- 1 Impact of Contextual Learning on Reinforcement Learning Performance in Anorexia Nervosa
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Abstract

**Objective:** This study compared individuals with Restrictive Anorexia Nervosa (R-AN; n = 15 40) to Healthy Controls (HCs; n = 45) and healthy controls at RIsk of eating disorders (RI; 16 n = 36) in a Probabilistic Reversal Learning (PRL) task. The aim was to investigate 17 whether R-AN individuals perform similarly to HCs and RIs in neutral contexts but show 18 significant impairments in food-related contexts. Method: Participants completed a PRL 19 task, making choices related to their disorder or unrelated to it. Results: R-AN individuals showed lower learning rates for disorder-related decisions, but their performance on neutral 21 decisions was similar to the HC and RI groups. Additionally, only the R-AN patients exhibited reduced learning rates for food-related decisions compared to food-unrelated 23 decisions. **Discussion:** These findings suggest that contextual cues, like food images, negatively impact Reinforcement Learning (RL) processes in individuals with R-AN. This 25 raises questions about whether the impaired RL performance should be solely attributed to compromised learning mechanisms, especially when RL abilities appear intact in neutral contexts. The study's insights may have implications for developing interventions that target decision-making processes in individuals with R-AN.

Keywords: anorexia nervosa, reinforcement learning, contextual learning, probabilistic reversal learning

Word count: X

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33 Impact of Contextual Learning on Reinforcement Learning Performance in Anorexia Nervosa

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 44 the mechanisms underlying 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). In particular, cognitive inflexibility in AN refers to difficulties adapting thoughts and actions to new information. This rigidity can lead to repetitive behaviors. On the other hand, reinforcement learning is the brain's 50 way of optimizing decision-making based on action outcomes, where positive outcomes 51 encourage repetition and negative outcomes discourage it. In AN, cognitive inflexibility can 52 hinder updating of action-outcome associations, affecting adaptive behavior learning and leading to impaired reinforcement learning processes. This may contribute to difficulties recognizing the negative consequences of restrictive eating behaviors, perpetuating the disorder. While studies have explored reward processing abnormalities, our understanding of learning-related anomalies in AN remains limited (Schaefer & Steinglass, 2021).

In relation to dysfunctions reward responsiveness among individuals with AN, research

has revealed that the intense levels of dietary restriction and physical activity typically associated with AN can trigger the activation of reward pathways in the brain (Keating, 2010; Keating, Tilbrook, Rossell, Enticott, & Fitzgerald, 2012; Selby & Coniglio, 2020). 61 Additionally, individuals with AN may exhibit diminished reward responses specifically towards food-related stimuli (Wierenga et al., 2014). In a broader sense, research has shown that AN is associated with 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, reduced tolerance for uncertainty, increased anxiety, and heightened sensitivity to punishment (Fladung, Schulze, 67 Schöll, Bauer, & Groen, 2013; Jappe et al., 2011; Keating et al., 2012; O'Hara, Campbell, & Schmidt, 2015). These factors collectively contribute to an altered response to negative feedback and a propensity to actively avoid aversive outcomes (Jonker, Glashouwer, & Jong, 2022; Matton, Goossens, Braet, & Vervaet, 2013). Neuroimaging studies have further supported these findings by revealing neural dysfunctions in individuals with AN regarding their response to loss and aversive taste stimuli (Bischoff-Grethe et al., 2013; Monteleone et al., 2017; Wagner et al., 2007).

Given the crucial importance of RL in acquiring knowledge from past experiences,
extensive research has been conducted to examine potential deficits in RL among individuals
diagnosed with 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). However, the findings of these studies have been mixed. For example,
Ritschel et al. (2017) found that individuals who had recovered from AN had impaired RL
performance compared to healthy controls (HCs) on a Probabilistic Reversal Learning (PRL)
task, particularly in response to negative feedback. In contrast, Bernardoni et al. (2018)
found that AN patients had a higher learning rate from punishment than HCs. Similarly,
Sarrar et al. (2016) found no differences in task performance between individuals with acute
AN and HCs using the Probabilistic Object Reversal Task with neutral stimuli. Geisler et al.

<sup>86</sup> (2017) also found no group differences in a PRL task with neutral stimuli and monetary feedback.

To shed light on the potential reinforcement RL deficits in AN, researchers have incorporated food-related information into the PRL paradigm. For example, Zhang, Manson, Schiller, and Levy (2014) found that individuals with binge-eating disorder (BED) exhibited poorer performance when exposed to food-related feedback, indicating a vulnerability to food-related cues. However, attempts to replicate these findings in AN have yielded conflicting results. Hildebrandt et al. (2015) reported increased inflexibility in AN individuals using a PRL task with food-related feedback, while Hildebrandt et al. (2018) found no differences in PRL performance between AN patients and healthy controls (HCs) when employing the same paradigm.

Given the inconsistent findings in behavioral experiments regarding RL in AN, we propose that these discrepancies may be partly attribute to the predominant use of general stimuli instead of stimuli specifically relevant to the disorder (Schaefer & Steinglass, 2021). Furthermore, when disorder-related information has been incorporated, it has typically been limited to the feedback provided after the participant's choice, with the stimuli presented during the decision-making process unrelated to the disorder. This approach primarily emphasizes the consequences of the choices, neglecting the contextual factors surrounding the decision-making process.

From a theoretical perspective, the methodological choices made in previous studies overlook the critical role of context in learning processes. Contextual learning (Heald, Lengyel, & Wolpert, 2023) draws upon the notion, grounded in the human memory literature, that memory retrieval depends on the match between the conditions during learning and testing. When there is a mismatch, retrieval is impaired. Applying this concept to RL in AN (Rosas, Todd, & Bouton, 2013), it can be hypothesized that contextual factors, such as individual characteristics, long-term goals, and situational influences, can contribute

to impaired RL specifically in decision-making related to the disorder. This impairment can occur even when RL performance remains intact for decisions unrelated to the disorder (Haynos, Widge, Anderson, & Redish, 2022). In other words, we propose that intermittent impaired RL performance in AN may arise from contextual factors that activate specific learning modes, rather than indicating a fundamental alteration in the underlying learning processes in the brain (for a discussion, see Bernardoni et al., 2021).

To examine the proposed hypothesis, we conducted a study using a modified version of
the standard PRL task. Unlike previous studies that used general stimuli (Schaefer &
Steinglass, 2021), our task incorporated two distinct contexts. In one context, participants
made choices between a stimulus related to the disorder (e.g., a caloric food) and a stimulus
unrelated to the disorder (e.g., a lamp). In the other context, participants made choices
between two stimuli unrelated to the disorder (i.e., flower vs. objects).

Based on the responses to food stimuli often seen in individuals with AN, which
typically exhibit reduced reward, increased aversion, and inhibition (Haynos, Lavender,
Nelson, Crow, & Peterson, 2020), we hypothesized that there would be a more conservative
learning rate for disorder-related choices compared to disorder-unrelated choices within a
PRL task. Additionally, we anticipated a lower learning rate for disorder-related choices in
individuals with AN compared to HCs. Conversely, we expected no learning abnormalities in
individuals with AN for choices unrelated to the disorder.

131 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.

### 135 Participants

The study included 40 individuals diagnosed with Restricting-Type Anorexia Nervosa 136 (R-AN) according to the DSM-5 criteria and 45 healthy volunteers (Table 2). The 137 participants with R-AN were recruited from three facilities in Italy: the Specchidacqua 138 Institute in Montecatini (Pisa), the Villa dei Pini Institute in Firenze, and the Gruber 139 Center, Outpatient Clinic in Bologna. The treatment approach consisted of Cognitive 140 Behavioral Therapy and family-based treatment, with patients receiving treatment for 2 to 6 141 hours per day, 2 days per week. The treatment program included various components such 142 as individual therapy, family therapy, group therapy, nutritional counseling, psychiatric care, 143 and medical monitoring. The diagnosis of AN was made by specialized psychiatrists and 144 psychologists through a semi-structured interview based on the DSM-5 criteria, at the start 145 of treatment. 146

The study recruited additional 310 female adolescents or young adults through social 147 media or university advertisements, and they completed the Eating Attitudes Test-26 148 (EAT-26) screening tool. Those scoring above 20 on the EAT-26 and not receiving current 149 treatment for eating disorders were classified as "at-risk" [RI; Dotti and Lazzari (1998)], 150 resulting in 36 individuals. From the remaining participants scoring below 20 on the EAT-26 151 and not receiving current treatment for eating disorders, 45 females were randomly selected 152 and assigned to the healthy control (HC) group. Both the RI and HC groups had 153 participants with a normal Body Mass Index (BMI). More details about eligibility criteria 154 and sample characteristics can be found in the Supplementary Information (SI). 155

#### 6 Procedure

In the initial session, participants underwent a clinical interview to determine their eligibility for the study. Those who met the criteria proceeded to anthropometric measurements and completed a battery of psychometric scales: the Eating Attitude Test (EAT-26; Garner (1991)), the Body Shape Questionnaire-14 [BSQ-14; Dowson and

Henderson (2001)], the Social Interaction Anxiety Scale [SIAS; Mattick and Clarke (1998)],
the Depression Anxiety Stress Scale-21 [DASS-21; Lovibond and Lovibond (1995)], the
Rosenberg Self-Esteem Scale [RSES; Rosenberg (1965)], and the Multidimensional
Perfectionism Scale [MPS-F; Frost, Marten, Lahart, and Rosenblate (1990)]. In a subsequent
session, participants completed the PRL task. Participants were told they would be playing
a simple computer game with the objective of accumulating as many "virtual euro" as
possible (see Figure 1).

The stimuli shown in each trial were randomly selected from sets of food-related and food-unrelated images. All images used in the study were obtained from the International Affective Picture System (IAPS) database (Lang, Bradley, Cuthbert, et al., 1997) – for details, see the SI.

### 172 Data analysis

To analyze the temporal dynamics of the two-choice decision-making in the PRL task,
we employed a hierarchical reinforcement learning drift diffusion model (RLDDM), as
described in Pedersen, Frank, and Biele (2017) and Pedersen and Frank (2020). Cognitive
modeling analysis allows us to deconstruct decision-making task performance into its
component processes, which can help us identify deviations in the underlying mechanisms
that may not be evident in the overall task outcome.

We used a Bayesian approach in our study because estimating RLDDM models is

currently only possible using Markov chain Monte Carlo (MCMC) procedures. Additionally,

the Bayesian approach prioritizes estimation over hypothesis testing, which helps to

overcome 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.

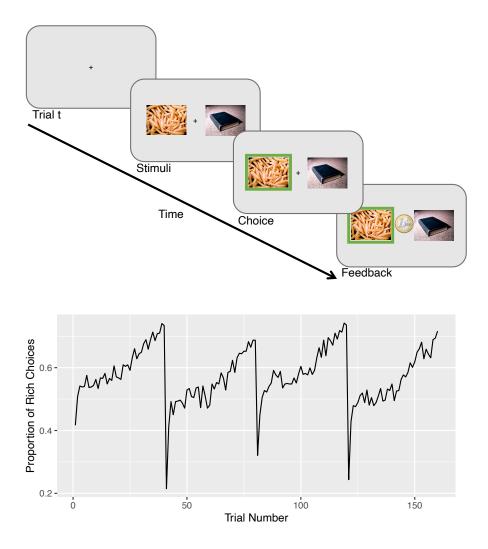


Figure 1. Top. During the PRL task, participants were presented with two images and had to choose the "correct" image based on trial-and-error feedback within 2.5 seconds. A euro coin image was displayed as a reward for correct responses, while a strike-through image of a euro coin served as a punishment for incorrect responses (left or right button press). The PRL task consisted of two blocks of 160 trials each. One block included pairs of food-related and food-unrelated images, while the other block only included food-unrelated images. The figure illustrates a single trial of the PRL task. **Bottom.** The trial-by-trial proportion of choosing the image with the highest probability of reward in the first epoch is shown for all participants. Initially, when participants have limited knowledge of the contingencies, the proportion of positive rewards is at chance level. However, as they engage in trial-and-error learning, their action selection improves, leading to enhanced performance and increased rewards. Following a context switch, there is an abrupt decline in performance, which is then followed by a gradual recovery that eventually levels off. It is worth noting that in this particular experiment, "correct choices" were rewarded positively only 70% of the time, thus establishing an upper limit of 0.7 on the plateau. Each session comprised 160 trials and included three context switches.

The RLDDM consists of two key components. The first component describes how reward feedback is used to update value expectations, using a delta learning rule (Rescorla & Wagner, 1972). The second component describes how an agent uses these expectations to arrive at a decision, using a drift-diffusion model (Ratcliff & McKoon, 2008). The DDM assumes that evidence for each option accumulates stochastically on each trial, until a decision is made (for details, see SI).

## The RLDDM has six basic parameters:

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- $\alpha^+$  and  $\alpha^-$ : These parameters quantify the learning rate in the Rescorla-Wagner delta learning rule. A higher learning rate results in rapid adaptation to reward expectations, while a lower learning rate results in slow adaptation. The parameter  $\alpha^+$  is computed from reinforcements, whereas  $\alpha^-$  is computed from punishments.
  - v: The drift rate is the average speed of evidence accumulation toward one decision.
  - a: The decision boundary is the distance between two decision thresholds. An increase of a increases the evidence needed to make a decision. The increase of a leads to a slower but more accurate decision; a decrease in a results in a faster but error-prone decision.
  - t: The non-decision time is the time spent for stimuli encoding or motor execution (i.e., time not used for evidence accumulation).
  - z: The starting point parameter captures a potential initial bias toward one or the other boundary in absence of any stimulus evidence.
- To assess the presence of context-dependent learning, we conditioned the model's parameters on two contexts: disorder-related choices and disorder-unrelated choices. This allowed us to examine how the model's parameters varied in response to these different contextual conditions.

210 Results

#### 211 Models selection

We evaluated context-dependent learning by comparing several RLDDM models that 212 differed in how they conditioned the model's parameters on group (R-AN, HC, RI) and 213 context (disorder-related choices and disorder-unrelated choices). We used the Deviance 214 Information Criterion (DIC) to balance model fit and complexity, and selected the model 215 with the lowest DIC as the best trade-off. The following RLDDM models were examined. 216 Model M1: Standard RLDDM without conditioning. DIC = 39879.444. Model M2: Separate 217 learning rates for positive and negative reinforcements. DIC = 39124.890 Model M3: 218 Group-based  $\alpha^+$  and  $\alpha^-$  parameters. DIC = 39194.763. Model M4: Group and 219 context-based  $\alpha^+$  and  $\alpha^-$  parameters. DIC = 38197.467. Model M5: Group and 220 context-based  $\alpha^+$ ,  $\alpha^-$ , and a parameters. DIC = 36427.448. Model M6: Group and 221 context-based  $\alpha^+$ ,  $\alpha^-$ , a, and drift rate (v) parameters. DIC = 36185.146. Model M7: Group 222 and context-based  $\alpha^+$ ,  $\alpha^-$ , a, v, and non-decision time (t) parameters. DIC = 34904.053. 223 Model M8: Group and context-based  $\alpha^+$ ,  $\alpha^-$ , a, v, t, and starting point (z) parameters. DIC 224 = 34917.762. Among the evaluated models, Model M7 had the lowest DIC, indicating the 225 best trade-off between goodness of fit and model complexity. In Model M7, the parameters  $\alpha^+$ ,  $\alpha^-$ , a, v, and t (excluding z) were conditioned on both the group and the context.

#### 228 Modelling results

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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. The  $\hat{R}$  values for all parameters in Model M7 were below 1.1, indicating that the model converged well. 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 Model 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  $(\alpha)$  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 provided in parentheses.

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	$\alpha^{-}$	1.815 (1.081)	0.738 (1.096)	0.2349	-0.432
R-AN	$\alpha^+$	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
НС	t	0.183 (0.009)	0.172 (0.009)	0.8228	-0.280
НС	$\alpha^{-}$	2.780 (0.874)	3.442 (0.980)	0.6993	0.298
НС	$\alpha^+$	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	$\alpha^-$	$2.857 \ (1.067)$	2.904 (1.062)	0.5101	0.015
RI	$\alpha^+$	1.573 (0.847)	$0.739 \ (0.752)$	0.2247	-0.438

Let's first consider the evidence of context-dependent learning from within-group comparisons (Figure 2, panel B). We found that individuals in the R-AN group had a

reduced learning rate from rewards for disorder-related choices, compared to disorder-unrelated choices (Cohen's d=-1.206, p=0.0098). However, no credible difference was found in the learning rate between disorder-related and disorder-unrelated choices in the HC (p=0.5544) or RI (p=0.2247) groups. We found no credible difference in the learning rate from punishments between disorder-related and disorder-unrelated choices for any of the R-AN (p=0.2349), HC (p=0.6993), and RI (p=0.5101) groups. Moreover, we found that individuals with R-AN showed a higher decision threshold for disorder-related choices compared to disorder-unrelated choices (Cohen's d=0.802, p=0.0013) – Figure 3, panel B.

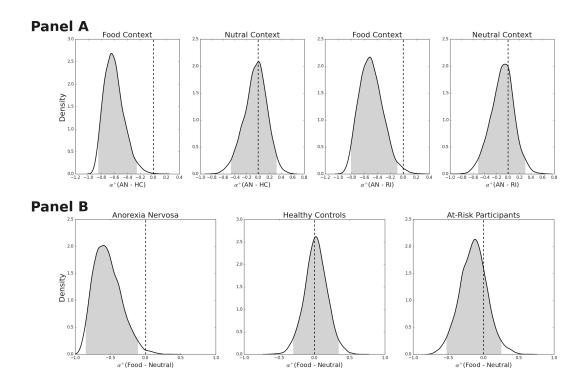


Figure 2. Panel A. Plots of the posterior distribution of the group effects (AN - HC; AN - RI) for parameter  $\alpha^+$  of the DDMRL, for disorder-related choices (Food context) and disorder-unrelated (Neutral context) choices. Panel B. Plots of the posterior distribution of the within-group effects  $(\alpha_{food}^+ - \alpha_{neutral}^+)$  across the three groups of participants.

Further evidence of context-dependent learning emerges from between-groups
comparisons. When making disorder-related choices, individuals with R-AN displayed a

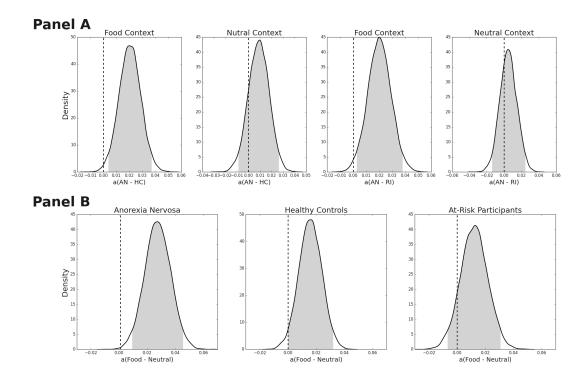


Figure 3. Panel A. Plots of the posterior distribution of the group effects (AN - HC; AN - RI) for parameter a of the DDMRL, for disorder-related choices (Food context) and disorder-unrelated (Neutral context) choices. Panel B. Plots of the posterior distribution of the within-group effects  $(a_{food} - a_{neutral})$  across the three groups of participants.

decreased learning rate from rewards compared to both HC (p = 0.0009, Cohen's d = 1.498) 249 and RI (p = 0.0085, Cohen's d = 1.209) – Figure 2, panel A. In contrast, no credible 250 difference in the learning rate from rewards was found between R-AN and HC (p = 0.4325), 251 as well as between R-AN and RI (p = 0.3232), for choices unrelated to disorder information. 252 Individuals with R-AN showed a higher decision threshold for disorder-related choices 253 compared to both HC (Cohen's d = -0.622, p = 0.0068) and RI (Cohen's d = -0.454, p =0.0118) participants, whereas no credible group differences were found for disorder-unrelated 255 choices (Figure 3, panel A). Finally, no credible differences were found, for both within-group and between-group comparisons, regarding the drift rate  $(\nu)$  and the non-decision time 257 parameters (t).

#### 259 Preferential choices

To investigate the presence of a bias against food choices in individuals with R-AN 260 during the PRL task, regardless of their past action-outcome history, we analyzed the 261 frequency of food choices in PRL blocks where a food image was paired with a neutral image. 262 Our results show that the AN-R group did not exhibit a bias against the food image, with a 263 proportion of food choices estimated at 0.49, 95% CI [0.46, 0.51]. Furthermore, there were no 264 credible differences in food choices between the R-AN group and the HC group (contrast 265 R-AN - HC = -0.007, 95% CI [-0.037, 0.024]) or between the R-AN group and the RI group 266 (contrast R-AN - RI = 0.013, 95% CI [-0.019, 0.046]). 267

# 268 Comorbidity

To examine the potential impact of comorbidity and medication status on the present 269 results, we compared R-AN participants who had diagnosed comorbidities (45% of the 270 sample) and those without any comorbid conditions using Model M7. We did not find any 271 credible differences in parameters between the two groups. Specifically, when considering the 272 disorder-related context, the parameter differences were as follows:  $\Delta \alpha^- = 2.614, 95\%$  CI 273  $[-3.173, 8.364]; \Delta \alpha^{+} = -0.635, 95\% \text{ CI } [-4.301, 2.449]; \Delta a = -0.034, 95\% \text{ CI } [-0.188, 0.124];$ 274  $\Delta v = 0.230, 95\%$  CI [-1.203, 1.586];  $\Delta t = 0.002, 95\%$  CI [-0.050, 0.055]. Similarly, for the disorder-unrelated context, the parameter differences were:  $\Delta \alpha^- = -0.768$ , 95% CI [-6.570, 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]. The correlation between comorbidity and medication was 0.78. 279

# 280 Discussion

Our study reveal a context-dependent learning asymmetry in individuals with R-AN, specifically in the positive learning rate ( $\alpha^+$ ). This asymmetry is evident when comparing their performance in the PRL task for disorder-related choices versus disorder-unrelated choices. Notably, this difference is not observed in the two control groups.

The presence of context-dependent learning asymmetry is also supported by between-group comparisons. Individuals with R-AN exhibited lower learning rates ( $\alpha^+$ ) compared to the HC and RI group. However, these differences were observed only for disorder-related choices. In contrast, no credible differences in learning rates were found among the three groups for choices unrelated to the disorder.

Support for context-dependent learning in R-AN is also provided by the DDM 290 parameters of the RLDDM model. Specifically, we observed that the R-AN group exhibited 291 a higher decision threshold (parameter "a" in the RLDDM model) compared to the HC and 292 RI groups, but this difference was only evident in the context of disorder-related choices. 293 Additionally, individuals with R-AN exhibited a higher decision threshold for disorder-related choices compared to disorder-unrelated choices, which was not seen in the HC and RI groups. Overall, these results suggest that individuals with R-AN tended to display a more cautious or conservative decision-making behavior in relation to choices related to the disorder (see also Caudek, Sica, Cerea, Colpizzi, & Stendardi, 2021; Schiff, 298 Testa, Rusconi, Angeli, & Mapelli, 2021). We did not find any credible contextual effects or group differences for the parameters  $\nu$  and t. 300

The analysis of preferential choices supports the conclusion that the learning
performance asymmetry observed in individuals with R-AN is not due to a preferential
selection of the disorder-unrelated image during the learning task. Additionally, our analysis
examining the relationship between the model's parameters and the presence of
comorbidities indicates that the learning performance asymmetry in individuals with R-AN
cannot be attributed to comorbid conditions.

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#### General discussion

In this study, we investigated reinforcement learning using a behavioral paradigm that included two distinct learning contexts: one involving choices related to food and the other involving choices unrelated to food. We compared the performance of patients with R-AN to age-, gender-, and education-matched healthy controls, as well as healthy controls at-risk of developing eating disorders. Consistent with our hypotheses, our findings revealed a lower learning rate in the disorder-related context for individuals with R-AN, whereas both healthy participants and at-risk individuals learned equally well in both contexts.

In PRL tasks, a participant's performance can be influenced by two potential factors. 315 First, there may be a learning impairment, where participants struggle to accurately update 316 the value of the stimuli. Second, there may be a decision impairment, where participants 317 may still select the wrong stimulus despite having intact learning processes. Our results show 318 that individuals with R-AN may struggle with both accurately updating the value of 319 disorder-related stimuli and making appropriate decisions based on this information. 320 However, we did not observe similar impairments in decision making for disorder-unrelated 321 choices. These findings provide evidence for context-dependent learning in individuals with 322 R-AN, where the inclusion of disorder-related information negatively impacts their RL 323 performance. It is important to note that this effect is specific to the disorder-related context 324 and does not suggest a generalized RL deficit in individuals with R-AN. Thus, our results 325 challenge the notion of a domain-general RL mechanism impairment in this population (see 326 Bernardoni et al., 2021). 327

Previous studies have demonstrated that reward and punishment processing in individuals with AN is influenced by stimulus properties and contextual factors. For instance, predictable and controllable behaviors such as calorie counting or purging are often perceived as rewarding, providing individuals with a sense of control and accomplishment. Conversely, unpredictable and uncontrollable situations, such as social outcomes, can be perceived as punishing, leading to heightened anxiety and distress (Haynos et al., 2020).
While previous studies have predominantly examined the impact of context on the subjective value attributed to experiences in AN, our study expands on this research by demonstrating that context plays a crucial role in the actual learning process itself (Heald et al., 2023).
This goes beyond solely influencing subjective value and provides valuable insights into how reward and punishment processing operates in AN.

Other recent studies have focused on investigating context-specific learning in eating 339 disorders. One task specifically designed for this purpose is the two-step Markov decision 340 task, which distinguishes between automatic or habitual (model-free) learning and controlled 341 or goal-directed (model-based) learning. For instance, studies conducted by Foerde et al. 342 (2021) and Onysk and Seriès (2022) employed similar experiments using the two-step task 343 paradigm. Foerde et al. (2021) compared a monetary two-step task and a food-related 344 two-step task, while Onysk and Seriès (2022) utilized stimuli unrelated to food or body 345 images (i.e., pirate ships and treasure chests) with rewards associated with body image 346 dissatisfaction. The results of these studies consistently demonstrated that individuals with 347 AN tend to exhibit a stronger inclination towards habitual control over goal-directed control 348 across different domains compared to healthy controls. However, these studies did not 349 identify significant differences in learning rates based on context or between AN patients and 350 healthy controls. In contrast, the present study reveals that, in individuals with R-AN, the 351 learning process per se (i.e., the learning rates) can be influenced by contextual 352 (disorder-related) information, even when contextual information is not directly relevant to 353 the task outcome.

The finding that individuals with R-AN demonstrated a conservative learning rate specifically for rewards in response to disorder-related context, but not for punishments, supports a neurobiological model suggesting that AN symptoms are maintained by diminished responses to rewarding stimuli and exaggerated responses to aversive stimuli,

potentially due to an overreliance on cognitive control brain circuitry (Wierenga et al., 2014). 359 A study by Bernardoni et al. (2018), which used a PRL task with disorder-unrelated stimuli, 360 revealed increased learning rates specifically after punishments in AN. This study suggested 361 that AN individuals, when faced with negative feedback, tend to critically reassess their 362 beliefs more quickly than healthy controls (HCs), leading them to base decisions on more 363 recent experiences. Such inclination may be linked to pre-existing harm-avoidant traits in 364 AN patients, characterized by a reduced tolerance for negative outcomes. Considering these 365 factors, we speculate that the lack of contextual effect on negative learning rates in our study may arise from a trade-off between the conservative learning induced by disorder-related cues 367 and the increased learning rate observed after punishment. 368

The hypothesis proposing that reinforcement learning (RL) anomalies in individuals 369 with anorexia nervosa (AN) may be influenced by contextual factors carries significant 370 implications for treatment strategies. Currently, Cognitive Remediation Therapy (CRT) is 371 utilized to address cognitive inflexibility in AN and other eating disorders. CRT involves 372 cognitive exercises and behavioral interventions aimed at improving central coherence 373 abilities, reducing cognitive and behavioral inflexibility, and enhancing thinking style 374 comprehension (Tchanturia, Davies, Reeder, & Wykes, 2010). A key aspect of CRT is to 375 avoid addressing symptom-related themes and instead utilize neutral stimuli in cognitive and 376 behavioral exercises. This approach aims to establish a therapeutic alliance and reduce drop-out rates, particularly among individuals with AN. However, recent evidence suggests 378 that CRT may not consistently improve central coherence abilities, cognitive flexibility, or 379 symptoms associated with eating disorders (Hagan, Christensen, & Forbush, 2020; Tchanturia, Giombini, Leppanen, & Kinnaird, 2017). In response to these findings, Trapp, Heid, Röder, Wimmer, and Hajak (2022) propose modifications to address practical 382 challenges encountered in the application of CRT. They question the use of neutral stimuli 383 and draw support from Beck's cognitive theory of depression (Beck & Alford, 2009). This 384 proposition aligns with the hypothesis of our study. If further studies consistently

demonstrate that maladaptive RL is context-dependent, it would necessitate a shift in intervention approaches.

There are few important limitations and questions for future research. 1) One aspect 388 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 rewards and punishments were merely symbolic, and it is unclear how the use of concrete, 391 non-symbolic rewards and punishments would impact the findings. Additionally, the 392 subjective value of one euro, or the loss of one euro, may vary among participants. Therefore, 393 future studies could aim to determine the equivalence of subjective values for rewards and 394 punishments to enhance the understanding of the underlying processes. 2) Our study only 395 included individuals with R-AN who were not in the most severe stage of the illness, as they 396 were recruited from a center for voluntary medical and psychological support. We did not 397 examine R-AN patients who require hospitalization due to the life-threatening nature of 398 their illness. It is possible that at the later stages of the illness, associative learning abilities, 390 which were preserved in the present sample under neutral conditions, may become impaired. 400 Therefore, investigating the impact of illness severity on context-dependent learning in R-AN 401 patients is an important avenue for future research. 3) While we observed no difference in 402 the choice behavior of R-AN patients, as measured by the relative frequency of image choices, 403 when selecting between a neutral image and a food image, we did find a slower learning rate 404 and lower decision threshold for R-AN patients compared to healthy controls in the RLDDM 405 model when compared to choosing between two neutral images. It is possible that the higher 406 "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 408 relative frequency of image choices. This warrants further exploration in future studies. 4) It 400 is worth noting that our study excluded women under the age of 18. However, this age range 410 is a critical period as the onset of AN during this stage may have a more profound impact on 411 associative learning, given the ongoing cognitive development and less-developed protective 412

413 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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 $\begin{tabular}{ll} Table 2 \\ Summary \ of \ Sample's \ Demographic \ and \ Clinical \ Characteristics. \end{tabular}$ 

	R-AN ( $n = 40$	)HC $(n = 45)$	RI (n = 36)	AN - HC	AN - RI	AN - HC	AN - RI
	Mean (SD)	Mean (SD)	Mean (SD)	PE (95% CI)	PE (95% CI)	Cohen's d	Cohen's d
Age (years) Education (years) BMI $(kg/m^2)$	21.11 (4.33) 14.53 (1.11) 17.79 (2.85)	19.49 (2.32) 14.11 (0.98) 21.78 (3.53)	21.31 (4.82) 13.89 (0.78) 21.64 (4.11)	-0.00 (-0.22, 0.18) 0.08 (-0.14, 0.33) -2.74 (-3.67, -1.79)	0.01 (-0.21, 0.25) 0.13 (-0.11, 0.41) -3.22 (-4.32, -2.07)	0.09 -0.08 2.67	-0.18 -0.13 3.15
EAT-26 Total score EAT-26 Dieting EAT-26 Bulimia EAT-26 Oral control BSQ-14 Total score RSES Total score DASS-21 Stress DASS-21 Depressio DASS-21 Anxiety SIAS Total score MPS Cmd MPS Ps MPS Pepc MPS Or	19.11 (11.24) 7.17 (3.95) ol 9.61 (6.23) e 139.78 (35.26) 22.69 (5.29) 12.86 (4.67) n 10.61 (5.49)	28.33 (5.76) 9.13 (3.55) 6.82 (4.33) 5.76 (4.26)		1.76 (1.32, 2.20) 53.96 (32.78, 80.9) 1.36 (0.99, 1.72) 1.53 (1.12, 1.96) 17.50 (11.30, 23.91) -5.601 (-8.12, -3.15) 3.73 (1.89, 5.38) 3.78 (1.76, 6.14) 2.48 (0.50, 4.33) 9.63 (3.12, 15.84) 5.46 (2.05, 9.02) 3.33 (0.89, 5.86) -0.63 (-3.49, 2.42) 0.84 (-1.49, 3.17)	0.11 (-0.17, 0.41) 0.81 (0.42, 1.20) -3.40 (-10.10, 3.15)	-1.84 -4.54 -2.33 -1.95 -1.21 -1.22 -0.94 -0.77 -0.56 -0.66 -0.69 -0.60 0.09 -0.17	-0.18 -0.36 -0.18 -1.03 0.24 0.23 -0.18 0.12 -0.16 0.12 0.48 0.06 0.57 -0.34