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Food restriction level and reinforcement schedule differentially influence behavior during acquisition and devaluation procedures in mice.

Maxime Chevée[1#], Courtney J. Kim[1#], Nevin Crow[1], Emma G. Follman[1], Michael Z. Leonard[1], Erin S. Calipari[1,2,3,4,5]

[1] Department of Pharmacology, Vanderbilt University, Nashville, TN, USA
[2] Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN, USA
[3] Vanderbilt Center for Addiction Research, Vanderbilt University, Nashville, TN, USA
[4] Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville, TN, USA
[5] Department of Psychiatry and Behavioral Sciences, Vanderbilt University, Nashville, TN, USA

# Authors contributed equally to this work

***Corresponding Author**
Erin S. Calipari, PhD
Associate Director
Vanderbilt Center for Addiction Research

Associate Professor
Department of Pharmacology
Department of Molecular Physiology and Biophysics
Department of Psychiatry and Behavioral Sciences
Vanderbilt Brain Institute
Vanderbilt University
865F Light Hall
2215 Garland Avenue, Nashville, TN 37232
Phone: 615-343-5792
Email: erin.calipari@vanderbilt.edu

ABSTRACT

Behavioral strategies are often classified based on whether reinforcer value controls reinforcement. Value-sensitive behaviors, in which animals update their actions when reinforcer value is changed, are classified as goal-directed; conversely, value-insensitive actions, where behavior remains consistent when the reinforcer is removed or devalued, are considered habitual. Basic reinforcement principles can help to bias behavior toward either process: random ratio (RR) schedules are thought to promote the formation of goal-directed behaviors while random intervals (RI) promote habitual control. However, how the schedule-specific features of these tasks interact with other factors that influence learning to control behavior has not been well characterized. Using male and female mice, we asked how distinct food restriction levels, a strategy often used to increase task engagement, interact with RR and RI schedules to control performance during task acquisition and devaluation procedures. We determined that food restriction level has a stronger effect on the behavior of mice following RR schedules compared to RI schedules, and that it promotes a decrease in response rate during devaluation procedures that is best explained by the effects of extinction rather than devaluation. Surprisingly, food restriction accelerated the decrease in response rates observed following devaluation across sequential extinction sessions, but not within a single session. Our results support the idea that the relationships between schedules and control strategies are not clear-cut and suggest that an animal's engagement in a task must be accounted for, together with the structure of reinforcement schedules, to appropriately interpret the cognitive underpinnings of behavior.

SIGNIFICANCE STATEMENT:

Understanding the basic learning principles that control behavior is essential to developing therapies for psychiatric disorders such as addiction or obsessive-compulsive disorder. Reinforcement schedules are thought to control the reliance on habitual versus goal-directed control during adaptive behaviors. However, external factors that are independent of training schedules also influence behavior, for example, by modulating motivation or energy balance. In this study, we find that food restriction levels are at least equally important as reinforcement schedules in shaping behavioral output. Our results add to a growing body of work which supports the argument for a nuanced distinction between habitual and goal-directed behavior.

INTRODUCTION

Understanding how animals learn to control their actions is a fundamental goal of behavioral science. One useful framework classifies operant behaviors into two categories: those that are driven by the pursuit of a valuable goal and those that rely on value-insensitive processes (Graybiel, 2008; Smith & Graybiel, 2014). The assessment of these two types of behavior is done in operant conditioning tasks where behavior is maintained by the presentation of an appetitive reinforcer – typically sucrose or food. By devaluating the reinforcer prior to a probe test conducted under extinction conditions, either by providing *ad libitum* access to it or by pairing it with a negative consequence before the operant session, it is possible to determine whether a behavior is goal-directed: animals whose response rate drops following devaluation are considered to be implementing a goal-directed strategy while continued responding is evidence of a non-goal-directed strategy (often referred to as habitual) (Dickinson et al., 1983; Gremel & Costa, 2013; Killcross & Coutureau, 2003; Schreiner et al., 2020). Both the decreased value of the primary reinforcer and the degradation in action-outcome relationship experienced during the extinction sessions are thought to independently contribute to the decrease in response rate that reflects goal-directed control (Schreiner et al., 2020). Thus, this behavioral framework has guided a large amount of work focused on identifying the cognitive and neuronal processes distinguishing value sensitive and insensitive behaviors (Balleine & Dickinson, 1998; Graybiel & Grafton, 2015; Yin & Knowlton, 2006).

Two types of reinforcement schedules are known to engender different sensitivity to reinforcer devaluation, as assessed via extinction tests (Dickinson et al., 1983). In random ratio (RR) schedules, a reinforcer is delivered after a randomly selected number of responses is produced; this generates behavior that is goal-directed and sensitive to reinforcer devaluation procedures. Alternatively, random interval (RI) schedules allow access to a reinforcer after a randomly selected amount of time has elapsed. While interval schedules still require an operant

response, responses are only reinforced following an elapsed period (Ferster & Skinner, 1957). These schedules often generate behavior over time that is insensitive to changes in the reinforcer and thus more resistant to extinction, when the reinforcer in omitted entirely (Dickinson et al., 1983). Although this dichotomy is a useful framework to study these types of behaviors, it has been challenged by experimental observations (Schreiner et al., 2020). For example, there is conflicting evidence regarding whether extended training on RR schedules becomes devaluation-insensitive over time (Adams, 1982; Adams & Dickinson, 1981; Dickinson, 1985; Miyachi et al., 1997) or remains goal-directed (Colwill & Rescorla, 1985, 1988; Colwill & Triola, 2002; Garr et al., 2021) and specific manipulations of the intervals used in RI schedules have been shown to produce behaviors that remain sensitive to reinforcer devaluation (Garr et al., 2020). Furthermore, the devaluation procedures used to evaluate whether animals are sensitive to the value of the reinforcer can suffer from the influence of extinction: during the probe extinction sessions that follow reinforcer/control devaluation, animals experience a degradation of the contingency between action and outcome that likely affects behavior (Delamater & Westbrook, 2014; Schreiner et al., 2020). Thus, while both devaluation and extinction affect value-dependent features of learning, the exact procedure implemented to perform devaluation tests may change the balance between the effects of devaluation and extinction on response rates.

While reinforcement schedule has a clear influence on operant behavior and sensitivity to devaluation procedures, schedule-independent factors – such as food restriction or stress – can also have effects on behavior that likely differ depending on the schedule under which the behavior occurs. For example, the same dose of systemic pentobarbital can increase or decrease the rate of food reinforcement depending on whether food delivery was reinforced under a ratio or interval schedule, respectively (Dews, 1955, 1956). In the behaviors discussed above - which are maintained by caloric foods - one particularly important factor is the food

127 restriction state of the animal. Indeed, food intake is often restricted to increase response rates
128 in operant tasks. While varying food restriction levels affects response rates and response
129 patterns under certain conditions (Blakely & Schlinger, 1988; Lowe et al., 1974; Powell, 1969;
130 Schlinger et al., 1990; Sidman & Stebbins, 1954), the effects of this common manipulation on
131 RR compared to RI schedules, and on the subsequent sensitivity to devaluation procedures, are
132 not known. Because RR schedules permit animals to control their own rate of reinforcement,
133 while RI schedules necessarily constrain reinforcement rates to those allowed by the interval,
134 we hypothesize that food restriction levels influence performance on RR schedules more
135 strongly than performance on RI schedules and contribute to sensitivity to outcome devaluation
136 procedures independently of schedule.
137
138 To explore this idea, we restricted the daily food intake of mice to various degrees and
139 trained them on either RR or RI schedules for which we adjusted the number of responses
140 required in RR schedules to match the actions-per-outcome mice of each restriction group
141 achieved on an RI schedule. This strategy allowed us to mitigate the effect of differences in
142 reinforcement efficiency and to compare the effects of food deprivation levels on performance
143 during acquisition and devaluation procedures across RI and RR schedules. We found that
144 deprivation had a combinatorial effect on operant behavior: increased food restriction was more
145 effective at increasing response rates under RR compared to RI schedules. Furthermore,
146 devaluation tests showed that the order of session, rather than the type of pre-feeding, drove
147 the decrease in response rates we observed during extinction tests. This decrease was different
148 across food restriction groups such that more restricted animals extinguished their responses
149 more strongly than mildly restricted animals but was unaffected by the training schedule.
150 Surprisingly, this difference only manifested across consecutive extinction sessions but was not
151 apparent within a single session.
152

Together, our results suggest that external factors such as food restriction level must indeed be accounted for, together with the structure of reinforcement schedules, to appropriately interpret the cognitive underpinnings of behavior.

MATERIALS AND METHODS

Subjects

Experiments were approved by the Institutional Animal Care and Use Committee of Vanderbilt University Medical Center and conducted according to the National Institutes of Health guidelines for animal care and use. Eighty-seven 8-week-old animals were used for this study. C57BL/6J mice (43 males and 44 females) were acquired from Jackson Laboratory (Bar Harbor, ME; SN: 000,664) and maintained on an 8am/8pm 12-h reverse light cycle. Experiments were performed during the dark phase. Animals were single housed for the duration of the study with unlimited access to water.

The experiments were performed in five separate rounds using different mice each time.

1) 20 mice (10 females, 10 males) were mildly food restricted (3g/day) for one week. They were then trained on FR1 until acquisition criteria were met (see **Procedure** below) and assigned to a RR10/RR20 schedule or RI30/RI60 schedule such that time to acquisition and sex were balanced across the two groups. This training session resulted in N = 5 females, 5 males performing an RR10/RR20 task under “Mild Restriction” conditions and N = 4 females, 5 males performing an RI30/RI60 task under “Mild Restriction” conditions (one female failed to acquire FR1 for 10 consecutive days).

2) 20 mice (10 females, 10 males) were mildly food restricted (3g/day) for one week. They were then trained on FR1 until acquisition criteria were met (see **Procedure** below) and

assigned to either a “No Restriction” group, which had unlimited access to food, or to a “Strong Restriction” group which received 2g chow per day, such that time to acquisition and sex were balanced across the two groups. All animals went on to perform an RI30/RI60 task. This training session resulted in N = 5 females, 5 males performing an RI30/RI60 task under “No Restriction” conditions and N = 5 females, 5 males performing an RI30/RI60 task under “Strong Restriction” conditions.

3) 20 mice (10 females, 10 males) were mildly food restricted (3g/day) for one week. They were then trained on FR1 until acquisition criteria were met (see **Procedure** below) and assigned to either a “No Restriction” group, which had unlimited access to food, or to a “Strong Restriction” group which received 2g chow per day, such that time to acquisition and sex were balanced across the two groups. Mice assigned to the “No Restriction” group then followed an RR2.8/RR3.4 schedule (ratios matched to the performance of the “No Restriction” group on RI30/RI60) and mice assigned to the “Strong Restriction” group followed an RR5.1/RR9.3 schedule (ratios matched to the performance of the “Strong Restriction” group on RI30/RI60). This training session resulted in N = 4 females, 5 males performing an RR2.8/RR3.4 task under “No Restriction” conditions (one female failed to acquire FR1 for 10 consecutive days) and N = 3 females, 5 males performing an RR5.1/RR9.3 task under “Strong Restriction” conditions (one female was a statistical outlier and one female was erroneously given unlimited access to food in the middle of the experiment and removed from the cohort).

4) 10 mice (5 females, 5 males) were mildly food restricted (3g/day) for one week. They were then trained on FR1 until acquisition criteria were met (see **Procedure** below) and then followed a RR3.4/RR5.2 schedule (ratios matched to the performance of the “Mild Restriction” group on RI30/RI60). This training session resulted in N = 5 females, 5 males performing an RR3.4/RR5.2 task under “Mild Restriction” conditions.

5) 17 mice (8 males, 9 females) were trained to increase sample sizes of all groups and perform additional control experiments (Post devaluation preference tests). Mice were mildly

food restricted (3g/day) for one week and trained on FR1 until acquisition criteria were met. They were then split such that time to acquisition and sex were balanced across groups as follows: 5 mice (3 males, 2 females) were mildly food restricted (3g/day) and trained on RI30/RI60; 4 mice (1 male, 3 females) were strongly food restricted (2g/day) and trained on RI30/RI60; 5 mice (2 males, 3 females) were mildly food restricted (3g/day) and trained on RR3.4/RR5.2; 2 mice (1 male, 1 female) were strongly food restricted (2g/day) and trained on RR5.1/RR9.3. One mouse did not acquire FR1 within 10 days. This additional cohort underwent post devaluation preference tests to confirm the efficacy of the devaluation procedure.

The number of animals included in each analysis is specified in the figure legends.

Apparatus

Mice were trained and tested daily in individual standard-wide mouse operant conditioning chambers (Med Associates Inc., St. Albans, Vermont) outfitted with a retractable lever. A 3D-printed divider was inserted in each chamber, limiting the available space to a small square area providing access to a sucrose port and a lever (area: 13 × 13 = 169 cm^2). A custom-made 3D-printed wall insert was used to hold and display a stainless-steel cannula (lick port, 18 gauge, 0.042'' ID, 0.05'' OD, 0.004''wall thickness), which was connected to a syringe pump for sucrose delivery. An illumination light was affixed above the lick port.

Procedure

General Procedural Information: All sessions lasted until the maximum number of rewards was obtained (51) or 1 hour was reached, whichever came first. White noise signaled the beginning of the session and was on for the entire duration of the session. All animals but a subset of the RI_MildRestriction group (N=9) were weighed before each session.

Task Design: Mice were first trained on a fixed ratio 1 (FR1) schedule of reinforcement. Each lever press resulted in the delivery of 8 µl of a 10% sucrose solution. Additional presses performed after sucrose delivery but before sucrose collection had no programmed consequence and did not count toward obtaining the next reinforcer. Once the reinforcer was collected, lever presses counted again. Mice were considered to have met the acquisition criteria once they had obtained 51 rewards within the allotted 1 h for two consecutive days. Upon meeting the criteria, mice were assigned to different tasks (see *Subjects* above) such that time to acquisition and sex were balanced across groups.

Random Interval (RI) training: RI schedules consisted of three days operating under an RI30 schedule, in which a lever press resulted in sucrose delivery only after an interval of time averaging 30 seconds (range: 0 to 125 seconds, generated according to $f(x) = (\frac{1}{\mu})e^{-\frac{x}{\mu}}$, where µ=30) had passed since consuming the last reinforcer, followed by four days operating under an RI60 schedule (range: 0 to 208 seconds).These intervals were determined in keeping with previous studies, which suggested that this training procedure produces habitual actions (Gremel & Costa, 2013; Hilario et al., 2007).

Random Ratio (RR) training: For the cohort reported in Figure 1, the RR schedules consisted of three days operating under an RR10 schedule, in which a lever press resulted in sucrose delivery only after a specific amount of responses (10 on average, range: 0 to 44, generated according to $f(x) = (\frac{1}{\mu})e^{-\frac{x}{\mu}}$, where µ=10) had been performed, followed by four days operating under an RR20 schedule (20 on average, range: 0 to 73). For the three cohorts with distinct food restriction levels, the ratios were calculated to match the responses-per-reinforcer ratio of their counterparts who

performed the RI task and are detailed in the Result section (**Figure 2B,C**) as well as in *Subject* above. No-Restriction RR2.8 (range: 0 to 11), RR3.4 (range: 0 to 14); Mild-Restriction RR3.4 (range: 0 to 14), RR5.1 (range: 0 to 19); Strong-Restriction RR5.2 (range: 0 to 21), RR9.3 (range: 0 to 45).

Outcome devaluation tests: Upon completing the seven days of RI or RR training, each mouse underwent an outcome devaluation test. This procedure consists of providing access to the reinforcer (10% sucrose, devalued condition) or to another familiar food source that was not used as a reinforcer (chow, valued condition) *ad libitum* for one hour prior to a 10 minute extinction session, in which the lever presses have no programmed consequences and do not result in reinforcer delivery. Within each cohort, half the mice were assigned to perform this test "Day1: valued, Day2: devalued" or "Day1: devalued, Day2: valued". Mice which consumed less than 0.2g during either pre-feeding sessions were excluded from the analysis of outcome devaluation tests, as well as one RR-StrongRestriction animal whose response rate during the extinction session was a statistical outlier (z=3.6), resulting in a dataset of N=41 mice included in these analyses (RI-MildRestrcition N=8, RI-StrongRestriction N=14, RR-MildRestriction N=10, ,RR-StrongRestriction N=9). A devaluation index was calculated for each mouse ($\frac{Rvalued}{Rvalued+Rdevalued}$, where R_{valued} is the response rate during the valued extinction session and $R_{devalued}$ is the response rate during the devalued extinction session), such that an index close to 1 indicates sensitivity to outcome devaluation (ie. goal-directed control). Similarly, the extinction index was defined as ($\frac{R2nd}{R1st+R2nd}$, where R_{1st} is the response rate during the first extinction session and R_{2nd} is the response rate during the second extinction session) for across sessions (**Figure 4**) and as ($\frac{R2nd}{R1st+R2nd}$, where R_{1st} is the response rate during the first minute of the first extinction session and R_{2nd} is the response rate during the second minute of the first extinction session) for within session analyses (**Figure 5**).

Post devaluation preference test: A subset of mice (N=16, 5th cohort described in *Subjects* above) underwent an additional test to validate the effectiveness of the devaluation procedure. Following each extinction session, mice were given free access to both sucrose and chow for 10 minutes. The amounts consumed were measured and a preference index was used to determine whether mice preferred to consume what they had not had access to during the devaluation period preceding the extinction test. The preference index following sucrose devaluation was defined as:

$$\frac{S_S}{S_S + S_C} - \frac{C_S}{C_S + C_C}$$

S_S = sucrose consumed during preference test following sucrose devaluation.

S_C = sucrose consumed during preference test following chow devaluation.

C_S = chow consumed during preference test following sucrose devaluation.

C_C = chow consumed during preference test following chow devaluation.

Thus, an index close to 1 indicates preference for sucrose and an index close to -1 indicates preference for chow.

Analysis

Statistical Analyses: All analyses were performed using custom code in Python (v3.6.13). The SciPy package (v1.5.3) was used to perform independent Student's t tests (**Figures 1B-D**) and the Pingouin package (v0.3.12) was used to perform two-way and three-way ANOVAs as well as the corresponding post-hoc Tukey tests (**Figures 2E, 2-1A, 2-1B, 3B-C, 3-1B, 3-1D, 4C, 4E, 4-1A-C, 5B-D**). All data are reported as Mean ± SEM and all statistical tests used are specified in the Results section or in figure legends as well as in the statistical table (**Table 1**).

RESULTS

RI and RR schedules in mice can produce different response rates and different responses-per-reinforcer ratios.

The stronger relationship between action and outcome in RR schedules compared to RI schedules is often cited as the primary reason for differences in sensitivity to outcome devaluation (Dickinson, 1985; Pérez et al., 2019; although see Garr et al., 2020). Mice on RR can increase their reinforcer rate by increasing their response rate while the rate of reinforcer delivery on RI schedules does not correlate with response rate (**Figure 1A**). Therefore, an animal's response rate can result in distinct responses-per-reinforcer ratios that are dependent on schedule. To illustrate this phenomenon, we compared food-restricted mice trained on RI and RR schedules using commonly used ratios/intervals (Gremel & Costa, 2013; Hilario et al., 2007). First, we restricted the mice's daily food intake to 3g per day to increase their engagement in the task and trained them to respond for sucrose under a Fixed-Ratio 1 (FR1) schedule of reinforcement. Upon acquisition of FR1, mice went on to a two-phase schedule comprised of either 1.) three days of RI30 followed by four days of RI60 or 2.) three days of RR10 followed by four days of RR20. When reinforcer delivery rate (**Figure 1B**, RI: 0.67±0.02 reinforcers/minute, N=9; RR: 0.12±0.02 reinforcers/minute, N=10) and response rate were assessed (**Figure 1C**, RI: 3.43±0.13 responses/minute, N=9; RR: 2.19±0.30 responses/minute, N=10), we found that during phase 2 the RI group had both a faster reinforcer delivery rate (independent Student's t test p=5.3e-14) and a faster response rate (independent Student's t test p=0.0021) compared to the RR group. This result indicates that, under these food restriction conditions, an RI30/RI60 training schedule is more effective than a RR10/RR20 schedule at increasing reinforcer and response rates.

Interestingly, the response-per-reinforcer ratio was much larger for the RR group than for the RI group during both phases of training (**Figure 1D**, Phase 1 - RI: 3.33±0.21, N=9; RR: 12.3±0.45, N=10, Welch's t test p=2.2e-10; Phase 2 - RI: 5.11±0.12, N=9; RR: 24.8±3.19, N=10, Welch's t test p=1.6e-4). In other words, reinforcer rates between RR and RI schedules were not comparable (they would only have been comparable at 20 responses/min, **Figure 1A** - dotted line). Thus, the differences in behavior following training under RI vs RR tasks are confounded with differences in response rates, which themselves are determined by reinforcement rate. We next set out to test whether the reinforcement rate or the schedule contingency better predicted operant performance and sensitivity to devaluation procedures.

Designing RR schedules to match the responses-per-reinforcer ratios observed in mice following RI30/RI60 schedules under distinct levels of food restriction.

To determine whether differences in response rates rather than differences in schedule contingencies best explain operant performance and sensitivity to reinforcer devaluation procedures, we first had to tailor RR schedules to produce a similar relationship between response rate and reinforcer delivery (responses-per-reinforcer) compared to RI schedules. To this end, mice were first mildly food restricted (3g/day) and trained on a FR1 lever pressing task until acquisition criteria were met (see Material and Methods, **Figure 2-1A**) and subsequently split into three groups which followed RI30/RI60 schedules under different food restriction conditions (No Restriction, Mild Restriction, Strong Restriction, **Figure 2A**). Animals had either unlimited access to food in their home cage (No Restriction), received 3g of chow per day (Mild Restriction) or received only 2g of chow per day (Strong Restriction, **Figure 2-1B**). For each group and each phase of training, we determined the mean response rate as well as the mean reinforcer delivery rate and computed the RR schedule at which the responses-per-reinforcer ratio would match that of the RI schedule given the observed response rates (defined as response rate / reinforcer delivery rate - **Figure 2B,C**).

We then trained three groups on the identified RI-matched RR schedules for each food restriction condition (**Figure 2D**) and compared the responses-per-reinforcer ratios during each phase of training to validate our strategy. During phase 1, a two-way ANOVA revealed that there was a main effect of restriction group but not of task schedule (RI_NoRestriction: 2.74±0.19, N=10; RR_NoRestriction: 3.61±0.06, N=9; RI_MildRestriction: 4.08±0.32, N=14; RR_MildRestriction: 3.98±0.03, N=15; RI_StrongRestriction: 5.34±0.36, N=14; RR_StrongRestriction: 5.80±0.05, N=10; two-way ANOVA, effect of task: df=1, F=3.02, p=0.087; effect of restriction: df=2, F=47.4, p= 1.70e-13). Post hoc comparisons confirmed there were no significant differences between each pair of restriction-matched RI-RR group (RI_NoRestriction-versus-RR_NoRestriction Tukey HSD p-adjusted=0.22; RI_MildRestriction-versus-RR_mildRestriction Tukey HSD p-adjuted=1.0; RI_StrongRestriction-versus-RR_StrongRestriction Tukey HSD p-adjusted=0.76). Results during phase two were similar (RI_NoRestriction: 3.25±0.25, N=10; RR_NoRestriction: 4.18±0.11, N=9; RI_MildRestriction: 6.19±0.49, N=14; RR_MildRestriction: 6.06±0.21, N=15; RI_StrongRestriction: 9.33±0.39, N=14; RR_StrongRestriction: 9.98±0.08, N=10; two-way ANOVA, effect of task: df=1, F=2.23, p=0.14; effect of restriction: df=2, F=145, p=6.65e-25) and post hoc tests again confirmed no differences between each pair of restriction-matched RI-RR group (RI_NoRestriction-versus-RR_NoRestriction Tukey HSD p-adjusted=0.50; RI_MildRestriction-versus-RR_mildRestriction Tukey HSD p-adjusted=1.0; RI_StrongRestriction-versus-RR_StrongRestriction Tukey HSD p-adjusted=0.75). Thus, our training strategy successfully produced three pairs of RI-RR groups with distinct levels of food restrictions and matched responses-per-reinforcer ratios, allowing us to compare the effects of restriction and task schedule on behavior and outcome devaluation.

Food restriction increases response rates more effectively in mice following RR schedules than in mice following RI schedules.

We first analyzed differences in performance (**Figure 3A**) by testing how food restriction and task schedule influenced response rates by the end of training (**Figure 3B**, RI_NoRestriction: 1.43±0.19 responses/minute, N=10; RR_NoRestriction: 1.66±0.29 responses/minute, N=9; RI_MildRestriction: 4.48±0.67 responses/minute, N=14; RR_MildRestriction: 7.15±1.19 responses/minute, N=15; RI_StrongRestriction: 9.17±0.37 responses/minute, N=14; RR_StrongRestriction: 16.3±2.41 responses/minute, N=10) and found that both restriction and task schedule had a main effect on response rate (two-way ANOVA, effect of task: df=1, F=15.2, p=2.3e-4; effect of restriction: df=2, F=45.6, p=3.6e-13). The interaction term was also significant (two-way ANOVA, interaction between task and restriction df=2, F=4.64, p=0.013), suggesting restriction and task schedule interacted to influence operant behavior. These effects were similar when we analyzed reinforcer delivery rates (**Figure 3-1A,B**). To further test whether restriction and schedule combined to influence task acquisition, we repeated this analysis using the fold change in response rate between the last and first session of training post FR1 acquisition (**Figure 3C**, RI_NoRestriction: 0.64±0.12 responses/minute, N=10; RR_NoRestriction: 0.53±0.11 responses/minute, N=9; RI_MildRestriction: 0.90±0.11 responses/minute, N=14; RR_MildRestriction: 1.25±0.19 responses/minute, N=15; RI_StrongRestriction: 1.45±0.13 responses/minute, N=14; RR_StrongRestriction: 3.19±0.79 responses/minute, N=10). Like final response rates, the fold change in response rates was influenced by the interaction between food restriction level and task schedule (two-way ANOVA, effect of task: df=1, F=8.29, p=6.9e-3; effect of restriction: df=2, F=15.7, p=5.0e-6, interaction: df=2, F=4.83, p=0.011).

Next, we asked whether schedule and restriction differentially affected response variability. We analyzed the inter-response interval coefficients of variation (defined as standard deviation / mean) across restriction groups and schedules and found that while RI animals respond with more regular intervals, stronger food restriction also promoted low variability

(**Figure 3-1C,D**, RI_NoRestriction: 1.03±0.09, N=10; RR_NoRestriction: 1.24±0.06, N=9; RI_MildRestriction: 0.59±0.11, N=14; RR_MildRestriction: 0.83±0.10, N=15; RI_StrongRestriction: 0.35±0.04, N=14; RR_StrongRestriction: 0.61±0.0, N=10; two-way ANOVA, effect of task: df=1, F=11.1, p=1.4e-3). Unlike for response rate, there was clearly no interaction between schedule and restriction (effect of restriction: df=2, F=26.2, p=4.3e-9, interaction: df=2, F=0.026, p=0.97).

We draw three conclusions from these results. First, they show that when the responses-per-reinforcer ratios are matched, mice trained on RI schedules do not achieve a higher response rate than their counterparts trained on RR schedules under any circumstances. Second, both food restriction and task schedule independently influenced reinforcer delivery rate and response rate, with more restricted mice and mice on RR schedules achieving higher rates than less restricted mice and mice on RI schedules, respectively. Response rate variability was also independently influenced by each factor such that RI schedules and strong restriction promoted lower variability compared to RR schedules and mild restriction, respectively. Third, there was a clear combinatorial effect of restriction and task schedule: food restriction increased reinforcer delivery rates and response rates more effectively in mice following RR schedules than in mice following RI schedules, but they did not interact to affect response rate variability.

The effects of extinction dominate the behavioral read-out during devaluation tests and are sensitive to food restriction but not to schedule of reinforcement.

After completing the seven days of RI or RR training, all mice underwent sequential outcome devaluation sessions. Animals were first pre-fed the reinforcer (devalued condition) or chow (control, valued condition) and subsequently tested in a 10min extinction session in which responses have no programmed consequences. On the following day, each mouse underwent the same test with the pre-feed it did not receive on the first day (see methods for more details).

Thus, both sensory-specific satiety and degradation of the action-outcome relationship experienced during the extinction session have the potential to influence response rates. To establish the effectiveness of the devaluation procedure, a subset of mice further performed a preference test following each extinction session during which it had access to both the sucrose reinforcer and chow (**Figure 4A** and **Figure 4-1**). Mice who had *Ad lib* access to food were not included in this analysis because they responded with rates too low to detect a decrease. The raw results of each session for each mouse are depicted in **Figure 4B** and a three-way ANOVA was performed on the devaluation index derived from these data (**Figure 4C** left, RI_MildRestriction_1st: 0.52±0.07, N=4; RI_MildRestriction_2nd: 0.44±0.05, N=4; RR_MildRestriction_1st: 0.48±0.06, N=5; RR_MildRestriction_2nd: 0.39±0.04, N=5; RI_StrongRestriction_1st: 0.66±0.03, N=8; RI_StrongRestriction_2nd: 0.32±0.04, N=6; RR_StrongRestriction_1st: 0.58±0.04, N=5; RR_StrongRestriction_2nd: 0.34±0.10, N=4) to identify the effects of task schedule, food restriction and session order on outcome devaluation. We found that only session order had a significant main effect on the devaluation index (three-way ANOVA, main effect of order df=1, F=32.1, p=3.0e-6) while task schedule and restriction level had no effect (three-way ANOVA, main effect of schedule df=1, F=1.18, p=0.28; main effect of restriction df=1, F=0.42, p=0.52). To illustrate this result, we plotted the means for groups collapsed by task schedule, restriction and session order (**Figure 4C** right). In addition, there was a significant interaction between restriction and session order (df=1, F=7.7, p=9.1e-3). Taken together, these results show that when performing a devaluation test with sequential extinction sessions, the observed decrease in response rates largely reflects the effects of the degraded action-outcome relationship experienced by animals during the extinction sessions.

Because our analysis of devaluation indices revealed an interaction between session order and restriction in addition to the clear effect of order, we sought to determine how food restriction affected extinction across the two sessions (**Figure 4D**). Similar to the devaluation

index, we computed an extinction index and asked whether it was influenced by food restriction or task schedule (**Figure 4E left**, RI_MildRestriction: 0.46±0.04, N=8; RR_MildRestriction: 0.46±0.04, N=10; RI_StrongRestriction: 0.33±0.03, N=14; RR_StrongRestriction: 0.38±0.05, N=9). A two-way ANOVA revealed that only food restriction, but not schedule, influenced the magnitude of the decrease in response rate from the first extinction session to the second extinction session (two-way ANOVA, main effect of schedule df=1, F=0.54, p=0.47; main effect of restriction df=1, F=7.1, p=0.011; interaction: df=1, F=0.41, p=0.53). To illustrate this result, we plotted the means for groups collapsed by task schedule and restriction (**Figure 4E** right). Thus, our results suggest that the observed decreases in response rates during sequential devaluation sessions largely reflect the effects of extinction and are sensitive to the food restriction state of the animal but not to the schedule used to reinforce behavior before the test.

The effects of restriction are only apparent across days and not within an extinction session.

Our results suggest that food restriction influences how rapidly animals decrease their response rates upon experiencing a degradation of the action-outcome relationship underlying extinction sessions. To further explore this possibility, we plotted the response rates during the first extinction session across time (10 one-minute bins, **Figure 5A**). When we compared the response rates during the first minute (**Figure 5B**, RI-MildRestriction: 6.25±1.0, N=8; RR-MildRestriction: 7.80±1.55, N=10; RI-StrongRestriction: 12.5±2.1, N=14; RR-StrongRestriction: 22.6±4.3, N=9), we found that both restriction and schedule had an effect on response rates (two-way ANOVA main effect of restriction group df=1, F=16.3, p=2.6e-4; main effect of schedule df=1, F=5.99, p=0.019), as would be predicted from the responses during training (**Figure 3**). The interaction between schedule and restriction was not significant (df=1, F=2.7, p=0.11), which would also be expected in the absence of reinforcement. However, when we repeated this analysis using an extinction index capturing the change in response rate from the

first to second minute within the session (**Figure 5C,** RI-MildRestriction: 0.38±0.04, N=8; RR-MildRestriction: 0.41±0.07, N=10; RI-StrongRestriction: 0.36±0.04, N=14; RR-StrongRestriction: 0.38±0.04, N=9), we found that neither restriction group nor schedule had a significant influence (two-way ANOVA main effect of restriction group df=1, F=0.21, p=0.65; main effect of schedule df=1, F=0.26, p=0.61; interaction df=1,F=0.0087, p=0.93). This result was confirmed when we plotted the number of responses each animal produced before its inter-response interval surpassed 2 standard deviations above the mean of a rolling window of length five responses – a measure capturing the number of actions it took for mice to slow down their responses – as again neither restriction nor schedule showed a significant effect (**Figure 5D**, RI-MildRestriction: 8.5±1.31, N=8; RR-MildRestriction: 8.8±1.0, N=10; RI-StrongRestriction: 9.0±0.75, N=14; RR-StrongRestriction: 9.11±0.82, N=9; two-way ANOVA main effect of restriction group df=1, F=0.18, p=0.68; main effect of schedule df=1, F=0.041, p=0.84; interaction df=1, F=0.0095, p=0.92). These results show that while food restriction influenced extinction across days, it had no impact on the decrease in response rates observed during a single session.

DISCUSSION

Our results show that the levels of food restriction under which animals learn and operate affect their performance differently based on schedule of reinforcement. Indeed, food restriction increased response rates and reinforcer delivery rates more strongly in mice following RR schedules compared to mice following RI schedules. In parallel, animals were rendered more sensitive to extinction experienced during devaluation procedures by increasing levels of food restriction. Thus, task schedule fundamentally interacted with food restriction level to shape behavioral output during task acquisition, yet it showed little effect on behavior during extinction compared to food restriction level. Overall, our results show that schedule of reinforcement must be considered in combination with other factors that may influence motivation when attempting to identify the cognitive basis underlying operant behaviors.

Our results are consistent with previous studies showing that when reinforcer delivery rate is matched, animals following RR schedules generally achieve higher response rates than those following RI schedules – and this effect appears consistent across species (rats: Dawson & Dickinson, 1990; pigeons: Catania et al., 1977; Peele et al., 1984; Zuriff, 1970; humans: McDowell & Wixted, 1986; Pérez et al., 2019; Wit et al., 2018). Consistent with the idea that RR schedules, by virtue of their strong action-outcome correlation (Dickinson, 1985; Ferster & Skinner, 1957; Pérez et al., 2019 although see Garr et al., 2020), allow for factors like motivation to influence response rates, we found that response rates were more sensitive to food restriction level in mice trained on RR schedules compared to RI schedules. However, whether the effects of food restriction and schedule of reinforcement interact differently across species is less clear. For example, previous work has shown that while training schedule has little effect on motivation in mice (Johnson et al., 2022), food restriction does impact measures of motivation in both rats (Dietze et al., 2016; Malikovic et al., 2018) and mice (Mifune et al., 2020). The effects of schedule specific features, such as the preferential reinforcement of long inter-response times (IRT) in RI schedules (Krame & Rilling, 1970; Kuch & Platt, 1976) or task parameters more generally (Follman et al., 2022), may also influence behavior in distinct species differently. By manipulating food restriction levels, our findings provide further support to the notion that the ability to control one's own reinforcement rate explains the difference in response rates generated by RR and RI schedules in mice.

Several studies have explored the effects of changes in reinforcer value or in food restriction levels on performance (Balleine, 1992; Blakely & Schlinger, 1988; Lowe et al., 1974; Parkes et al., 2017; Powell, 1969; Schlinger et al., 1990; Sidman & Stebbins, 1954). However, these studies were largely focused on evaluating the effects of acute changes in value or in feeding schedule rather than understanding the systematic relationship between food restriction

and reinforcement structure. Nevertheless, changes in reinforcer value have been shown to have a stronger effect on actions temporally close to the reinforcer delivery compared to those further away (Dickinson & Balleine, 1995; Holland & Rescorla, 1975). Our findings support this idea because they suggest that tasks that promote a high response rate, either via food restriction or via richer schedules, are more likely to appear sensitive to value. This is also supported by the observation that leaner RI schedules are more likely to produce devaluation-insensitive behaviors (Garr et al., 2020) and that as long as animals continue to perform and remain in control of their own reinforcement rate, they remain goal-directed even for long periods of time (Colwill & Rescorla, 1985, 1988; Colwill & Triola, 2002; Corbit et al., 2012; Garr et al., 2021). We also found that stronger food restriction, together with RI schedules of reinforcement, promoted less variable response rates, however it is not clear whether these effects are related. Indeed, strong food restriction may increase task engagement and thus continued responding, while RI schedule may promote stable response rates by maintaining relatively high uncertainty as to whether a response will produce a reinforcer. Overall, our findings support the idea that schedule-dependent and -independent factors interact to influence behavior and that studies must carefully match reinforcement rates, intrinsic reinforcer value and exposure to action-outcome contingencies when using response rates as a measure of operant behavior.

The results from our devaluation experiments reveal several insights. First, a limitation of our study is that we used chow as both regular food and as the control during devaluation procedures. Thus, we cannot completely rule out that pre-feeding on sucrose versus chow did not influence the animals' motivation and engagement differently. Nonetheless, our results do not support a scenario in which more strongly restricted animals experienced a larger decrease in motivation following pre-feeding as all groups showed similar drops in their response rate within the first extinction session (**Figure 5**). Instead, our results suggest that food restriction

affected the ability of animals to remember the degraded action-outcome relationship experienced in extinction session 1 the following day (**Figure 4D,E**). This effect supports a role for energy homeostasis in memory consolidation that has been observed in other learning contexts (Diano et al., 2006; Verma et al., 2016) but is rarely considered in operant conditioning. Second, we performed the devaluation procedures sequentially, without re-training between days. While this approach is commonly used (Hadjas et al., 2019; Parkes et al., 2017; Renteria et al., 2018), we show here that under these circumstances, the testing order dominates the observed decreases in response rate (**Figure 4B,C**) – not the valued versus devalued state of the animal – despite the confirmation that devaluation procedures selectively reduced the value of the pre-fed food (**Figure 4-1**). This result is a clear indication that counter-balancing the order in which reinforcer and control food are devalued is essential when attempting to determine sensitivity to value. Shorter probe tests and retraining between extinction sessions can also reduce the effects of extinction. While devaluation and extinction likely independently contribute to behavior, as revealed when training and extinction are performed in different contexts (Thrailkill & Bouton, 2015) or when multiple levers with distinct contingencies to reward are available (Dickinson et al., 1998), our results show that the interplay between these two factors must be carefully accounted for when interpreting devaluation procedures.

Finally, our results add to the growing evidence against a clear-cut relationship between schedule and cognitive basis of behavior, in which RR training produces goal-directed actions and RI training produces habitual actions (Colwill & Rescorla, 1990; Dezfouli & Balleine, 2012; Garr & Delamater, 2019; Schreiner et al., 2020; Wit et al., 2018). While the two schedules produce inherently distinct features such as reinforcement uncertainty (de Russo et al., 2010), the temporal distribution of reinforcers and of responses (Adams, 1982; Doughty & Lattal, 2003; Urcelay & Jonkman, 2019), the correlation between action and outcome or the preferential reinforcement of long IRTs (Krame & Rilling, 1970; Kuch & Platt, 1976), that all likely contribute

to differences in value sensitivity, external factors are at least equally important. Our data show that food restriction, together with schedule of reinforcement, affects how animals learn and support evidence that external factors such as reinforcer value, on-board drug or stimulus saliency (Vandaele et al., 2017), both contribute to, and can fundamentally control, the underlying cognitive basis of behavior.

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778 **LEGENDS**

779

780 **Figure 1 – RI30/RI60 and RR10/RR20 produce different operant behavior and different**
781 **response-per-reinforcer ratios. (A)** Schematic showing the relationship between response
782 rate and reinforcer delivery rate under 4 example schedules. The red dotted line indicates the
783 mean response rate a subject must perform to achieve equal reinforcer delivery rates under
784 RI30 or RR10 schedules. The value is the same for achieving equal reinforcer delivery rates
785 between RI60 and RR20. **(B)** Mean reinforcer delivery rates across training, split by schedule.
786 **(C)** Mean response rates across training, split by schedule. **(D)** Mean responses-per-reinforcer
787 ratio during each phase of training. (Note: animals on RR20 can have mean response/reinforcer
788 ratio larger than 20 because response only counted once the previous reinforcer had been
789 collected). Individual data points are shown separated by sex within each group (Females: left,
790 Males: right). RI: N=9 mice, RR: N=10 mice, * indicates independent Student's t test $p<0.05$.
791 Data are shown as mean±sem (error bars are occluded by mean symbol in panel B).

792

793 **Figure 2 – Designing RR schedules to match the responses-per-reinforcer ratios**
794 **observed in mice following RI schedules under distinct levels of food restriction.**
795 **(A)** Schematic showing the training strategy for three groups distinguished by their level of food
796 restriction. Each mouse underwent 3 days of RI30, 4 days of RI60 and 2 days of outcome
797 devaluation testing. **(B)** Plot showing that each pair of response rate/reinforcer delivery rate can
798 be achieved by a specific RR (shown as a color map). The response rate/reinforcer delivery rate
799 values observed for each phase/restriction group are depicted as circles color-coded to match
800 (A). **(C)** Summary of Figure 2B showing the RR that matches each RI based on the
801 performance of each RI group. **(D**) Schematic showing the training strategy for three groups
802 distinguished by their level of food restriction. Each group followed the RR schedule identified in
803 (B-C). **(E)** Mean responses-per-reinforcer ratios for each restriction/schedule group, separated

by phase of training. Individual data points are shown separated by sex within each group (Females: left, Males: right). RI-noRestriction N=10 mice, RR-noRestriction=9 mice, RI-MildRestriction N=14 mice, RR-MildRestriction=15 mice, RI-strongRestriction N=14 mice, RR-strongRestriction=10 mice; * indicates two-way ANOVA $p<0.05$ (E). ns indicates two-way ANOVA $p>0.05$ (E) and post hoc Tukey HSD $p>0.5$ (E). Data are shown as mean±sem. See also Figure 2-1.

Figure 3 - Food restriction increases response rates more effectively in mice following RR schedules than in mice following RI schedules. (A) Mean response rates across training, split by restriction and schedule. **(B)** Mean response rates on the last day of training summarizing the data used to perform a two-way ANOVA. **(C)** Mean ratio of response rate on last session over first session (post FR1 acquisition) summarizing the data used to perform a two-way ANOVA. Individual data points are shown separated by sex within each group (Females: left, Males: right). RI-noRestriction N=10 mice, RR-NoRestriction N=9 mice, RI-MildRestriction N=14 mice, RR-MildRestriction N=15 mice, RI-strongRestriction N=14 mice, RR-strongRestriction N=10 mice; black * indicates two-way ANOVA $p<0.05$ (B,C); grey * indicates $p<0.05$ post hoc Tukey HSD test for matched RR-RI pairs (B,C). ANOVA results and post hoc Tukey HSD tests are reported in the statistical table (Table 1). Data are shown as mean±sem. See also Figure 3-1.

Figure 4 – The effects of food restriction and schedule on performance during devaluation procedures are dominated by extinction. (A) Diagram describing the devaluation procedure, extinction test and preference test. **(B)** Summary of response rates during devaluation sessions, grouped by devaluation (valued/food, devalued/sucrose). Valued conditions consisted of 1 hour access to regular chow and devalued 1 hour access to 10% sucrose. The two test sessions were performed on consecutive days and the order

counterbalanced within each group. (valued-RI-MildRestriction: 4.3±0.56 responses/min, devalued-RI-MildRestriction: 4.95±0.91 responses/min, N=8; valued-RR-MildRestriction: 4.88±1.08 responses/min; devalued-RR-MildRestriction: 6.40±1.21 responses/min, N=10; valued-RI-StrongRestriction: 6.54±0.92 responses/min; devalued-RI-StrongRestriction: 6.74±1.16 responses/min, N=14; valued-RR-StrongRestriction: 9.18±1.46 responses/min; devalued-RR-StrongRestriction: 10.82±2.05 responses/min, N=9) **(C)** Same data as shown in (**B**) summarized as a devaluation index for each mouse (valued response rate / (valued response rate + devalued response rate)). Means for the mice grouped by schedule, restriction and testing order are also shown on the right. **(D)** Same data as shown in (B), grouped by session number (1st extinction session, 2nd extinction session). (1st-RI-MildRestriction: 4.95±0.74 responses/min, 2nd-RI-MildRestriction: 4.30±0.77 responses/min, N=8; 1st-RR-MildRestriction: 6.48±1.08 responses/min; 2nd-RR-MildRestriction: 4.80±0.62 responses/min, N=10; 1st-RI-StrongRestriction: 9.01±1.05 responses/min; 2nd-RI-StrongRestriction: 4.27±0.47 responses/min, N=14; 1st-RR-StrongRestriction: 12.91±1.99 responses/min; 2nd-RR-StrongRestriction: 7.09±0.66 responses/min, N=9). **(E)** Same data as shown in (D) summarized as an extinction index for each mouse (2nd session response rate / (1st session response rate + 2nd session response rate)). Means for the mice grouped by schedule and by restriction are also shown on the right. * indicates two-way ANOVA $p<0.05$ (C,E). ns indicates two-way ANOVA $p>0.05$ (C,E). Data are shown as mean±sem. Individual data points are shown separated by sex within each group (Females: left, Males: right). See also Figure 4-1.

Figure 5 – The effects of food restriction on extinction are not apparent within a session. **(A)** Response rates during the first extinction session. Data are shown across the duration of the session in 1 minute time bins. **(B)** Response rates during the first minute of the extinction session show similar results as by the end of acquisition. **(C)** Graph showing the ratio of the number of responses in the second minute over the number of responses during the first and

second minutes capturing the magnitude of the decrease in response rate. **(D)** Graph showing the number of responses executed before the inter-response interval became larger than mean+2std based on a rolling window of five responses. Data are shown as mean±sem. Individual data points are shown separated by sex within each group (Females: left, Males: right). RI-MildRestriction: N=8, RR-MildRestriction: N=10, RI-StrongRestriction: N=14, RR-StrongRestriction: N=9).

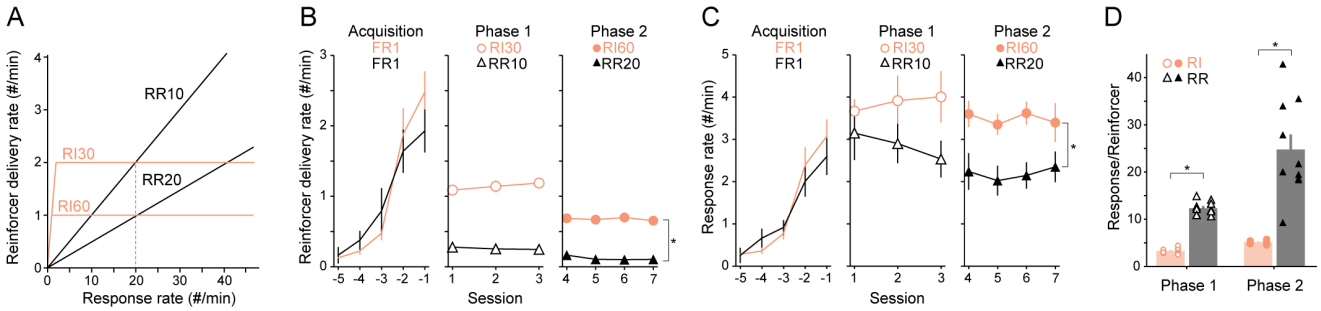
Figure 2-1 – No difference in time to acquisition across restriction/schedule and in the efficacy of food restriction across sex. (A) Graph showing the time to acquisition across training schedules and restriction groups. (RI-NoRestriction: 4.1±0.5 sessions (N=10), RI-MildRestriction: 4.29±0.62 sessions (N=14), RI-StrongRestriction: 3.86±0.49 sessions (N=14), RR-NoRestriction: 3.78±0.52 sessions (N=9), RR-MildRestriction: 3.93±0.45 sessions (N=15), RR-StrongRestriction: 3.4±0.45 sessions (N=10)). A two-way ANOVA revealed no effects of restriction group (two-way ANOVA F=0.45, df=2, p=0.64) and no effect of task schedule (two-way ANOVA F=0.77, df=1, p=0.38). These results are expected as we assigned mice to groups post FR1 acquisition to avoid any differences. **(B)** Graph showing the effects of food restriction across time as the fraction of initial body weight. (Data on session 7: Females/NoRestriction: 1.02±0.02 (N=9), Females/MildRestriction: 0.99±0.03 (N=10), Females/StrongRestriction: 0.79±0.01 (N=12), Males/NoRestriction: 1.02±0.01 (N=10), Males/MildRestriction: 0.92±0.02 (N=10), Males/StrongRestriction: 0.76±0.01 (N=12)). A two-way ANOVA on the last day (sessions7) revealed a significant effect of restriction group (two-way ANOVA F=90.1, df=2, p=2.3e-18) but no effect of sex (two-way ANOVA F=3.48, df=1, p=6.7e-2).

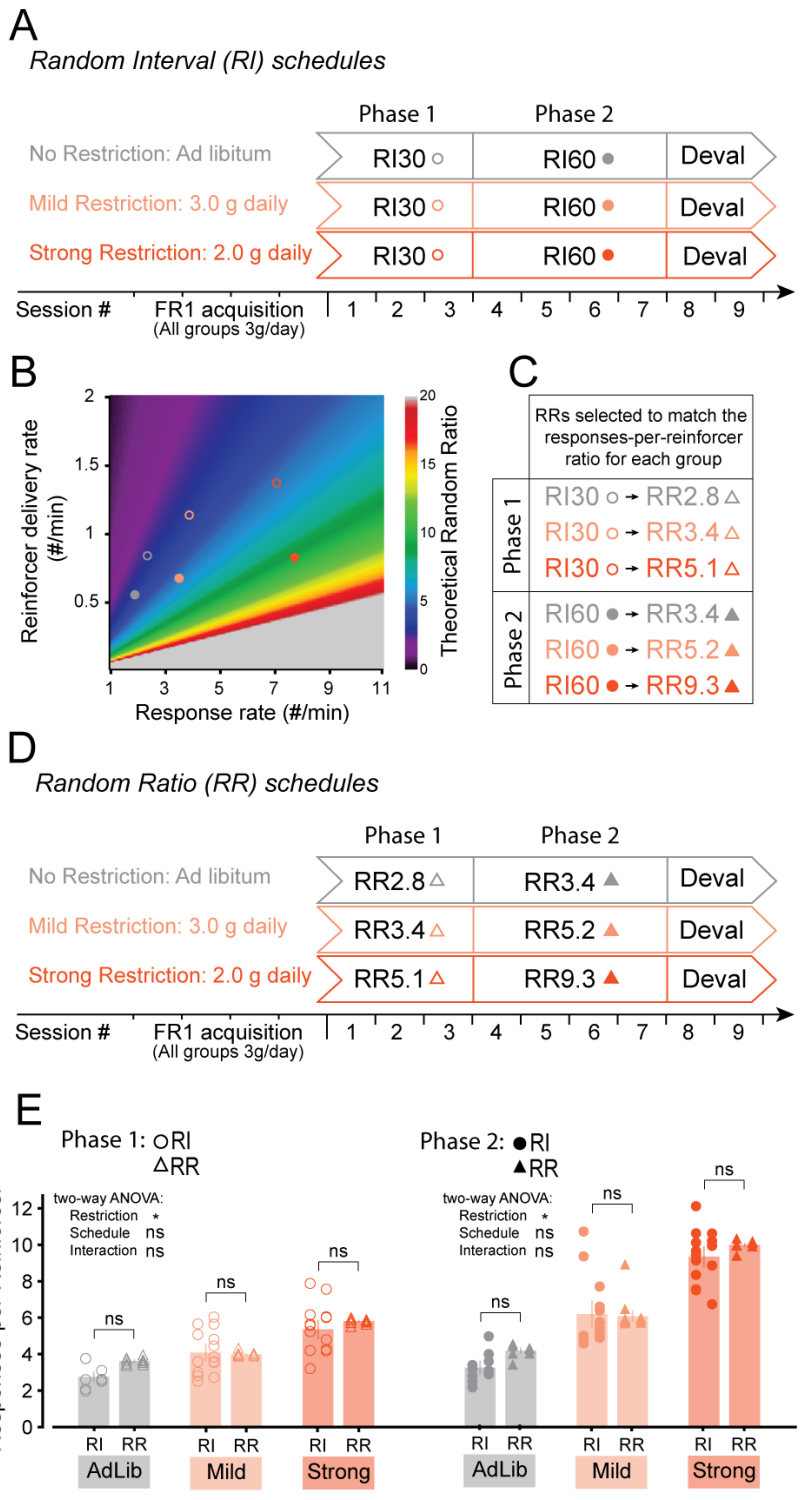
Figure 3-1 –Food restriction and schedule influenced reinforcer delivery rates and response rate variability. (A) Mean reinforcer delivery rates across training, split by restriction and schedule. **(B)** Mean reinforcer delivery rates on the last day of training summarizing the

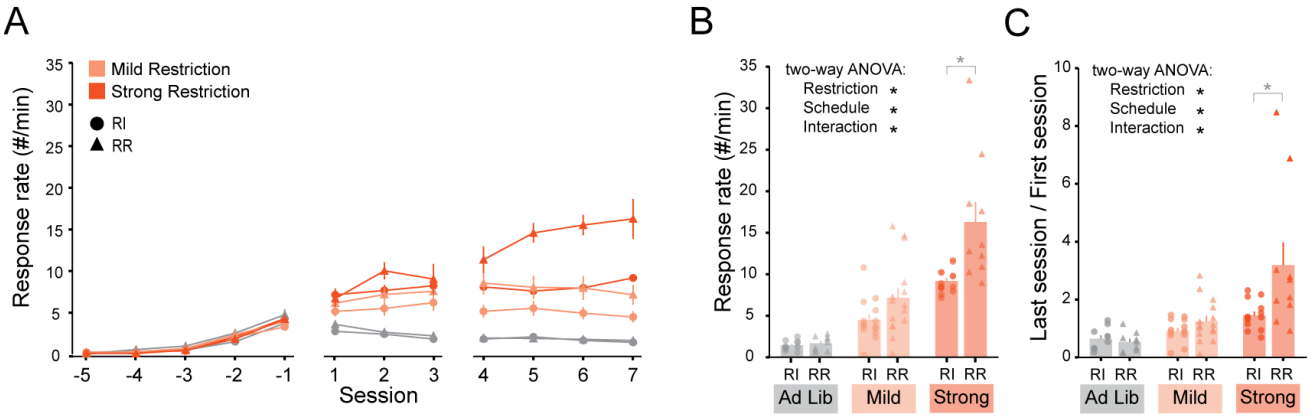
data used to perform a two-way ANOVA. **(C)** Mean coefficient of variation of the inter-response interval across training, split by restriction and schedule. **(D)** Mean coefficient of variation on the last day of training summarizing data used to perform a two-way ANOVA. RI-noRestriction N=10 mice, RR-NoRestriction N=9 mice, RI-MildRestriction N=14 mice, RR-MildRestriction N=15 mice, RI-strongRestriction N=14 mice, RR-strongRestriction N=10 mice; black * indicates two-way ANOVA $p<0.05$ (B,D); grey * indicates $p<0.05$ post hoc Tukey HSD test for matched RR-RI pairs (B,D). ANOVA results and post hoc Tukey HSD tests are reported in the statistical table. Data are shown as mean±sem. Individual data points are shown separated by sex within each group (Females: left, Males: right).

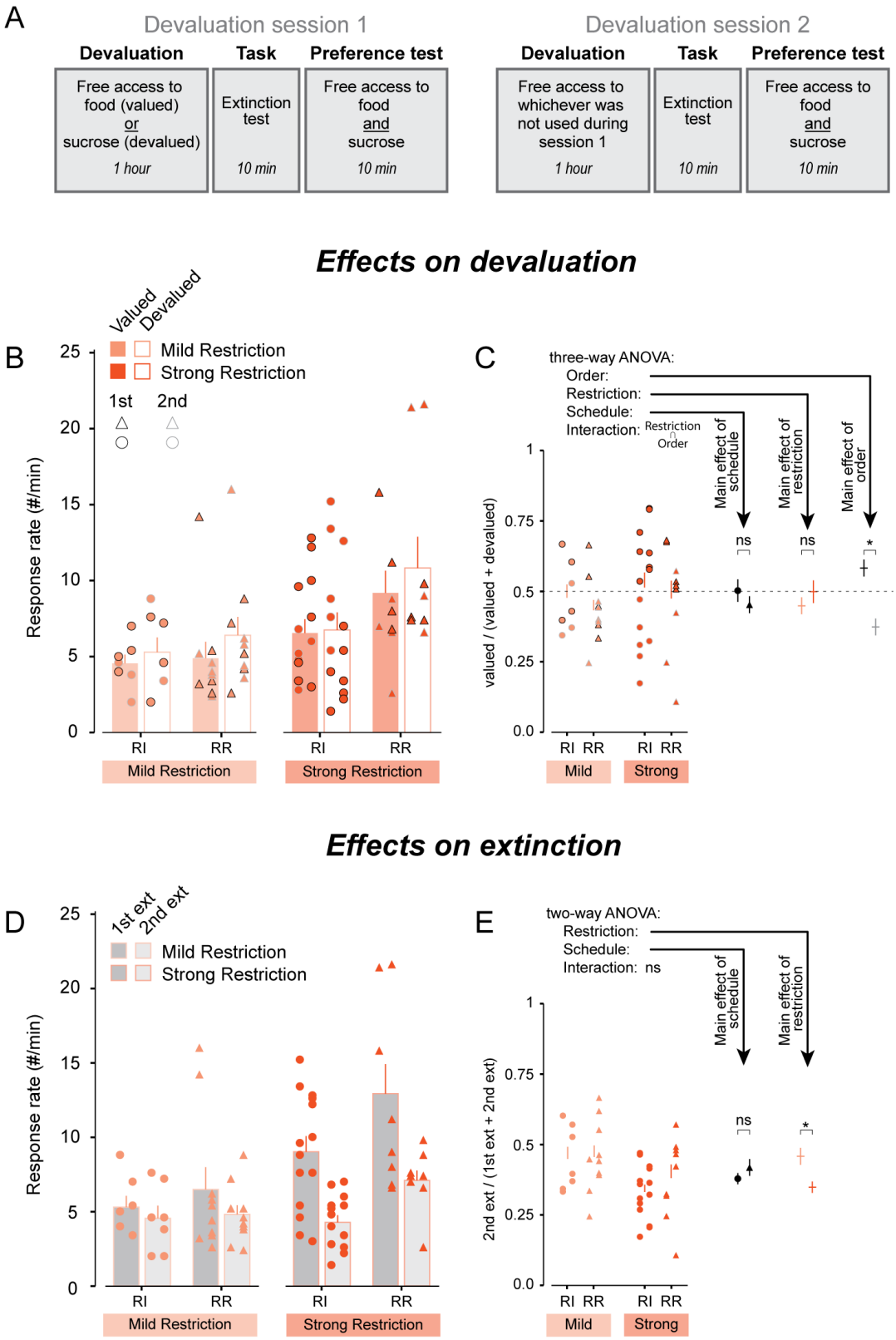
Figure 4-1 – Pre-feeding selectively and effectively reduced mice's preference for the pre-fed food. (A) Graphs showing how much food (left; RI-MildRestriction: 1.08±0.24 g (N=8), RR-MildRestriction: 0.94±0.17 g (N=10), RI-StrongRestriction: 1.25±0.09 g (N=14), RR-StrongRestriction: 1.52±0.16 g (N=10); two-way ANOVA main effect of restriction group df=1,F=4.35, p=0.044; main effect of schedule df=1,F=0.15, p=0.70; interaction df=1,F=2.39, p=0.13) or sucrose (right; RI-MildRestriction: 1.62±0.44 g (N=8), RR-MildRestriction: 1.65±0.40 g (N=10), RI-StrongRestriction: 2.9±0.22 g (N=14), RR-StrongRestriction: 3.16±0.18 g (N=10); two-way ANOVA main effect of restriction group df=1,F=18.6, p=1.15e-4; main effect of schedule df=1,F=0.24, p=063; interaction df=1,F=0.15, p=0.70) mice consumed during the 1 hour pre-feeding session preceding the extinction test. **(B)** Graphs showing consumption during the post-devaluation preference test, during which mice have free access to both food and sucrose for 10 minutes, for food (left; RI-MildRestriction_postSucDeval: 0.52±0.04 g (N=5), RI-MildRestriction_postFoodDeval: 0.24±0.07 g (N=5), RR-MildRestriction_postSucDeval: 0.48±0.09 g (N=4), RR-MildRestriction_postFoodDeval: 0.27±0.11 g (N=4), RI-StrongRestriction_postSucDeval: 0.45±0.05 g (N=4), RI-StrongRestriction_postFoodDeval: 0.15±0.05 g (N=4), RR-StrongRestriction_postSucDeval: 0.55±0.05 g (N=2), RR-

908 StrongRestriction_postFoodDeval: 0.10±0.10 g (N=2); three-way ANOVA main effect of
909 restriction group df=1,F=1.68, p=0.21; main effect of schedule df=1,F=0.014, p=0.91; main
910 effect of pre-feed df=1,F=30.8, p=1.4e-5; interactions all showed p>0.05) and for sucrose (right;
911 RI-MildRestriction_postSucDeval: 0.24±0.11 g (N=5), RI-MildRestriction_postFoodDeval:
912 1.26±0.28 g (N=5), RR-MildRestriction_postSucDeval: 0.22±0.05 g (N=4), RR-
913 MildRestriction_postFoodDeval: 1.22±0.36 g (N=4), RI-StrongRestriction_postSucDeval:
914 0.10±0.04 g (N=4), RI-StrongRestriction_postFoodDeval: 1.35±0.28 g (N=4), RR-
915 StrongRestriction_postSucDeval: 0.15±0.15 g (N=2), RR-StrongRestriction_postFoodDeval:
916 0.65±0.55 g (N=2); three-way ANOVA main effect of restriction group df=1,F=0.59, p=0.45;
917 main effect of schedule df=1,F=0.59, p=0.45; main effect of pre-feed df=1,F=33.5, p=8.0e-6;
918 interactions all showed p>0.05). **(C)** Preference index based on data shown in (B) showing all
919 groups preferred the non-devalued option equally. Negative values indicate preference for food
920 and positive values indicate preference for sucrose (following sucrose devaluation - RI-
921 MildRestriction: -0.59±0.12 (N=5), RR-MildRestriction: -0.45±0.15 (N=4), RI-StrongRestriction: -
922 0.66±0.05 (N=4), RR-StrongRestriction: -0.76±0.24 (N=2). Indices following food devaluation
923 are the opposite. two-way ANOVA main effect of restriction group df=1, F=1.49, p=0.25; main
924 effect of schedule df=1, F=0.15, p=0.70; interaction df=1,F=0.74, p=0.41). Data are shown as
925 mean±sem. Individual data points are shown separated by sex within each group (Females: left,
926 Males: right).
927
928 **Table 1 – Statistical table.**
929









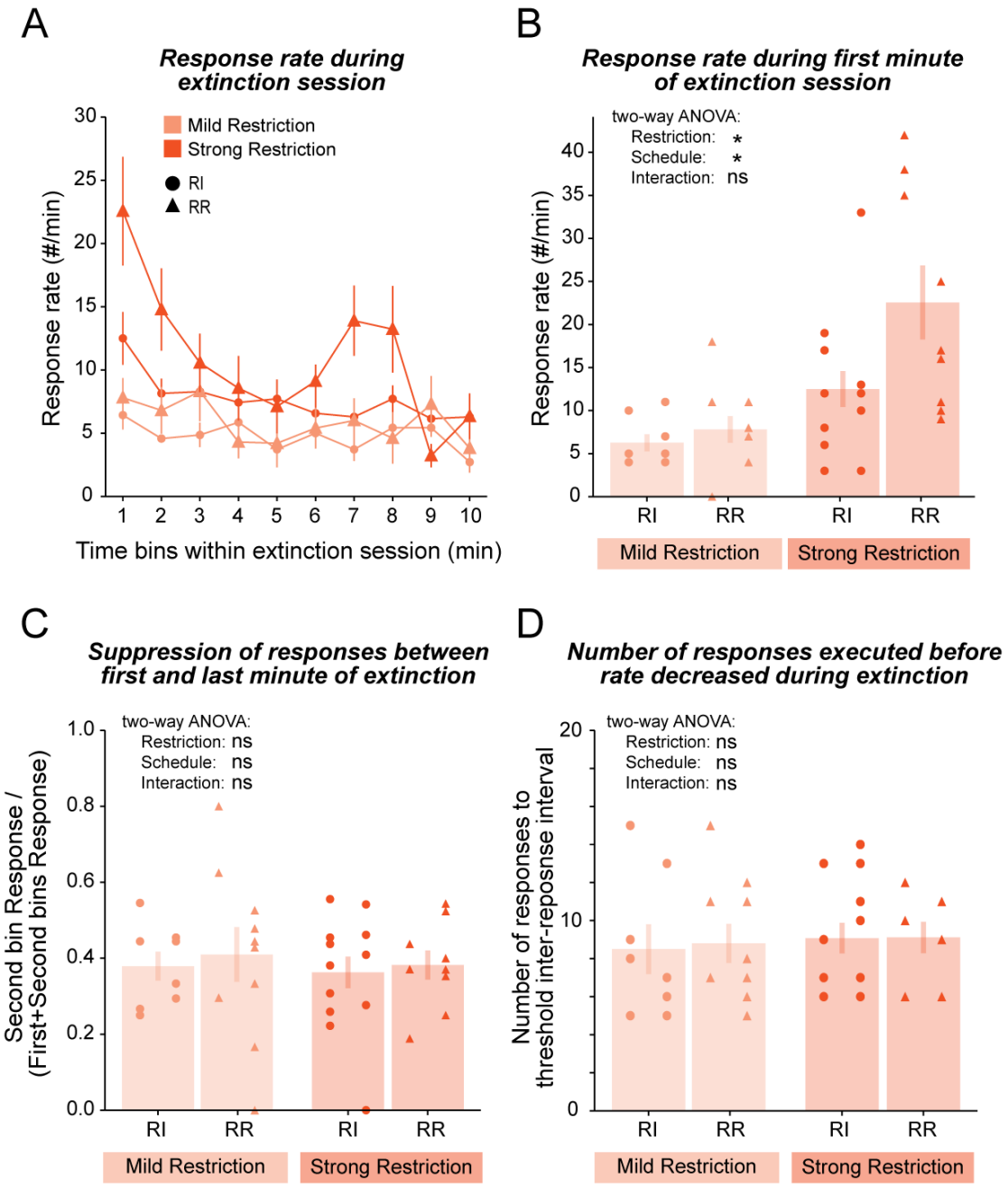


Figure 1B

Data Structure	Type of test	Statistic	Significance
Normal distribution	Student's t test	t=22.2	p=5.2E-14

Figure 1C

Data Structure	Type of test	Statistic	Significance
Normal distribution	Student's t test	t=3.6	p=2.1E-3

Figure 1D (phase 1)

Data Structure	Type of test	Statistic	Significance
Normal distribution	Welch's t test	t=-18.2	p=2.2E-10

Figure 1D (phase 2)

Data Structure	Type of test	Statistic	Significance
Normal distribution	Welch's t test	t=-6.17	p=1.63E-4

Figure 2 E Phase 1

Data Structure	Type of test
Normal distribution	two-way ANOVA with Tukey HSD post hoc test

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	2.075114644	1	2.075115	3.024752	0.086665	0.043821
group	65.09672171	2	32.54836	47.44351	1.7E-13	0.589774
task * group	2.774285271	2	1.387143	2.021943	0.140518	0.057734
Residual	45.27893798	66	0.686045			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Fed	RI / Restricted	2.6046	0	1.5981	3.6112	TRUE
RI / Fed	RR / Restricted	3.0644	0	1.9772	4.1517	TRUE
RR / Fed	RR / Restricted	2.199	0	1.082	3.316	TRUE
RR / Mild	RR / Restricted	1.8221	0	0.8296	2.8145	TRUE
RI / Mild	RR / Restricted	1.7251	0.0001	0.7185	2.7316	TRUE
RI / Restricted	RR / Fed	-1.7392	0.0001	-2.7778	-0.7005	TRUE
RI / Restricted	RR / Mild	-1.3622	0.0005	-2.2657	-0.4588	TRUE
RI / Mild	RI / Restricted	1.2653	0.0019	0.3464	2.1841	TRUE
RI / Fed	RI / Mild	1.3394	0.0029	0.3328	2.3459	TRUE
RI / Fed	RR / Mild	1.2424	0.0061	0.2499	2.2349	TRUE
RI / Fed	RR / Fed	0.8655	0.2194	-0.2515	1.9825	FALSE
RI / Restricted	RR / Restricted	0.4598	0.7613	-0.5467	1.4664	FALSE
RI / Mild	RR / Fed	-0.4739	0.7622	-1.5126	0.5648	FALSE

RR / Fed	RR / Mild	0.3769	0.8879	-0.6481	1.402	FALSE
RI / Mild	RR / Mild	-0.097	0.9996	-1.0004	0.8064	FALSE

Figure 2 E Phase 2

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	2.962500458	1	2.9625	2.231765	0.139965	0.032709
group	385.7566029	2	192.8783	145.3026	6.65E-25	0.814921
task * group	3.680881158	2	1.840441	1.386475	0.257139	0.04032
Residual	87.61003367	66	1.327425			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Fed	RI / Mild	2.9344	0	1.5342	4.3345	TRUE
RI / Fed	RI / Restricted	6.0789	0	4.6787	7.479	TRUE
RI / Fed	RR / Mild	2.8089	0	1.4283	4.1894	TRUE
RI / Fed	RR / Restricted	6.7249	0	5.2126	8.2372	TRUE
RI / Mild	RI / Restricted	3.1445	0	1.8663	4.4226	TRUE
RI / Mild	RR / Restricted	3.7905	0	2.3904	5.1907	TRUE
RI / Restricted	RR / Fed	-5.1491	0	-6.5939	-3.7043	TRUE
RI / Restricted	RR / Mild	-3.27	0	-4.5266	-2.0133	TRUE
RR / Fed	RR / Restricted	5.7951	0	4.2414	7.3489	TRUE
RR / Mild	RR / Restricted	3.916	0	2.5355	5.2965	TRUE
RI / Mild	RR / Fed	-2.0046	0.0017	-3.4494	-0.5598	TRUE
RR / Fed	RR / Mild	1.8791	0.0033	0.4533	3.305	TRUE
RI / Fed	RR / Fed	0.9298	0.5005	-0.624	2.4835	FALSE
RI / Restricted	RR / Restricted	0.646	0.7536	-0.7541	2.0462	FALSE
RI / Mild	RR / Mild	-0.1255	0.9997	-1.3821	1.1312	FALSE

Figure 2-1A

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	2.554019999	1	2.55402	0.771959	0.382799	0.011561
group	2.964468026	2	1.482234	0.448009	0.640827	0.013394
task * group	0.056019468	2	0.02801	0.008466	0.991571	0.000256
Residual	218.3603175	66	3.30849			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Mild	RR / Restricted	-0.8857	0.8466	-3.0962	1.3247	FALSE
RI / Fed	RR / Restricted	-0.7	0.9544	-3.0875	1.6875	FALSE

RR / Mild	RR / Restricted	-0.5333	0.9791	-2.7129	1.6462	FALSE
RI / Mild	RR / Fed	-0.5079	0.9863	-2.7889	1.773	FALSE
RI / Mild	RI / Restricted	-0.4286	0.9889	-2.4464	1.5893	FALSE
RI / Restricted	RR / Restricted	-0.4571	0.9902	-2.6676	1.7533	FALSE
RI / Mild	RR / Mild	-0.3524	0.9951	-2.3363	1.6315	FALSE
RR / Fed	RR / Restricted	-0.3778	0.9975	-2.8307	2.0752	FALSE
RI / Fed	RR / Fed	-0.3222	0.9988	-2.7752	2.1307	FALSE
RI / Fed	RI / Restricted	-0.2429	0.9995	-2.4533	1.9676	FALSE
RI / Fed	RI / Mild	0.1857	0.9999	-2.0247	2.3962	FALSE
RI / Fed	RR / Mild	-0.1667	0.9999	-2.3462	2.0129	FALSE
RI / Restricted	RR / Fed	-0.0794	1	-2.3603	2.2016	FALSE
RI / Restricted	RR / Mild	0.0762	1	-1.9077	2.0601	FALSE
RR / Fed	RR / Mild	0.1556	1	-2.0954	2.4066	FALSE

Figure 2-1B

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
sex	0.013471967	1	0.013472	3.482002	0.067188	0.057571
group	0.696884779	2	0.348442	90.0594	2.27E-18	0.759614
sex * group	0.012494214	2	0.006247	1.614645	0.207928	0.053617
Residual	0.220534633	57	0.003869			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
F / Fed	F / Restricted	-0.2313	0	-0.3122	-0.1504	TRUE
F / Fed	M / Restricted	-0.2523	0	-0.3332	-0.1714	TRUE
F / Mild	F / Restricted	-0.2023	0	-0.2808	-0.1238	TRUE
F / Mild	M / Restricted	-0.2233	0	-0.3018	-0.1448	TRUE
F / Restricted	M / Fed	0.2328	0	0.1542	0.3113	TRUE
M / Fed	M / Restricted	-0.2538	0	-0.3323	-0.1752	TRUE
M / Mild	M / Restricted	-0.155	0	-0.2335	-0.0765	TRUE
F / Restricted	M / Mild	0.134	0.0001	0.0555	0.2126	TRUE
M / Fed	M / Mild	-0.0988	0.0097	-0.1808	-0.0167	TRUE
F / Fed	M / Mild	-0.0973	0.0147	-0.1816	-0.013	TRUE
F / Mild	M / Mild	-0.0683	0.1553	-0.1503	0.0137	FALSE
F / Mild	M / Fed	0.0305	0.8811	-0.0515	0.1125	FALSE
F / Fed	F / Mild	-0.029	0.9109	-0.1133	0.0553	FALSE
F / Restricted	M / Restricted	-0.021	0.9614	-0.0959	0.0539	FALSE
F / Fed	M / Fed	0.0015	1	-0.0828	0.0857	FALSE

Figure 3B

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table						
Source	**SS**	**DF**	**MS**	**F**	**p-unc**	**np2**
task	214.6959521	1	214.696	15.2026	0.000229	0.187218
group	1289.035016	2	644.5175	45.63824	3.59E-13	0.580357
task * group	131.1364602	2	65.56823	4.642881	0.012985	0.12334
Residual	932.0727255	66	14.12231			

Tukey HSD post hoc tests						
group1	**group2**	**meandiff**	**p-adj**	**lower**	**upper**	**reject**
RI / Fed	RR / Restricted	14.8384	0	9.9056	19.7711	TRUE
RI / Mild	RR / Restricted	11.7919	0	7.2251	16.3588	TRUE
RR / Fed	RR / Restricted	14.6096	0	9.5416	19.6775	TRUE
RR / Mild	RR / Restricted	9.1195	0	4.6165	13.6225	TRUE
RI / Fed	RI / Restricted	7.7407	0.0001	3.1738	12.3075	TRUE
RI / Restricted	RR / Fed	-7.5119	0.0002	-12.2244	-2.7993	TRUE
RI / Restricted	RR / Restricted	7.0977	0.0003	2.5309	11.6645	TRUE
RI / Fed	RR / Mild	5.7189	0.0052	1.2159	10.2218	TRUE
RR / Fed	RR / Mild	5.49	0.0116	0.8394	10.1407	TRUE
RI / Mild	RI / Restricted	4.6942	0.0184	0.5253	8.8632	TRUE
RI / Fed	RI / Mild	3.0464	0.3773	-1.5204	7.6133	FALSE
RI / Mild	RR / Mild	2.6724	0.4032	-1.4265	6.7713	FALSE
RI / Mild	RR / Fed	-2.8176	0.5014	-7.5302	1.8949	FALSE
RI / Restricted	RR / Mild	-2.0218	0.698	-6.1207	2.0771	FALSE
RI / Fed	RR / Fed	0.2288	1	-4.8391	5.2967	FALSE

Figure 3C

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table						
Source	**SS**	**DF**	**MS**	**F**	**p-unc**	**np2**
task	8.288507957	1	8.288508	7.772326	0.006923	0.105356
group	31.31301957	2	15.65651	14.68147	5.31E-06	0.307907
task * group	10.29197934	2	5.14599	4.825514	0.011068	0.127573
Residual	70.38324338	66	1.066413			

Tukey HSD post hoc tests						
group1	**group2**	**meandiff**	**p-adj**	**lower**	**upper**	**reject**
RI / Fed	RR / Restricted	2.5488	0	1.1933	3.9043	TRUE
RI / Mild	RR / Restricted	2.2906	0	1.0356	3.5455	TRUE
RR / Fed	RR / Restricted	2.6579	0	1.2653	4.0506	TRUE
RR / Mild	RR / Restricted	1.9423	0.0003	0.7049	3.1797	TRUE
RI / Restricted	RR / Restricted	1.7393	0.0017	0.4843	2.9942	TRUE
RI / Restricted	RR / Fed	-0.9187	0.3092	-2.2137	0.3763	FALSE
RI / Fed	RI / Restricted	0.8095	0.4154	-0.4454	2.0645	FALSE
RR / Fed	RR / Mild	0.7156	0.5733	-0.5624	1.9936	FALSE
RI / Fed	RR / Mild	0.6065	0.7036	-0.6309	1.8439	FALSE

RI / Mild	RI / Restricted	0.5513	0.7194	-0.5943	1.6969	FALSE
RI / Mild	RR / Mild	0.3482	0.9433	-0.7781	1.4746	FALSE
RI / Mild	RR / Fed	-0.3674	0.9603	-1.6624	0.9276	FALSE
RI / Fed	RI / Mild	0.2582	0.9904	-0.9967	1.5132	FALSE
RI / Restricted	RR / Mild	-0.2031	0.9948	-1.3294	0.9233	FALSE
RI / Fed	RR / Fed	-0.1092	0.9999	-1.5018	1.2835	FALSE

Figure 3-1B

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	3.448541654	1	3.448542	15.33447	0.000216	0.188536
group	6.104268212	2	3.052134	13.57179	1.16E-05	0.291416
task * group	1.602648516	2	0.801324	3.563212	0.033923	0.097453
Residual	14.84261983	66	0.224888			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Fed	RR / Restricted	1.1235	0	0.5011	1.746	TRUE
RR / Fed	RR / Restricted	1.1677	0	0.5282	1.8072	TRUE
RI / Mild	RR / Restricted	0.934	0.0002	0.3577	1.5103	TRUE
RR / Fed	RR / Mild	0.7747	0.0033	0.1879	1.3616	TRUE
RI / Fed	RR / Mild	0.7306	0.0045	0.1623	1.2988	TRUE
RI / Restricted	RR / Restricted	0.7078	0.0076	0.1315	1.2841	TRUE
RI / Mild	RR / Mild	0.541	0.0352	0.0238	1.0583	TRUE
RI / Restricted	RR / Fed	-0.4599	0.2211	-1.0546	0.1348	FALSE
RI / Fed	RI / Restricted	0.4157	0.2913	-0.1606	0.992	FALSE
RR / Mild	RR / Restricted	0.393	0.337	-0.1753	0.9612	FALSE
RI / Restricted	RR / Mild	0.3148	0.4814	-0.2024	0.8321	FALSE
RI / Mild	RI / Restricted	0.2262	0.8042	-0.2999	0.7523	FALSE
RI / Mild	RR / Fed	-0.2337	0.8569	-0.8284	0.361	FALSE
RI / Fed	RI / Mild	0.1895	0.9272	-0.3868	0.7658	FALSE
RI / Fed	RR / Fed	-0.0442	1	-0.6837	0.5954	FALSE

Figure 3-1D

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.985917139	1	0.985917	11.1338	0.001395	0.144344
group	4.632669074	2	2.316335	26.15798	4.31E-09	0.442172
task * group	0.004708376	2	0.002354	0.026585	0.973775	0.000805
Residual	5.844413481	66	0.088552			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject
RI / Fed	RI / Restricted	-0.676	0	-1.0376	-0.3143	TRUE
RI / Mild	RR / Fed	0.6494	0	0.2762	1.0226	TRUE
RI / Restricted	RR / Fed	0.8862	0	0.513	1.2593	TRUE
RR / Fed	RR / Restricted	-0.6339	0.0002	-1.0352	-0.2326	TRUE
RI / Restricted	RR / Mild	0.4748	0.0008	0.1502	0.7994	TRUE
RI / Fed	RI / Mild	-0.4392	0.0086	-0.8008	-0.0776	TRUE
RR / Fed	RR / Mild	-0.4114	0.0198	-0.7796	-0.0431	TRUE
RI / Fed	RR / Restricted	-0.4237	0.0258	-0.8143	-0.0331	TRUE
RI / Mild	RR / Mild	0.238	0.2741	-0.0866	0.5626	FALSE
RI / Mild	RI / Restricted	-0.2368	0.2975	-0.5669	0.0934	FALSE
RI / Restricted	RR / Restricted	0.2522	0.3277	-0.1094	0.6138	FALSE
RR / Mild	RR / Restricted	-0.2226	0.4528	-0.5791	0.134	FALSE
RI / Fed	RR / Mild	-0.2012	0.5652	-0.5577	0.1554	FALSE
RI / Fed	RR / Fed	0.2102	0.6418	-0.1911	0.6115	FALSE
RI / Mild	RR / Restricted	0.0155	1	-0.3462	0.3771	FALSE

Figure 4C

Data Structure	Type of test
Normal distribution	three-way ANOVA

ANOVA table						
Source	SS	DF	MS	F	p-unc	np2
task	0.016042488	1	0.016042	1.183358	0.284555	0.034618
group	0.005627884	1	0.005628	0.415135	0.523828	0.012424
deval_order	0.435258432	1	0.435258	32.10639	2.58E-06	0.493137
task * group	0.000682343	1	0.000682	0.050332	0.823869	0.001523
task * deval_orde	0.006540706	1	0.006541	0.482468	0.492168	0.01441
group * deval_or	0.104020907	1	0.104021	7.672996	0.009131	0.188651
task * group * de	0.005000038	1	0.005	0.368823	0.547803	0.011053
Residual	0.44737282	33	0.013557			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject
RI / Restricted / C	RI / Restricted / 1	-0.3387	0.0001	-0.542	-0.1354	TRUE
RI / Restricted / C	RR / Restricted / 1	-0.3209	0.0018	-0.5514	-0.0904	TRUE
RI / Restricted / C	RR / Mild / 1	-0.2694	0.0062	-0.4839	-0.0548	TRUE
RI / Restricted / 1	RR / Restricted / 0	0.264	0.0141	0.0361	0.4919	TRUE
RR / Restricted / (	RR / Restricted / 1	-0.2462	0.0603	-0.4987	0.0063	FALSE
RI / Mild / 1	RI / Restricted / 0	0.2226	0.0645	-0.0079	0.4531	FALSE
RI / Restricted / C	RR / Mild / 0	-0.1827	0.1425	-0.3973	0.0318	FALSE
RI / Mild / 0	RI / Restricted / 1	-0.2046	0.1516	-0.4476	0.0384	FALSE
RR / Mild / 1	RR / Restricted / 0	0.1947	0.1767	-0.0434	0.4327	FALSE
RI / Mild / 0	RR / Restricted / 1	-0.1868	0.3401	-0.4529	0.0794	FALSE
RI / Restricted / 1	RR / Mild / 0	0.156	0.3708	-0.072	0.3839	FALSE
RI / Mild / 1	RR / Restricted / 0	0.1479	0.5642	-0.1046	0.4004	FALSE

RI / Mild / 0	RI / Restricted / 0	0.1341	0.5727	-0.0964	0.3646	FALSE
RR / Mild / 0	RR / Restricted / 1	-0.1381	0.6443	-0.3906	0.1144	FALSE
RI / Mild / 0	RR / Mild / 1	-0.1352	0.6676	-0.3877	0.1173	FALSE
RI / Mild / 1	RI / Restricted / 1	-0.1161	0.7782	-0.359	0.1269	FALSE
RR / Mild / 0	RR / Restricted / 0	0.1081	0.8186	-0.13	0.3461	FALSE
RI / Mild / 1	RR / Restricted / 1	-0.0983	0.9282	-0.3644	0.1679	FALSE
RR / Mild / 0	RR / Mild / 1	-0.0866	0.9331	-0.3247	0.1514	FALSE
RI / Restricted / 0	RR / Restricted / 0	-0.0747	0.9464	-0.2893	0.1399	FALSE
RI / Mild / 0	RI / Mild / 1	-0.0885	0.9576	-0.3547	0.1776	FALSE
RI / Restricted / 1	RR / Mild / 1	0.0693	0.9737	-0.1586	0.2973	FALSE
RI / Mild / 0	RR / Restricted / 0	0.0594	0.994	-0.1931	0.3119	FALSE
RR / Mild / 1	RR / Restricted / 1	-0.0515	0.9975	-0.304	0.201	FALSE
RI / Mild / 0	RR / Mild / 0	-0.0486	0.9983	-0.3011	0.2039	FALSE
RI / Mild / 1	RR / Mild / 1	-0.0467	0.9987	-0.2992	0.2058	FALSE
RI / Mild / 1	RR / Mild / 0	0.0399	0.9995	-0.2126	0.2924	FALSE
RI / Restricted / 1	RR / Restricted / 1	0.0178	1	-0.2252	0.2608	FALSE

Figure 4E

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.007507134	1	0.007507	0.541598	0.466412	0.014427
group	0.098837447	1	0.098837	7.130566	0.011193	0.161579
task * group	0.005676861	1	0.005677	0.409554	0.526139	0.010948
Residual	0.512860453	37	0.013861			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Restricted	RR / Mild	0.1244	0.0682	-0.0067	0.2555	FALSE
RI / Mild	RI / Restricted	-0.1235	0.1016	-0.2638	0.0169	FALSE
RR / Mild	RR / Restricted	-0.0754	0.5114	-0.2209	0.0701	FALSE
RI / Mild	RR / Restricted	-0.0744	0.5682	-0.2283	0.0795	FALSE
RI / Restricted	RR / Restricted	0.049	0.7643	-0.0862	0.1843	FALSE
RI / Mild	RR / Mild	0.001	1	-0.1493	0.1512	FALSE

Figure 4-1A (food)

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.092493243	1	0.092493	0.354666	0.555014	0.009247
group	1.424152334	1	1.424152	5.460927	0.024818	0.125651
task * group	0.413756757	1	0.413757	1.586555	0.215501	0.040078
Residual	9.91	38	0.260789			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject
RR / Mild	RR / Restricted	0.58	0.0697	-0.0335	1.1935	FALSE
RI / Mild	RR / Restricted	0.445	0.2723	-0.2058	1.0958	FALSE
RI / Restricted	RR / Mild	-0.31	0.4674	-0.878	0.258	FALSE
RI / Restricted	RR / Restricted	0.27	0.5829	-0.298	0.838	FALSE
RI / Mild	RI / Restricted	0.175	0.866	-0.433	0.783	FALSE
RI / Mild	RR / Mild	-0.135	0.944	-0.7858	0.5158	FALSE

Figure 4-1A (sucrose)

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table						
Source	SS	DF	MS	F	p-unc	np2
task	0.257804805	1	0.257805	0.264173	0.610244	0.006904
group	19.53710278	1	19.5371	20.01968	6.75E-05	0.34505
task * group	0.139306306	1	0.139306	0.142747	0.707667	0.003742
Residual	37.084	38	0.975895			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject
RR / Mild	RR / Restricted	1.51	0.0079	0.3231	2.6969	TRUE
RI / Mild	RR / Restricted	1.535	0.0116	0.2761	2.7939	TRUE
RI / Restricted	RR / Mild	-1.25	0.0204	-2.3488	-0.1512	TRUE
RI / Mild	RI / Restricted	1.275	0.0292	0.0988	2.4512	TRUE
RI / Restricted	RR / Restricted	0.26	0.9198	-0.8388	1.3588	FALSE
RI / Mild	RR / Mild	0.025	0.9999	-1.2339	1.2839	FALSE

Figure 4-1B (sucrose)

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table						
Source	SS	DF	MS	F	p-unc	np2
group	0.134444444	1	0.134444	0.591674	0.449953	0.02619
task	0.134444444	1	0.134444	0.591674	0.449953	0.02619
pre	7.600333333	1	7.600333	33.44816	8.09E-06	0.603233
group * task	0.15	1	0.15	0.660132	0.425218	0.029132
group * pre	0.003402778	1	0.003403	0.014975	0.903714	0.00068
task * pre	0.153402778	1	0.153403	0.675107	0.420092	0.029773
group * task * pr	0.222041667	1	0.222042	0.977179	0.333645	0.042528
Residual	4.999	22	0.227227			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject

RI / Restricted / f	RI / Restricted / suc	-1.25	0.0225	-2.3754	-0.1246	TRUE
RI / Mild / food	RI / Restricted / suc	-1.16	0.0269	-2.2276	-0.0924	TRUE
RI / Mild / suc	RI / Restricted / food	1.11	0.0377	0.0424	2.1776	TRUE
RI / Mild / food	RI / Mild / suc	-1.02	0.0455	-2.0266	-0.0134	TRUE
RI / Restricted / f	RR / Mild / suc	-1.125	0.0501	-2.2504	0.0004	FALSE
RI / Restricted / s	RR / Mild / food	1.125	0.0501	-0.0004	2.2504	FALSE
RI / Mild / food	RR / Mild / suc	-1.035	0.0618	-2.1026	0.0326	FALSE
RI / Mild / suc	RR / Mild / food	0.985	0.0849	-0.0826	2.0526	FALSE
RR / Mild / food	RR / Mild / suc	-1	0.1062	-2.1254	0.1254	FALSE
RI / Restricted / f	RR / Restricted / suc	-1.2	0.1192	-2.5783	0.1783	FALSE
RI / Mild / food	RR / Restricted / suc	-1.11	0.1502	-2.4416	0.2216	FALSE
RR / Mild / food	RR / Restricted / suc	-1.075	0.2067	-2.4533	0.3033	FALSE
RI / Restricted / f	RR / Restricted / fooc	-0.7	0.6899	-2.0783	0.6783	FALSE
RI / Mild / food	RR / Restricted / fooc	-0.61	0.7841	-1.9416	0.7216	FALSE
RR / Mild / food	RR / Restricted / fooc	-0.575	0.851	-1.9533	0.8033	FALSE
RI / Restricted / s	RR / Restricted / fooc	0.55	0.8767	-0.8283	1.9283	FALSE
RR / Restricted /	RR / Restricted / suc	-0.5	0.9609	-2.0915	1.0915	FALSE
RR / Mild / suc	RR / Restricted / fooc	0.425	0.9645	-0.9533	1.8033	FALSE
RI / Mild / suc	RR / Restricted / fooc	0.41	0.9648	-0.9216	1.7416	FALSE
RI / Mild / suc	RI / Restricted / suc	-0.14	0.9998	-1.2076	0.9276	FALSE
RI / Restricted / f	RR / Mild / food	-0.125	0.9999	-1.2504	1.0004	FALSE
RI / Restricted / s	RR / Mild / suc	0.125	0.9999	-1.0004	1.2504	FALSE
RR / Mild / suc	RR / Restricted / suc	-0.075	1	-1.4533	1.3033	FALSE
RI / Mild / suc	RR / Restricted / suc	-0.09	1	-1.4216	1.2416	FALSE
RI / Restricted / s	RR / Restricted / suc	0.05	1	-1.3283	1.4283	FALSE
RI / Mild / suc	RR / Mild / suc	-0.015	1	-1.0826	1.0526	FALSE
RI / Mild / food	RR / Mild / food	-0.035	1	-1.1026	1.0326	FALSE
RI / Mild / food	RI / Restricted / food	0.09	1	-0.9776	1.1576	FALSE

Figure 4-1B (food)

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
group	0.033611111	1	0.033611	1.680556	0.208285	0.070968
task	0.000277778	1	0.000278	0.013889	0.907255	0.000631
pre	0.616333333	1	0.616333	30.81667	1.4E-05	0.583465
group * task	0.0015	1	0.0015	0.075	0.786746	0.003398
group * pre	0.020069444	1	0.020069	1.003472	0.327363	0.043623
task * pre	6.94444E-05	1	6.94E-05	0.003472	0.953543	0.000158
group * task * pr	0.022041667	1	0.022042	1.102083	0.305205	0.047705
Residual	0.44	22	0.02			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
food / Restricted	suc / Mild / RI	0.37	0.0147	0.0533	0.6867	TRUE

food / Restricted	suc / Mild / RI	0.42	0.0319	0.025	0.815	TRUE
food / Restricted	suc / Restricted / RR	0.4	0.0582	-0.0089	0.8089	FALSE
food / Restricted	suc / Mild / RR	0.325	0.0602	-0.0089	0.6589	FALSE
food / Restricted	suc / Restricted / RR	0.45	0.0692	-0.0222	0.9222	FALSE
food / Mild / RI	suc / Mild / RI	0.28	0.0768	-0.0186	0.5786	FALSE
food / Restricted	suc / Mild / RR	0.375	0.0881	-0.0339	0.7839	FALSE
food / Restricted	suc / Restricted / RI	0.3	0.0995	-0.0339	0.6339	FALSE
food / Restricted	suc / Restricted / RI	0.35	0.1308	-0.0589	0.7589	FALSE
food / Mild / RI	suc / Restricted / RR	0.31	0.2011	-0.085	0.705	FALSE
food / Mild / RR	suc / Mild / RI	0.245	0.2144	-0.0717	0.5617	FALSE
food / Mild / RI	suc / Mild / RR	0.235	0.2556	-0.0817	0.5517	FALSE
food / Mild / RR	suc / Restricted / RR	0.275	0.3646	-0.1339	0.6839	FALSE
food / Mild / RI	suc / Restricted / RI	0.21	0.3814	-0.1067	0.5267	FALSE
food / Mild / RR	suc / Mild / RR	0.2	0.5038	-0.1339	0.5339	FALSE
food / Mild / RR	suc / Restricted / RI	0.175	0.6571	-0.1589	0.5089	FALSE
food / Mild / RR	food / Restricted / RF	-0.175	0.8345	-0.5839	0.2339	FALSE
food / Mild / RR	food / Restricted / RI	-0.125	0.9073	-0.4589	0.2089	FALSE
food / Mild / RI	food / Restricted / RF	-0.14	0.9284	-0.535	0.255	FALSE
food / Mild / RI	food / Restricted / RI	-0.09	0.9771	-0.4067	0.2267	FALSE
suc / Restricted /	suc / Restricted / RR	0.1	0.9902	-0.3089	0.5089	FALSE
suc / Mild / RI	suc / Restricted / RI	-0.07	0.9947	-0.3867	0.2467	FALSE
suc / Mild / RR	suc / Restricted / RR	0.075	0.9983	-0.3339	0.4839	FALSE
suc / Mild / RI	suc / Mild / RR	-0.045	0.9997	-0.3617	0.2717	FALSE
food / Mild / RI	food / Mild / RR	0.035	0.9999	-0.2817	0.3517	FALSE
food / Restricted	food / Restricted / RF	-0.05	0.9999	-0.4589	0.3589	FALSE
suc / Mild / RR	suc / Restricted / RI	-0.025	1	-0.3589	0.3089	FALSE
suc / Mild / RI	suc / Restricted / RR	0.03	1	-0.365	0.425	FALSE

Figure 4-1C

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.009358172	1	0.009358	0.151296	0.704724	0.013568
group	0.091969156	1	0.091969	1.486886	0.248202	0.119076
task * group	0.045702355	1	0.045702	0.73888	0.408363	0.062943
Residual	0.680389033	11	0.061854			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RR / Mild	RR / Restricted	-0.3072	0.5099	-0.9554	0.341	FALSE
RI / Restricted	RR / Mild	0.2121	0.6357	-0.3171	0.7414	FALSE
RI / Mild	RR / Mild	0.1391	0.8374	-0.363	0.6412	FALSE
RI / Mild	RR / Restricted	-0.1681	0.8495	-0.7943	0.4582	FALSE
RI / Restricted	RR / Restricted	-0.0951	0.9699	-0.7433	0.5531	FALSE
RI / Mild	RI / Restricted	-0.073	0.9707	-0.5751	0.4291	FALSE

Figure 5B

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	387.0925612	1	387.0926	5.985578	0.019296	0.139246
group	1052.684141	1	1052.684	16.27756	0.000263	0.305524
task * group	177.5151682	1	177.5152	2.744901	0.106022	0.069063
Residual	2392.822222	37	64.67087			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Mild	RR / Restricted	16.3056	0.001	5.795	26.8161	TRUE
RR / Mild	RR / Restricted	14.7556	0.0016	4.817	24.6941	TRUE
RI / Restricted	RR / Restricted	10.0556	0.0285	0.814	19.2971	TRUE
RI / Mild	RI / Restricted	6.25	0.3115	-3.3367	15.8367	FALSE
RI / Restricted	RR / Mild	-4.7	0.5003	-13.6559	4.2559	FALSE
RI / Mild	RR / Mild	1.55	0.977	-8.7103	11.8103	FALSE

Figure 5C

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.006490882	1	0.006491	0.260709	0.612667	0.006997
group	0.00520252	1	0.005203	0.208961	0.650256	0.005616
task * group	0.000216574	1	0.000217	0.008699	0.926194	0.000235
Residual	0.921191629	37	0.024897			

Tukey HSD post hoc tests

group1	group2	meandiff	p-adj	lower	upper	reject
RI / Restricted	RR / Mild	0.0492	0.8745	-0.1265	0.225	FALSE
RI / Mild	RR / Mild	0.0308	0.9762	-0.1706	0.2321	FALSE
RR / Mild	RR / Restricted	-0.0279	0.9804	-0.2229	0.1671	FALSE
RI / Restricted	RR / Restricted	0.0214	0.9888	-0.16	0.2027	FALSE
RI / Mild	RI / Restricted	-0.0185	0.9934	-0.2066	0.1696	FALSE
RI / Mild	RR / Restricted	0.0029	1	-0.2033	0.2091	FALSE

Figure 5D

Data Structure	Type of test
Normal distribution	two-way ANOVA with

ANOVA table

Source	SS	DF	MS	F	p-unc	np2
task	0.380085517	1	0.380086	0.041062	0.840529	0.001109
group	1.643659472	1	1.643659	0.177569	0.675909	0.004776
task * group	0.087547333	1	0.087547	0.009458	0.923051	0.000256
Residual	342.4888889	37	9.256456			

Tukey HSD post hoc tests						
group1	group2	meandiff	p-adj	lower	upper	reject
RI / Mild	RR / Restricted	0.6111	0.9758	-3.3653	4.5875	FALSE
RI / Mild	RI / Restricted	0.5	0.9823	-3.1269	4.1269	FALSE
RR / Mild	RR / Restricted	0.3111	0.996	-3.4489	4.0711	FALSE
RI / Mild	RR / Mild	0.3	0.9968	-3.5817	4.1817	FALSE
RI / Restricted	RR / Mild	-0.2	0.9985	-3.5883	3.1883	FALSE
RI / Restricted	RR / Restricted	0.1111	0.9998	-3.3852	3.6075	FALSE