the potential discrepancies in the literature (described above), there still are some unanswered questions that may potentially be accounted for by specific aspects of the tasks employed [see 7]. In terms of impulsive choice, Hellemans, Nobrega [5] reported greater impulsivity in environmentally-enriched rats when the LL delay to sugar pellets increased within each session [see 75]. In contrast, Kirkpatrick, Marshall [16] reported reduced impulsivity in environmentally-enriched rats in an impulsive choice task in which LL magnitude (i.e., grain-based food pellets) increased across blocks of sessions. While both tasks have been assumed to measure “impulsive choice”, differential task structure may elicit differences in learning about the environments [e.g., relative reward rate, delay/magnitude contrast; see 76]. For example, adjusting delay procedures promote greater impulsivity, poorer learning of delays, and more random choices [76, 77], and any of these factors could interact with differential rearing effects on behavior. Future research should consider how task structure and differential rearing interact to produce a given behavior in various paradigms.

Alternatively, the previously reported empirical contradictions may reflect the structure of the housing conditions [see 7]. Here, the presence of a single novel object or conspecific differentiated impulsive behaviors in separate tasks (Figures 1B and 3). In the impulsive choice task, the effect of novelty enrichment was stronger for SC rats (Figure 1B). Relatedly, Brenes, Lackinger [34] reported stronger effects of novelty over social enrichment in rats when comparing pair-housed rats to rats housed six to a group. One explanation for this finding may be that increases in the levels of enrichment have nonlinear effects on behavior. For instance, there may be a stronger effect of social enrichment when enriching one rat with one conspecific (present study) compared to enriching two rats with four conspecifics. Enrichment may be a continuous factor, in that enrichment effects ultimately depend on the placement of and distance between various conditions along an “enrichment continuum” [see 78]. Given that the effects of social and novelty enrichment in the present study were obtained with one social companion and one novel object, future environmental enrichment research may be feasible without the use of large enrichment cages.

Lastly, the empirical inconsistencies amongst previous research may potentially be due to individuals’ sensitivity to social and novelty enrichment, such that “sensitivity to enrichment” is in fact a measurable individual difference variable itself [see 79, 80]. For example, in the impulsive choice task (Figure S1), IC– Rat 3 and IC+ Rat 3 exhibited relatively comparable behavior with good sensitivity to LL magnitude, while IC– Rat 5 showed poor sensitivity to LL magnitude. It is worth noting that one advantage of mixed effects models is that such individual differences can be accounted for in the model by including random effects. While the individual differences may be explained by differences in the specific mechanisms of choice behavior, they may also reflect differential sensitivities to enrichment. Even though such subjective effects of enrichment sensitivity could not be

analyzed in the present experiment, it is conceivable that some rats may be more or less susceptible to the effects of social and/or novelty enrichment than other rats and that some types of enrichment may be more effective for some rats than others. Thus, analyzing an individual difference variable of “sensitivity to enrichment” in future research may illuminate the psychological and neurobiological mechanisms of various behaviors (e.g., drug abuse, impulsivity).

Over the past several decades, the environmental enrichment literature has continued to provide considerable insight into the neurobiological and behavioral consequences of individuals’ early environmental experiences [e.g., 7, 9]. It is becoming clearer how the individual components of the enriched environment affect behavior. While there have been previous studies investigating the independence of differential enrichment techniques in rodents [34–37, 81, 82], this is the first experiment, to our knowledge, that has disentangled the effects of such enrichment techniques on individual differences in behaviors that were operationalized as measuring impulsive choice, impulsive action, and behavioral flexibility. Both novelty and social enrichment significantly differentiated impulsive choice while social enrichment alone did the same regarding impulsive action. These results and the accumulating evidence regarding enrichment effects are critical, as environmental enrichment seems to be a key deterrent of drug abuse [83]. Overall, a summary of the effects of differential enrichment techniques is not without its complexities and contradictions, but the continuation of such research will ultimately unveil the critical environmental elements that collectively shape an individual’s brain and behavior.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- The independent effects of social and novelty enrichment were investigated.
- Impulsive choice, impulsive action, and behavioral flexibility were analyzed.
- Novelty enrichment increased impulsive choice.
- Social enrichment decreased impulsive choice and increased impulsive action.
- Novelty and social enrichment produce distinct effects on behavior.

Figure 1.

A: Mean proportion of choices for the LL outcome as a function of LL magnitude for the different social- (IC, SC) and novelty-enrichment conditions (–, +). B: Mean overall proportion of choices for the LL outcome as a function of the rats' social- and novelty-enrichment conditions. Error bars ($\pm$ SEM) were computed with respect to the estimated marginal means of the fitted generalized linear mixed-effects model.

Figure 2.

A: Mean proportion of correct choices as a function of the rats' social-enrichment condition (IC, SC), novelty-enrichment condition (–, +), and phase of the behavioral flexibility task. Error bars (+/– SEM) were computed with respect to the estimated marginal means of the fitted generalized linear mixed-effects model. V = visual discrimination phase; R = response discrimination phase. B: Mean perseverative (PERS.), regressive (REG.), and never-reinforced (NR) errors as a function of the rats' enrichment conditions in the first session of the response discrimination phase of the behavioral flexibility task. Error bars (+/– SEM) were computed with respect to the estimated marginal means of the fitted generalized linear models.

Figure 3.

A: Probability of inter-response times (IRTs) as a function of the rats' social- (IC, SC) and novelty-enrichment conditions (–, +). The abscissa is on a log₁₀ scale. The gray shaded area indicates rewarded IRTs. B: Mean proportion of rewarded IRTs as a function of the rats' social- and novelty-enrichment conditions. Error bars (+/– SEM) were computed with respect to the estimated marginal means of the fitted generalized linear mixed-effects model.

Figure 4.

A: Mean proportion of rewarded inter-response times (IRTs) in the impulsive action task plotted against the behavioral flexibility index from the behavioral flexibility task. B: Mean proportion of choices for the larger-later (LL) outcome in the impulsive choice task when the LL choice delivered 2 or 3 pellets [i.e., overall self-control (SELF-CONT.) index] plotted against the behavioral flexibility index from the behavioral flexibility task. C: Mean proportion of choices for the LL outcome in the impulsive choice task when the LL choice delivered 2 or 3 pellets (i.e., overall self-control index) plotted against the mean proportion of rewarded IRTs in the impulsive action task. D: Mean proportion of choices for the LL outcome in the impulsive choice task when the LL choice delivered 1 pellet (i.e., delay sensitivity index) plotted against the mean proportion of rewarded IRTs in the impulsive action task. E: Mean proportion of choices for the LL outcome in the impulsive choice task when the LL choice delivered 1 pellet (i.e., delay sensitivity index) plotted against the behavioral flexibility index from the behavioral flexibility task. The dotted lines in Panels

A–E represent the best fitting overall regression line, and the variance accounted for by the best overall fit is shown (R^2). F: The same data as presented in Panel E but differentiated by social-enrichment condition. The solid and dash-dot lines in (E) represent simple linear fits to the SC and IC data, respectively.