- When Food Becomes a Distraction: The Impact of Food-Related Information on Reward
 Learning in Anorexia Nervosa
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15 Abstract

Objective: This study utilized a within-subject design to examine whether individuals with 16 restrictive anorexia nervosa (R-AN; n=40) perform similarly to healthy controls (HCs; n=17 45) and healthy controls at risk of eating disorders (RI; n=36) in a reinforcement learning 18 (RL) tasks. Specifically, we aimed to determine if RL performance is comparable between 19 groups for disorder-unrelated choices, but significantly impaired for disorder-related choices. 20 Method: RL performance was assessed using a Probabilistic Reversal Learning (PRL) task, 21 where participants were asked to perform disorder-related choices or disorder-unrelated 22 choices. Results: R-AN individuals demonstrated lower learning rates for disorder-related 23 decisions, while their performance on neutral decisions was comparable to participants with Bulimia Nervosa, Healthy Controls (HCs), and HCs at risk of eating disorders. Additionally, only AN patients exhibited reduced learning rates for outcome-irrelevant food-related 26 decisions in reward-based learning, as opposed to food-unrelated decisions. **Discussion:** Impaired RL task performance in individuals with AN may be attributed to external factors rather than compromised learning mechanisms. These findings indicate that AN may significantly impact the cognitive processing of food-related information, even when AN patients do not show learning rate disadvantages compared to HCs in decision-making 31 involving food-unrelated information. This study provides valuable insights into the reinforcement learning processes of individuals with AN and emphasizes the need to consider the influence of food-related information on cognitive functioning in this patient population. The findings have potential implications for the development of interventions targeting 35 decision- making processes in individuals with AN

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Introduction

Anorexia Nervosa (AN) is one of the most common eating disorders characterized by distorted body perception and pathological weight loss, particularly in its restricting type (R-AN) (American Psychiatric Association, 2022). Lifetime prevalence for AN has been reported at 1.4% for women and 0.2% for men (Galmiche, Déchelotte, Lambert, & Tavolacci, 2019; Smink, Hoeken, & Hoek, 2013), with a mortality rate that can be as high as 5-20% (Qian et al., 2022). Treating AN is extremely challenging (Atwood & Friedman, 2020; Linardon, Fairburn, Fitzsimmons-Craft, Wilfley, & Brennan, 2017), highlighting the importance of gaining a deeper understanding of its underlying mechanisms (Chang, Delgadillo, & Waller, 2021).

Executive functions have gained significant attention in the research on understanding
the mechanisms underlying anorexia nervosa (AN). Impairments in executive processes, such
as cognitive inflexibility, decision-making difficulties, and inhibitory control problems, have
been identified as potential risk and perpetuating factors in AN (Bartholdy, Dalton, O'Daly,
Campbell, & Schmidt, 2016; Guillaume et al., 2015; Wu et al., 2014). Within this domain,
Reinforcement Learning (RL) in the context of associative learning has received considerable
interest. In fact, the presence of persistent maladaptive eating behaviors in individuals with
AN, despite experiencing negative consequences, along with indications of altered reward and
punishment sensitivity, has led to the proposal of abnormal reward responsiveness and reward
learning in AN (Schaefer & Steinglass, 2021). While there is strong evidence supporting the
presence of anomalies in reward responsiveness in individuals with AN, our current
understanding of potential abnormalities in AN-related reward learning remains limited.

In relation to the dysfunctions observed in reward responsiveness among individuals with AN, research has revealed that the intense levels of dietary restriction and physical

activity characteristic of AN can indeed activate reward pathways (Keating, 2010; Keating, Tilbrook, Rossell, Enticott, & Fitzgerald, 2012; Selby & Coniglio, 2020). Additionally, individuals with AN may exhibit diminished reward responses specifically towards food (Wierenga et al., 2014). In a broader sense, research has shown that AN is associated with 68 reduced subjective reward sensitivity and decreased neural response to rewarding stimuli. Moreover, individuals with AN may experience disruptions in processing aversive stimuli, leading to heightened harm avoidance, intolerance of uncertainty, increased anxiety, and 71 oversensitivity to punishment (Fladung, Schulze, Schöll, Bauer, & Groen, 2013; Jappe et al., 2011; Keating et al., 2012; O'Hara, Campbell, & Schmidt, 2015). These factors contribute to an altered response to negative feedback and a tendency to avoid aversive outcomes (Jonker, Glashouwer, & Jong, 2022; Matton, Goossens, Braet, & Vervaet, 2013). Neuroimaging 75 studies have further supported these findings by revealing neural dysfunction in AN's response to loss and aversive taste (Bischoff-Grethe et al., 2013; Monteleone et al., 2017; Wagner et al., 2007).

However, when it comes to reward learning abnormalities in AN (Bernardoni et al., 2018; Foerde et al., 2021; Foerde & Steinglass, 2017), the reported results have been inconsistent (Caudek, Sica, Cerea, Colpizzi, & Stendardi, 2021). For example, some studies have suggested RL deficits, while others have found no significant differences. [bla bla] Given the critical role of RL in learning from experience, understanding these processes is essential in elucidating the mechanisms underlying maladaptive eating behavior in AN (Bischoff-Grethe et al., 2013; Glashouwer, Bloot, Veenstra, Franken, & Jong, 2014; Harrison, Genders, Davies, Treasure, & Tchanturia, 2011; Jappe et al., 2011; Matton et al., 2013).

Recently, it has been proposed that the inconsistency in the results regarding potential anomalies in RL processing in AN may be explained by the assumption that RL is a context-independent unitary process. This assumption attributes RL anomalies in R-AN to deficits in the underlying RL mechanism [ref]. Instead, an alternative perspective posits that

atypical RL behavior in R-AN may arise from the interference of extraneous contextual factors, even in the presence of intact RL mechanisms (Haynos, Widge, Anderson, & Redish, 2022). This hypothesis suggests that contextual factors, encompassing personal characteristics, long-term goals, and situational influences, can exert a negative impact on RL performance, regardless of the presence of an underlying RL deficit. Individuals with R-AN, being particularly susceptible to the influence of symptom-related information such as food, body weight, and social pressure [ref], may experience heightened vulnerability to these interfering contextual factors.

To investigate the influence of contextual factors on decision-making in R-AN, we conducted a study using a Probabilistic Reversal Learning (PRL) task. This task measures RL and cognitive flexibility by allowing participants to learn from feedback and adjust their 101 behavior based on reward probabilities. The task reflects real-life situations where outcomes 102 are uncertain, requiring individuals to make decisions based on probabilities. By presenting 103 uncertain and varying reward probabilities, the task captures the complexities of 104 decision-making under uncertainty and provides insights into how individuals integrate 105 probabilistic information to guide their behavior. The PRL task involves unannounced 106 reversals of contingencies, demanding behavioral adaptation to changing environments. This 107 reversal learning aspect measures cognitive flexibility – i.e., the ability to shift behavior in 108 response to changing environmental demands. The PRL task has been extensively used in 100 neuroscience research and has shown associations with specific brain regions involved in 110 reinforcement learning and cognitive flexibility [ref]. Neuroimaging techniques like fMRI have 111 revealed neural activations and connectivity patterns during the task, corresponding to 112 reward processing, error monitoring, and cognitive control mechanisms. 113

In contrast to previous studies that utilized general stimuli (Schaefer & Steinglass, 2021), our study implemented the PRL task with two distinct conditions. Participants were asked to complete the PRL task under two different scenarios: one condition involved choices

between a stimulus related to the disorder and a stimulus unrelated to the disorder, while
the other condition involved choices between two stimuli unrelated to the disorder.

The putative learning process involves a computational mechanism known as the 119 reward prediction error (PE). Derived from the RL framework, PE quantifies the disparities 120 between received outcomes and expected outcomes, enabling the updating of stimulus, state, 121 or action values (Rescorla & Wagner, 1972; Sutton & Barto, 2018). The neural manifestation 122 of the PE during reversal learning consistently emerges in the ventral frontostriatal circuitry 123 of the human brain (O'Doherty et al., 2003). In the RL framework, PEs are solely dependent 124 on the relationship between outcomes and choices, making the image content irrelevant in a 125 PRL task. As a result, previous studies have not explored the impact of contextual factors 126 on learning rates using the PRL task. 127

However, recent research suggests that outcome-irrelevant information can influence
PRL performance. For example, Shahar et al. (2019) showed that spatial-motor associations,
which are irrelevant to the outcomes, can affect PRL performance. While optimal
decision-making should prioritize rewards regardless of spatial-motor associations, such as
the choice of a response key in the previous trial, Shahar et al. (2019) found that rewards
had a more pronounced influence on the likelihood of choosing between two images when the
chosen image was associated with the same response key in both the "n-1" and "n" trials.

The present study aimed to investigate the influence of outcome-irrelevant and disorder-relevant information on PRL performance in three groups: individuals with DSM-5 restricting-type AN, healthy controls (HCs), and individuals at risk of developing eating disorders (RIs). The primary objective was to utilize computational models of reinforcement learning to analyze and compare learning outcomes in two distinct contextual conditions: decision-making involving disorder-relevant information and decision-making without disorder-relevant information.

Based on the evidence suggesting that outcome-irrelevant information can impact PRL performance, the study hypothesized that differences in RL between R-AN patients and the control groups would primarily emerge in the disorder-relevant condition. Conversely, no substantial differences were expected in the disorder-unrelated condition. By incorporating both disorder-relevant and disorder-unrelated stimuli, the study aimed to examine and quantify anomalies in RL performance among individuals with R-AN, thereby shedding light on the role of contextual factors in their decision-making processes.

Evidence of contextual factors on RL learning in AN

TODO

Developing flexibility in decision-making necessitates acquiring knowledge about the most rewarding choices in the current context and adjusting one's decision-making accordingly.

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Concerning cognitive flexibility, research has produced mixed results for the influence of disorder-related information.

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The inconsistent findings in behavioral experiments can be partly explained by the
predominant use of general stimuli in the studies, as opposed to disorder-relevant stimuli
(Schaefer & Steinglass, 2021). Furthermore, when disorder-related information is utilized, it
is typically provided solely in the feedback following the participant's choice, while the
stimuli presented during the decision-making process are unrelated to the disorder.
Consequently, the manipulation primarily emphasizes the consequences of the choices rather
than the contextual factors surrounding the decision-making process. However, recent
theoretical developments have emphasized the significant role of context in RL (e.g., Collins

& McDougle, 2021). Regarding motor learning, for example, it has been shown that
contextual cues affect learning rate (Castro, Hadjiosif, Hemphill, & Smith, 2014; Herzfeld,
Vaswani, Marko, & Shadmehr, 2014). In line with these findings, we propose that contextual
cues, specifically disorder-related information, have the potential to activate a dysfunctional
"learning mode" in individuals with R-AN, even in the absence of a general deficit in the
underlying RL mechanisms.

172 Implications for treatment

The hypothesis of contextual maladaptive RL in individuals with R-AN has significant implications for treatment strategies. Current efforts aim to improve cognitive flexibility in individuals with R-AN to address their maladaptive eating behavior. However, existing interventions have predominantly concentrated on fostering adaptive behavioral choices in contexts unrelated to the disorder (e.g., Tchanturia, Davies, Reeder, & Wykes, 2010). Establishing evidence that maladaptive RL is context-dependent would necessitate a redirection of intervention approaches.

180 Methods

The study, which adhered to the Declaration of Helsinki, was approved by the
University of Florence's Ethical Committee (Prot. n. 0178082). All eligible participants
provided informed consent and willingly agreed to participate in the study.

84 Participants

The study recruited a total of 40 individuals meeting criteria for DSM-5 restricting-type AN, 213 healty volunteers, and 36 healthy individuals at risk of developing eating disorders. Individuals with R-AN were recruited from three facilities in Italy, namely the Specchidacqua Institute in Montecatini (Pisa), the Villa dei Pini Institute in Firenze, and the Gruber Center, Outpatient Clinic in Bologna. The treatment approach consisted of Cognitive Behavioral Therapy and family-based treatment. Patients received treatment for 2

to 6 hours per day, 2 days per week. The treatment program included various components, such as individual therapy, family therapy, group therapy, nutritional counseling, psychiatric care, and medical monitoring. AN diagnosis was determined by semi-structured interview performed by specialized psychiatrists and psychologists at treatment admission according to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria.

Patients diagnosed with R-AN (Restrictive Anorexia Nervosa) were included in the 196 study approximately 6 months (± 1 month) after starting treatment for eating disorders at 197 one of the participating facilities. The assessment of comorbidities in R-AN patients was 198 carried out by specialized psychiatrists and psychologists at the treatment centers using a 199 comprehensive approach. This approach involved regular and ongoing monitoring of 200 psychiatric symptoms and comorbid conditions throughout the treatment process. The 201 assessment process encompassed clinical interviews and the administration of specific 202 symptom inventories and rating scales to obtain a comprehensive evaluation of comorbid 203 psychiatric disorders. 204

The HC (healthy control) group consisted of 310 adolescent or young-adult females 205 recruited through social media or university advertisements. All participants completed the 206 Eating Attitudes Test-26 (EAT-26; Garner et al., 1982) screening tool. Females who scored 207 higher than 20 on the EAT-26 (Dotti & Lazzari, 1998) and did not report any current 208 treatment for eating disorders were classified as "at-risk" for the study's purposes and assigned to the RI (reference/independent) group, resulting in a total of 36 "at-risk" females. From the remaining participants who scored lower than 20 on the EAT-26 and did not report 211 any current treatment for eating disorders, a random sample of 45 females was selected and 212 assigned to the HC group. It was a requirement for both the HC and RI groups that 213 participants have a normal Body Mass Index. 214

To be eligible for participation, individuals needed to demonstrate proficient command over both spoken and written Italian language. Exclusion criteria for all participants included a history of alcohol or drug abuse or dependence, neurological disorders, and intellectual or developmental disability. Cognitive function within the normal range was assessed using the Raven's Standard Progressive Matrices test (Raven et al., 2000). The eligibility criteria for all participants were evaluated through psychologist interviews by trained psychologists. Body mass index (BMI) values were determined in the laboratory.

The study included a predominantly Caucasian sample, with 97.7% of the participants identifying as Caucasian. A smaller proportion of participants identified as Asian-Italian (1.7%) and African-Italian (0.6%). Additionally, all selected participants were right-handed and were unaware of the study's specific objectives, ensuring a blind study design.

226 Procedure

During the initial session, participants underwent a clinical interview to determine
their eligibility for the study. Those who met the criteria and were selected proceeded to
anthropometric measurements and were asked to complete the psychometric scales listed
below. In a subsequent session, participants completed the PRL task and were subsequently
provided with a debriefing.

We compared the characteristics of the clinical sample with the controls by
administering the following scales: the EAT-26, the Body Shape Questionnaire-14 (BSQ-14;
Dowson & Henderson, 2001), the Social Interaction Anxiety Scale (SIAS; Mattick & Clarke,
1998), the Depression Anxiety Stress Scale-21 (DASS-21; Lovibond & Lovibond, 1995), the
Rosenberg Self-Esteem Scale (RSES; Rosenberg, 1965), the Multidimensional Perfectionism
Scale (MPS-F; Frost et al., 1990), and the Raven's Standard Progressive Matrices (Raven et
al., 2000). The results of these statistical analyses are provided in the Supplementary
Information (SI).

During the Probabilistic Reversal Learning (PRL) task, participants were presented with two stimuli simultaneously on a screen and were instructed to select one within a

242 2.5-second time limit by pressing a key. Trials were presented in an interleaved manner, with
243 a randomly drawn inter-trial interval ranging from 0.5 to 1.5 seconds. Following each trial, a
244 euro coin image was displayed as a reward for correct responses, while a strike-through image
245 of a euro coin served as a punishment for incorrect responses. Feedback was provided for 2
246 seconds after each trial.

The PRL task consisted of two blocks, each containing 160 trials. One block included pairs of food-related and food-unrelated images, while the other block exclusively used food-unrelated images. The images were selected randomly from sets of food-related and food-unrelated categories.

All images used in the study were obtained from the International Affective Picture
System (IAPS) database (Lang et al., 2005). The food-related category consisted of images
of french fries, cake, pancake, cheeseburger, and cupcake (IAPS #7461, 7260, 7470, 7451,
7405), while the food-unrelated category included images of a lamp, book, umbrella, basket,
and clothespin (IAPS #7175, 7090, 7150, 7041, 7052). For the control task, five images were
used for each of the two food-unrelated categories, i.e., five images of flowers (IAPS #5000,
5001, 5020, 5030, 5202) and five images of objects (IAPS #7010, 7020, 7034, 7056, 7170).

The PRL task comprised four epochs, each consisting of 40 trials where the same 258 image was considered correct. Feedback during the task was probabilistic, with the correct 259 image being rewarded in 70% of the trials, while negative feedback was provided in the 260 remaining 30% of the trials. Both blocks of the task included three rule changes in the form 261 of reversal phases. Participants were informed that stimulus-reward contingencies would change, but not the specifics of how or when this would occur. The objective of the participants was to maximize their earnings, which were displayed at the end of each block. Participants underwent a training block consisting of 20 trials prior to the start of the actual 265 experiment. The Psychtoolbox extensions in MATLAB (MathWorks) were used to program 266 the tasks (Brainard, 1997). 267

268 Transparency Openness

We report all data exclusion criteria and how the sample size was determined. Data and analysis code are available upon request to the corresponding author. Data were analyzed using Python and R version 4.3.1. The study was not preregistered.

272 Data analysis

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To model the two-choice decision over time in the PRL task, we used a hierarchical reinforcement learning drift diffusion model (RLDDM), as described in Pedersen, Frank, and Biele (2017) and Pedersen and Frank (2020). The RLDDM was estimated in a hierarchical Bayesian framework using the HDDMrl module of the HDDM (version 0.9.7) Python package (Fengler et al., 2021; Wiecki et al., 2013). It has been shown that hierarchical modeling of reinforcement learning task provides the best predictive accuracy compared to other methods (Geen & Gerraty, 2021; e.g., Gershman, 2016).

We chose a Bayesian approach for our study because estimating RLDDM models is
currently limited to Markov Chain Monte Carlo (MCMC) procedures. Moreover, by
prioritizing estimation over hypothesis testing, the Bayesian approach overcomes the binary
nature of decision-making inherent in null hypothesis significance testing (NHST) (Kruschke
Liddell, 2018). We determined credible effects by examining 95% credible intervals or
assessing the proportion of posterior samples (97.5%) indicating the direction of the effect.

Cognitive modeling analysis allows us to deconstruct decision-making task performance into its component processes. This approach enables the identification of deviations in the underlying mechanisms that may not be evident in the overall task outcome. The RLDDM consists of two key components: one describes how reward feedback is employed to update value expectations and the other describes how an agent uses these expectations to arrive at a decision.

The first component characterizes the learning process in terms of the delta learning

rule (Rescorla & Wagner, 1972):

$$Q_{a,i} = Q_{a,i-1} + \alpha (I_{a,i-1} - Q_{a,i-1}),$$

where Q refers to the expected values for option a on trial i, I represents the reward (with values 1 or 0), and α is the leaning rate, which scales the difference between the expected and actual rewards. A higher learning rate results in rapid adaptation to reward expectations, while a lower learning rate results in slow adaptation. We estimated two α parameters: The parameter α^+ is computed from reinforcements, whereas α^+ is computed from punishments.

The second component describes the selection rule for reinforced options. Typically, a softmax function is used, where the probability of selecting option a depends on its expected value relative to other options n, scaled by the inverse temperature parameter β :

$$p_{a,i} = \frac{e^{\beta Q_{a,i}}}{\sum_{j=1}^{n} e^{\beta Q_{j,i}}}.$$

In the RLDDM, this second component of decision-making is replaced by a
Drift-Diffusion Model [DDM; Ratcliff and McKoon (2008)] which assumes a stochastic
accumulation of evidence on each trial. The DDM includes four parameters: A drift rate
parameter (v), which describes the rate of (noisy) evidence accumulation; a decision
threshold parameter (a), which represents the amount of evidence needed to make a decision;
a non-decision time parameter (t), which accounts for the time devoted to sensory processing,
motor preparation, and motor output, and a starting point parameter (z), which accounts
for any predispositions in the initial decision variable towards either boundary.

Results

Demographic and Psychopathology Measures

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Mean age and Body Mass Index (BMI) for each group of participant were as follows: 313 patients with AN, mean age = 21.18 (SD = 2.41), average Body Mass Index (BMI) = 16.88314 (SD = 1.55); patients with BN, mean age = 20.39 (SD = 1.88), average BMI = 30.09 (SD = 1.88)315 5.47); HCs, mean age = 19.77 (SD = 1.06), average BMI = 21.62 (SD = 3.03); healthy 316 individuals at risk of developing eating disorders, mean age = 20.36 (SD = 1.44), average 317 BMI = 22.41 (SD = 4.79). Bayesian statistical analysis revealed no credible age differences 318 among the four groups (AN, BN, HC, and RI). AN participants displayed a lower mean BMI 319 than HC participants, while BN participants had a higher mean BMI than HC participants. 320 No noteworthy difference in BMI was observed between HC and RI participants. 321 Furthermore, there is credible evidence that the Rosenberg Self-Esteem Scale scores of all three groups (AN, BN, and RI) are smaller than those of the HC group. We also found credible evidence that individuals with AN, BN, and RI exhibited higher levels of dissatisfaction with their body shape, as measured by the BSQ-14 questionnaire, when 325 compared to the HCs. Individuals with AN displayed higher stress, anxiety, and depression 326 levels (as measured by the DASS-21) than HCs. Additionally, individuals with AN showed 327 credibly higher levels of social interaction anxiety (as measured by the SIAS) than HCs. All 328 three AN, BN, and RI groups exhibited higher levels of Concerns over mistakes and doubts 329 scores of the MPS scale compared to HCs. Individuals with AN also showed higher levels of 330 Personal standard scores of the MPS scale compared to HCs. Moreover, individuals with AN 331 displayed higher values on all three subscales of the EAT-26 questionnaire relative to HCs. 332 For more detailed information regarding these comparisons, please refer to the 333 Supplementary Information (SI). 334

Sixteen individuals with R-AN were diagnosed with a comorbid anxiety disorder, 8

with OCD, 1 with social phobia, and 1 with DAP.

337 Models selection

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To test the interference of disease-related information on the decision process, we
compared several RLDDMs in which we conditioned either none, each or all model's
parameters on group and context (disorder-related vs. disorder-unrelated information). For
each model, we computed the Deviance Information Criterion (DIC), and we selected the
model with the best trade-off between the fit quality and model complexity (i.e., the model
with the lowest DIC). The following RLDDM models were examined.

- 1. Model M1: This is the standard RLDDM. DIC = 39879.444.
- 2. Model M2: Extending M1, it includes separate learning rates for positive and negative reinforcements. DIC = 39124.890
- 3. Model M3: In this model, the α^+ and α^- parameters are based on the diagnostic group. DIC = 39194.763.
- 4. Model M4: Building upon M3, the α^+ and α^- parameters are conditioned on both the diagnostic group and image category. DIC = 38197.467.
- 5. Model M5: Expanding on M4, it considers the potential influence of both the diagnostic group and image category on the a parameter. DIC = 36427.448.
- 6. Model M6: Extending M5, it takes into account the possible influence of both the diagnostic group and image category on the drift rate (v) parameter. DIC = 36185.146.
- 7. Model M7: Building upon M6, it considers the potential influence of both the diagnostic group and image category on the non-decision time (t) parameter. DIC = 34904.053.
- 8. Model M8: Adding to Model M7, it estimates a potential bias in the starting point (z) parameter. DIC = 34917.762.
 - All the models were estimated using Bayesian methods with weakly informative priors.

provided in parentheses.

The model with the lowest DIC was Model M7. In Model M7, the parameters α^+ , α^- , a, v, and t (excluding z) are conditioned on both the diagnostic group and image category.

Model M7 was estimated using 15,000 iterations, with a burn-in period of 5,000 iterations. Convergence of the Bayesian estimation was evaluated using the Gelman-Rubin statistic. For all parameters in Model M7, the \hat{R} values were below 1.1 (maximum = 1.025, mean = 1.002), indicating no significant convergence issues. Collinearity and posterior predictive checks were also used to evaluate model validity (see SI).

To investigate the impact of disorder-related versus disorder-unrelated information on RL learning, we compared the posterior estimates of the RLDDM parameters of M7 between the two conditions (see Table 1).

Table 1

Posterior Parameter Estimates of DDMRL Model M7 by Group (R-AN, HC, RI) and

Context of PRL Choice (disorder-related vs. disorder-unrelated information). The learning

rates (α) are shown on a logit scale. The probability (p) describes the Bayesian test that the

posterior estimate of the parameter in the disorder-related context is greater than the

posterior estimate of the parameter in the disorder-unrelated context. Standard deviations are

Group	Par.	Neutral choice	Food choice	p	Cohen's d
R-AN	a	1.273 (0.039)	1.442 (0.040)	0.0013	0.802
R-AN	V	1.403 (0.320)	1.776 (0.342)	0.7907	0.190
R-AN	t	0.188 (0.011)	0.174 (0.011)	0.8311	-0.253
R-AN	α^{-}	1.815 (1.081)	0.738 (1.096)	0.2349	-0.432
R-AN	α^+	1.006 (0.899)	-1.786 (0.756)	0.0098	-1.206
НС	a	1.222 (0.033)	1.314 (0.034)	0.0256	0.474
НС	V	$2.157 \ (0.265)$	1.790 (0.263)	0.1606	-0.358

Group	Par.	Neutral choice	Food choice	p	Cohen's d
НС	t	0.183 (0.009)	0.172 (0.009)	0.8228	-0.280
НС	α^{-}	2.780 (0.874)	3.442 (0.980)	0.6993	0.298
НС	α^+	1.198 (0.680)	1.326 (0.700)	0.5544	0.071
RI	a	1.245 (0.041)	1.316 (0.039)	0.1026	0.403
RI	V	2.197 (0.322)	1.849 (0.307)	0.2133	-0.381
RI	t	0.188 (0.011)	0.186 (0.011)	0.5462	0.166
RI	α^{-}	2.857 (1.067)	2.904 (1.062)	0.5101	0.015
RI	α^+	1.573 (0.847)	0.739 (0.752)	0.2247	-0.438

Let consider first the evidence of context-dependent learning from within-group 371 comparisons. We found that, on average, individuals in the R-AN group demonstrate a 372 reduced learning rate in response to positive prediction errors (PEs) for disorder-related 373 choices, as compared to disorder-unrelated choices (Cohen's d = 1.206, p = 0.0098). In contrast, no substantial evidence was found indicating a difference in the learning rate 375 between disorder-related and disorder-unrelated choices in the HC (p = 0.5544) and RI (p =0.2247) groups. We found no credible difference in the learning rate from negative prediction errors between disorder-related and disorder-unrelated choices for any of the R-AN (p =378 (0.2349), HC (p = 0.6993), and RI (p = 0.5101) groups. Moreover, we found that both the 379 R-AN (Cohen's d = 0.802, p = 0.0013) and HC (Cohen's d = 0.474, p = 0.0256) groups 380 showed a higher decision threshold for disorder-related choices compared to 381 disorder-unrelated choices. 382

Further evidence of context-dependent learning emerges from between-groups
comparisons. When making disorder-related choices, individuals with R-AN displayed a
decreased learning rate following positive prediction errors (PEs) compared to both HC and
RI. Specifically, the learning rate after positive PEs was lower for R-AN compared to HC, p

= 0.0009, Cohen's d = 1.498. Similarly, R-AN exhibited a lower learning rate after positive 387 PEs compared to RI (p = 0.0085, Cohen's d = 1.209). In contrast, no credible difference in 388 the learning rate after positive PEs was found between R-AN and HC (p = 0.4325), as well 389 as between R-AN and RI (p = 0.3232), for choices unrelated to disorder information. 390 Concerning the learning rate after negative PEs, we found that R-AN showed a lower 391 learning rate compared to HC, but only for disorder-related choices: (p = 0.0274, Cohen's d)392 = 1.144). Individuals with R-AN showed a higher decision threshold for disorder-related 393 choices compared to both HC (Cohen's d = 0.622, p = 0.0068) and RI (Cohen's d = 0.454, p = 0.454394 = 0.0118) participants. No credible group differences were found for disorder-unrelated 395 choices. Additionally, we observed that both HC (Cohen's d = 0.520, p = 0.0344) and RI 396 (Cohen's d = 0.529, p = 0.0392) participants exhibited a faster accumulation of evidence and 397 more confident decision-making, as indicated by a higher average drift rate parameter, compared to individuals with R-AN. This difference was only evident for disorder-unrelated choices. Finally, no credible differences were found, for both within-group and between-group comparisons, regarding the non-decision time parameter (t).

402 Biased choices

To investigate a potential bias against food choices in individuals with R-AN during
the PRL task, regardless of their past action-outcome history, we examined the frequency of
food choices in PRL blocks where a food image was paired with a neutral image. Our
findings indicate no bias against the food image in the AN-R group, with a proportion of
food choices of 0.49, 95% CI [0.46, 0.51]. Moreover, there were no credible differences
between groups: contrast R-AN - HC = -0.007, 95% CI [-0.037, 0.024]; contrast R-AN - RI =
0.013, 95% CI [-0.019, 0.046].

410 Comorbidity

To ensure the broader applicability of our findings to the psychiatric population (Woodside & Staab, 2006), we included individuals with R-AN who also had comorbid

psychiatric conditions. Among the 40 individuals with R-AN in our study, comorbidities 413 included anxiety disorder (n=16), OCD (n=8), social phobia (n=1), and DAP (n=1). In a 414 further statistical analysis, we examined whether these comorbid conditions influence the 415 conservative learning behavior observed in individuals with R-AN when making 416 disorder-related choices. We applied model M7 to the individuals with R-AN and categorized 417 them based on the presence or absence of diagnosed comorbidities. Our statistical analysis 418 revealed no credible differences in parameters between the two groups. For the 419 disorder-related context, the parameter differences were as follows: $\Delta \alpha^- = 2.614, 95\%$ CI 420 $[-3.173, 8.364]; \Delta \alpha^{+} = -0.635, 95\% \text{ CI } [-4.301, 2.449]; \Delta a = -0.034, 95\% \text{ CI } [-0.188, 0.124];$ 421 $\Delta v = 0.230, 95\%$ CI [-1.203, 1.586]; $\Delta t = 0.002, 95\%$ CI [-0.050, 0.055]. For the 422 disorder-unrelated context, the parameter differences were: $\Delta \alpha^- = -0.768$, 95% CI [-6.570, 423 4.401]; $\Delta \alpha^+ =$ -1.739, 95% CI [-6.184, 1.654]; $\Delta a =$ -0.126, 95% CI [-0.281, 0.025]; $\Delta v =$ 0.744, 95% CI [-0.453, 1.886]; $\Delta t = -0.003, 95\%$ CI [-0.057, 0.052].

426 Discussion

In this within-subjects study, we investigated the influence of disorder-related information on probabilistic reversal learning in females with restrictive anorexia nervosa (R-AN), healthy female participants (HC), and females at-risk of developing eating disorders (RI). Consistent with our hypotheses, the results show that participants with R-AN displayed a slower learning rate following positive outcomes for choices associated with the disorder compared to outcomes for choices unrelated to the disorder. In contrast, we did not observe any credible differences in the learning rate between disorder-related and disorder-unrelated choices in the HC and RI groups.

Additionally, our study revealed that individuals with R-AN demonstrated lower learning rates for both positive and negative prediction errors compared to the HC group, and specifically for positive prediction errors compared to the RI group, but only for disorder-related choices. When it came to disorder-unrelated choices, no credible difference in learning rates was observed between the R-AN group on one side, and the HC and RI groups on the other.

Together, these results indicate that individuals with rR-AN exhibit context-dependent learning, where the presence of disorder-related information adversely affects RL performance, despite the absence of a generalized RL deficit. These results challenge the belief of a domain-general RL mechanism impairment in this particular population.

We also observed contextual effects for the DDM parameters of the hDDMrl model.

Specifically, we found that, on average, the R-AN group had a higher decision threshold

(parameter "a" in the hDDMrl model) compared to the HC and RI groups, but only for

disorder-related choices. This indicates that individuals with R-AN displayed a more

cautious or conservative decision-making behavior than the HC and RI groups, but only for

disorder-related choices Schiff, Testa, Rusconi, Angeli, & Mapelli (2021).

Further evidence supporting context-related learning is evident from the result which indicate that both healthy control (HC) and at-risk (RI) participants exhibited a faster accumulation of evidence and displayed more confident decision-making, as reflected by a higher average drift rate parameter, compared to individuals with restrictive anorexia nervosa (R-AN). However, this difference was specifically observed for disorder-unrelated choices. It is noteworthy that individuals with R-AN displayed slower evidence accumulation and less confident decision-making specifically in disorder-unrelated contexts, whereas this group difference was not observed for disorder-related choices. This finding further supports the notion of context-dependent learning in individuals with R-AN, particularly in the context of food-related information.

Further evidence of context-related learning come also from the result indicating that both HC and RI participants exhibited a faster accumulation of evidence and more confident decision-making, as indicated by a higher average drift rate parameter, compared to individuals with R-AN. However, this difference was only evident for disorder-unrelated choices. The fact that individuals with R-AN showed slower accumulation of evidence and less confident decision-making for in disorder-unrelated contexts, but this group difference was not found for disorder-related choices could be interpreted could be interpreted, again, as evidence for the specificity of context-dependent learning, for individuals with R-AN, for choices related to food-information.

There is a growing consensus that reward and punishment processing in anorexia 470 nervosa (AN) is not a generic process, but rather influenced by complex interactions between stimulus properties (e.g., type of reward/punishment cue) and contextual factors (e.g., long-term objectives, personality traits, temperamental dispositions, physiological states like hunger, etc.). A recent comprehensive review by @Haynos, Lavender, Nelson, Crow, and Peterson (2020) demonstrated that how individuals with AN perceive their experiences as 475 rewarding or punishing is influenced by factors such as predictability, controllability, 476 immediacy, and effort. For instance, behaviors associated with AN that are predictable, 477 controllable, and immediate (e.g., calorie counting or purging) may be rewarding, providing 478 a sense of control and accomplishment. Conversely, behaviors that are unpredictable and 479 uncontrollable (e.g., social outcomes) may be perceived as punishing, leading to increased 480 anxiety and distress. 481

However, most previous studies have primarily focused on exploring the subjective value assigned to various experiences by individuals with AN, regardless of their inherent rewarding or punishing properties. In contrast, the current study investigates the impact of contextual factors on reinforcement learning (RL). To our knowledge, this is the first study to demonstrate that individuals with R-AN exhibit slower learning specifically for disorder-related choices, while maintaining intact RL performance for disorder-unrelated choices. These findings challenge the notion of a domain-general RL mechanism impairment in this population.

515

It is important to acknowledge that the experimental manipulation employed in this 490 study is irrelevant to the task outcome, meaning that optimal reinforcement learning (RL) 491 performance should not be affected by it. However, we observed a significant impact of this 492 manipulation on the PRL performance of individuals with R-AN, while no such impact was 493 observed in the performance of healthy controls (HCs) and healthy controls at risk of eating 494 disorders. In the existing literature, there are limited pieces of evidence regarding the 495 influence of outcome-irrelevant information on RL in the general population. Notably, 496 Shahar et al. (2019) demonstrated that image/effector response mapping can affect 497 associative learning in a PRL task, even if only image identity predicts rewards. As detailed 498 in the Supplementary Information (SI), we successfully replicated these findings across all 499 three groups included in our study, thus further supporting the notion that various forms of 500 outcome-irrelevant information can impact RL learning, both in the general population and in individuals with eating disorders. It is noteworthy that the effects of image/effector 502 response mapping described by Shahar et al. (2019) appear to be similar in both the general population and the patient groups, whereas the effects of outcome-irrelevant disorder-related 504 information were specific to the R-AN group. 505

Other recent studies have focused on investigating context-specific learning in eating 506 disorders. One task specifically designed for this purpose is the two-step Markov decision 507 task, which distinguishes between automatic or habitual (model-free) learning and controlled 508 or goal-directed (model-based) learning. For instance, studies conducted by Foerde et al. 509 (2021) and Onysk and Seriès (2022) employed similar experiments using the two-step task 510 paradigm. Foerde et al. (2021) compared a monetary two-step task and a food-related 511 two-step task, while Onysk and Seriès (2022) utilized stimuli unrelated to food or body 512 images (i.e., pirate ships and treasure chests) with rewards associated with body image 513 dissatisfaction.

The results of these studies consistently demonstrated that individuals with AN tend

to exhibit a stronger inclination towards habitual control over goal-directed control across
different domains compared to healthy controls. However, no significant differences were
observed in learning rates as a function of context, nor between AN patients and healthy
controls, according to these findings. In contrast, the present study reveals that the learning
process itself in individuals with R-AN can be influenced by disorder-related information,
even when such information is not directly relevant to the task outcome.

The implications of the present findings, if replicated by future studies, are relevant to 522 the treatment of anorexia nervosa (AN). Current treatment practices address the issue of 523 cognitive inflexibility in AN, with Cognitive Remediation Therapy (CRT) being proposed as 524 an adjunct treatment targeting specific cognitive processes in AN and other eating disorders. 525 CRT involves cognitive exercises and behavioral interventions aimed at improving central 526 coherence abilities, reducing cognitive and behavioral inflexibility, and enhancing thinking 527 style comprehension (Tchanturia et al., 2010). A key aspect of CRT is to avoid focusing on 528 symptom-related themes and instead utilize neutral stimuli in cognitive and behavioral 529 exercises. This approach aims to establish a therapeutic alliance and reduce drop-out rates, particularly among AN patients. 531

However, recent evidence suggests that CRT may not consistently enhance central coherence abilities, cognitive flexibility, or symptoms associated with eating disorders (Hagan, Christensen, & Forbush, 2020; Tchanturia, Giombini, Leppanen, & Kinnaird, 2017). In response to this, Trapp, Heid, Röder, Wimmer, and Hajak (2022) have proposed improvements to address practical issues encountered in the application of CRT. They question the use of neutral stimuli and draw support from Beck's cognitive theory of depression (Beck & Alford, 2009).

The proposition presented by Trapp et al. (2022) aligns with the hypothesis of our study, which suggests that contextual factors play a crucial role in the maladaptive eating behavior observed in individuals with R-AN, extending beyond deficits in the underlying

reinforcement learning mechanism alone. If abnormal reward learning is indeed identified as
a significant anomaly among individuals with R-AN, particularly in relation to
disorder-relevant choices, it would imply that treatments focused on enhancing cognitive
flexibility and reinforcement learning processes specific to disorder-relevant stimuli could
hold significant promise for this population.

There are several important questions that remain for future research. 1) One aspect to consider is the use of symbolic rewards and punishments in our study, represented by images of a one euro coin and a barred representation of a one euro coin, respectively. These 549 rewards and punishments were merely symbolic, and it is unclear how the use of concrete, 550 non-symbolic rewards and punishments would impact the findings. Additionally, the 551 subjective value of one euro, or the loss of one euro, may vary among participants. Therefore, 552 future studies could aim to determine the equivalence of subjective values for rewards and 553 punishments to enhance the understanding of the underlying processes. 2) Our study only 554 included individuals with R-AN who were not in the most severe stage of the illness, as they 555 were recruited from a center for voluntary medical and psychological support. We did not 556 examine R-AN patients who require hospitalization due to the life-threatening nature of 557 their illness. It is possible that at the later stages of the illness, associative learning abilities, 558 which were preserved in the present sample under neutral conditions, may become impaired. 559 Therefore, investigating the impact of illness severity on context-dependent learning in R-AN 560 patients is an important avenue for future research. 3) While we observed no difference in 561 the choice behavior of R-AN patients, as measured by the relative frequency of image choices, 562 when selecting between a neutral image and a food image, we did find a slower learning rate and lower decision threshold for R-AN patients compared to healthy controls in the RLDDM model when compared to choosing between two neutral images. It is possible that the higher "salience" of food images compared to neutral images could be better captured by other measures, such as fixation length or the number of fixations, rather than solely relying on the 567 relative frequency of image choices. This warrants further exploration in future studies. 4) It 568

is worth noting that our study excluded women under the age of 18. However, this age range is a critical period as the onset of AN during this stage may have a more profound impact on associative learning, given the ongoing cognitive development and less-developed protective factors. Therefore, future studies should take into consideration the inclusion of participants in this age range to better understand the influence of context-dependent learning in R-AN.

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