Contextual influence of reinforcement learning performance in Anorexia Nervosa

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Abstract

Objective: This study utilized a within-subject design to examine whether individuals with 15 restrictive anorexia nervosa (R-AN; n=40) perform similarly to healthy controls (HCs; n=16 45) and healthy controls at risk of eating disorders (RI; n=36) in a reinforcement learning 17 (RL) tasks. Specifically, we aimed to determine if RL performance is comparable between 18 groups for disorder-unrelated choices, but significantly impaired for disorder-related choices. 19 Method: RL performance was assessed using a Probabilistic Reversal Learning (PRL) task, 20 where participants were asked to perform disorder-related choices or disorder-unrelated 21 choices. Results: R-AN individuals demonstrated lower learning rates for disorder-related 22 decisions, while their performance on neutral decisions was comparable to participants with 23 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 25 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 27 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 involving food-unrelated information. This study provides valuable insights into the 31 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. 33 The findings have potential implications for the development of interventions targeting 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 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 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 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).

Given the critical role of reinforcement learning (RL) in learning from experience,
numerous attempts have been made to investigate RL deficits in individuals with Anorexia
Nervosa (AN) in order to gain insights into the underlying mechanisms responsible for their
maladaptive eating behaviors (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, results have been mixed. For example, Ritschel et
al. (2017) reported impaired RL performance in recovered AN patients compared to healthy
controls (HCs) using a probabilistic reversal learning (PRL) task, particularly in response to
negative feedback. In contrast, Bernardoni et al. (2018) observed a higher learning rate from
punishment in AN patients compared to HCs. Similarly, Sarrar et al. (2015) found no
differences in task performance between individuals with acute AN and HCs using the
Probabilistic Object Reversal Task (pORT) with neutral stimuli. Geisler et al. (2018) also
found no group differences in a PRL task with neutral stimuli and monetary feedback.

To clarify RL deficits in AN, some studies incorporated food-related feedback into the PRL paradigm. For example, Zang et al. (2014) demonstrated that patients with binge-eating disorder performed worse when exposed to food-related feedback, indicating vulnerability to food-related cues. However, attempts to replicate these findings in AN have produced conflicting results. Hildebrandt et al. (2015) reported increased rigidity 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 HCs using the same paradigm.

We speculate that the inconsistent findings in behavioral experiments about RL in AN may be partially attributed to the predominant use of general stimuli instead of disorder-relevant stimuli (see also Schaefer & Steinglass, 2021). Furthermore, when disorder-related information is incorporated, it is typically limited to the feedback provided after the participant's choice, while the stimuli during the decision-making process are unrelated to the disorder. This manipulation primarily highlights the consequences of the choices rather than the contextual factors surrounding the decision-making process.

This methodological choice of previous studies stems from the assumption that any 106 potential RL impairment in AN can be attributed to deficits in a singular, underlying RL mechanism [ref]. However, an alternative perspective proposes that the atypical RL behavior 108 observed in individuals R-AN may be better explained by contextual learning processes (Haynos, Widge, Anderson, & Redish, 2022). This hypothesis posits that contextual factors, such as individual characteristics, long-term goals, and situational influences, can have a 111 detrimental impact on RL performance, even when the underlying RL mechanisms remain 112 intact. In other words, it suggests that the deficits in RL performance observed in R-AN 113 may be the result of contextual factors influencing the learning process, rather than a 114 fundamental impairment in the RL mechanism itself. 115

To examine the proposed hypothesis, we conducted a study utilizing a modified version

of the standard PRL task. In contrast to previous studies that utilized general stimuli 117 (Schaefer & Steinglass, 2021), we incorporated two distinct contexts in our task. One context 118 involved choices between a stimulus related to the disorder (e.g., a caloric food) and a 119 stimulus unrelated to the disorder (e.g., a lamp), while the other context involved choices 120 between two stimuli unrelated to the disorder (i.e., flower vs objects). 121

Considering the heightened susceptibility of individuals with R-AN to symptom-related 122 information, such as food, body weight, and social pressure [ref], we anticipated that their 123 learning abilities would diminish when making decisions between a food item and a non-food 124 item. Conversely, we expected no learning anomaly in individuals with R-AN when making 125 choices between two non-food items in a Probabilistic Reversal Learning (PRL) task. 126

We tested the hypothesized learning asymmetry in PRL performance among three 127 groups: individuals with DSM-5 restricting-type Anorexia Nervosa (AN), healthy controls 128 (HCs), and individuals at risk of developing eating disorders (RIs). The main objective of this study was to employ computational models of reinforcement learning to analyze and compare 130 the learning outcomes within two distinct contextual conditions: decision-making involving disorder-relevant information and decision-making without disorder-relevant information.

The hypothesis of contextual maladaptive RL in individuals with R-AN has significant 133 implications for treatment strategies. Current efforts aim to improve cognitive flexibility in 134 individuals with R-AN to address their maladaptive eating behavior. However, existing 135 interventions have predominantly concentrated on fostering adaptive behavioral choices in 136 contexts unrelated to the disorder (e.g., Tchanturia, Davies, Reeder, & Wykes, 2010). Establishing evidence that maladaptive RL is context-dependent would necessitate a 138 redirection of intervention approaches. 130

Table 1 Annualized continuum and emission-line flux variability characteristics of Mrk 335.

λ_o (Å) / Line	$F_{\lambda} \pm \Delta F_{\lambda}$ (min)	$F_{\lambda} \pm \Delta F_{\lambda}$ (max)	$F_{\lambda} \pm \Delta F_{\lambda}$ (avg)	EW (Å)	$R_{max} \pm \Delta R_{max}$	$F_{var} \pm \Delta F_{var}$	ΔT (days)	N
2625 2687 2875 Si IV C IV C III] Mg II	$\begin{array}{c} 4.59 \pm 0.02 \\ 4.43 \pm 0.04 \\ 4.19 \pm 0.02 \\ \hline 1.99 \pm 0.1 \\ 6.13 \pm 0.1 \\ 1.85 \pm 0.07 \\ 0.98 \pm 0.05 \\ \end{array}$	$\begin{array}{c} 5.19 \pm 0.02 \\ 4.88 \pm 0.04 \\ 4.6 \pm 0.02 \\ \hline 1.53 \pm 0.08 \\ 6.41 \pm 0.06 \\ 6.38 \pm 0.06 \\ 0.79 \pm 0.05 \end{array}$	$\begin{array}{c} 4.89 \pm 0.02 \\ 4.66 \pm 0.04 \\ 4.4 \pm 0.02 \\ \hline 1.76 \pm 0.09 \\ 6.27 \pm 0.08 \\ 4.12 \pm 0.07 \\ 0.89 \pm 0.05 \end{array}$	1981 - - 19.24 73.39 40.66 16.42	$\begin{array}{c} 1.33 \pm 0.01 \\ 1.45 \pm 0.02 \\ 1.37 \pm 0.01 \\ \hline 1.3 \pm 0.09 \\ 1.05 \pm 0.02 \\ 0.52 \pm 0.19 \\ 1.45 \pm 0.12 \\ \end{array}$	$\begin{array}{c} 12.68 \pm 0.24 \\ 16.25 \pm 0.55 \\ 13.65 \pm 0.24 \\ 14.21 \pm 3.04 \\ 2.34 \pm 0.85 \\ 70.91 \pm 1.1 \\ 19.02 \pm 3.57 \\ \end{array}$	267 267 267 267 267 0.26 63	4 4 4 3 3 6 3
1350 1450 1605 1675 1812 Si IV C IV He II C III]	$\begin{array}{c} 10.57 \pm 0.03 \\ 9.32 \pm 0.06 \\ 10.46 \pm 0.06 \\ 9.26 \pm 0.03 \\ 7.71 \pm 0.03 \\ 2.38 \pm 0.09 \\ 6.73 \pm 0.08 \\ 2.39 \pm 0.07 \\ 3.29 \pm 0.06 \end{array}$	$\begin{array}{c} 10.58 \pm 0.04 \\ 8.93 \pm 0.07 \\ 9.98 \pm 0.06 \\ 8.31 \pm 0.04 \\ 7.2 \pm 0.02 \\ 1.97 \pm 0.08 \\ 6.37 \pm 0.07 \\ 2.65 \pm 0.08 \\ 1.08 \pm 0.07 \end{array}$	$\begin{array}{c} 10.58 \pm 0.04 \\ 9.13 \pm 0.07 \\ 10.22 \pm 0.06 \\ 8.79 \pm 0.04 \\ 7.46 \pm 0.03 \\ 2.18 \pm 0.09 \\ 6.55 \pm 0.08 \\ 2.52 \pm 0.08 \\ 2.19 \pm 0.07 \end{array}$	1982 - - - - 24.88 87.18 37.91 25.5	$\begin{array}{c} 1.06 \pm 0.01 \\ 1.16 \pm 0.01 \\ 1.18 \pm 0.01 \\ 0.9 \pm 0.01 \\ 1.13 \pm 0.01 \\ 1.21 \pm 0.07 \\ 1.16 \pm 0.02 \\ 1.34 \pm 0.06 \\ 3.14 \pm 0.22 \\ \end{array}$	$\begin{array}{c} 3.49 \pm 0.21 \\ 7.41 \pm 0.43 \\ 8.29 \pm 0.32 \\ 10.97 \pm 0.26 \\ 6.16 \pm 0.23 \\ 9.72 \pm 2.32 \\ 7.79 \pm 0.66 \\ 15.11 \pm 1.54 \\ 60.26 \pm 2.12 \end{array}$	0.26 0.26 0.26 0.26 0.26 0.14 0.14 0.14 0.07	3333333334
C III] C IV	$\begin{array}{c} \pm \\ 2.3 \pm 0.05 \\ 7 \pm 0.06 \end{array}$	$\begin{array}{c} \pm \\ 7.58 \pm 0.04 \\ 10.81 \pm 0.05 \end{array}$	4.94 ± 0.05 8.91 ± 0.06	1985 81.88 153.07	4.78 ± 0.11 1.54 ± 0.01	$\begin{array}{c} \pm \\ 85.59 \pm 0.95 \\ 23.7 \pm 0.41 \end{array}$	174 174	3 3
1350 1450 1605 1675 1812 2475 2625 2875 Lyα Si IV C IV He II C III]	$\begin{array}{c} 12.03 \pm 0.03 \\ 10.91 \pm 0.06 \\ 12.29 \pm 0.05 \\ 10.15 \pm 0.04 \\ 9.87 \pm 0.05 \\ 6.51 \pm 0.02 \\ 5.72 \pm 0.02 \\ 5.04 \pm 0.01 \\ \hline 14.37 \pm 0.04 \\ 1.82 \pm 0.08 \\ 6.32 \pm 0.06 \\ 3.16 \pm 0.08 \\ 3.96 \pm 0.06 \\ \end{array}$	$\begin{array}{c} 9.24 \pm 0.02 \\ 9.5 \pm 0.05 \\ 9 \pm 0.04 \\ 8.33 \pm 0.03 \\ 7.44 \pm 0.03 \\ 5.38 \pm 0.01 \\ 4.88 \pm 0.01 \\ 4.18 \pm 0.01 \\ \hline 13.2 \pm 0.1 \\ 3.08 \pm 0.07 \\ 6.26 \pm 0.09 \\ 4.1 \pm 0.05 \\ 1.19 \pm 0.09 \\ \end{array}$	$\begin{array}{c} 10.64 \pm 0.03 \\ 10.21 \pm 0.06 \\ 10.65 \pm 0.05 \\ 9.24 \pm 0.04 \\ 8.66 \pm 0.04 \\ 5.95 \pm 0.02 \\ 4.61 \pm 0.01 \\ 13.79 \pm 0.07 \\ 2.45 \pm 0.08 \\ 6.29 \pm 0.08 \\ 3.63 \pm 0.07 \\ 2.58 \pm 0.08 \\ \end{array}$	1989 - - - - - - - - - - - - -	$\begin{array}{c} 1.49 \pm 0.01 \\ 1.39 \pm 0.01 \\ 1.53 \pm 0.01 \\ 0.82 \pm 0 \\ 1.63 \pm 0.01 \\ 1.31 \pm 0.01 \\ 1.24 \pm 0.01 \\ 1.29 \pm 0 \\ \hline 1.43 \pm 0.01 \\ 2.12 \pm 0.1 \\ 1.33 \pm 0.02 \\ 2.24 \pm 0.06 \\ 5.49 \pm 0.43 \\ \end{array}$	$\begin{array}{c} 15.27 \pm 0.11 \\ 11.16 \pm 0.22 \\ 13.27 \pm 0.14 \\ 12.89 \pm 0.12 \\ 14.18 \pm 0.13 \\ 11.32 \pm 0.14 \\ 8.91 \pm 0.12 \\ 11.12 \pm 0.25 \\ \hline 11.4 \pm 0.22 \\ 26.58 \pm 1.63 \\ 9.79 \pm 0.38 \\ 28.59 \pm 0.95 \\ 71.22 \pm 1.87 \\ \end{array}$	182 182 182 182 182 182 182 182 182 29 58 29 54	10 7 10 11 11 6 6 6 6 9 7 9 7

Continued on the next page

λ_o (Å) / Line	$F_{\lambda} \pm \Delta F_{\lambda}$	$F_{\lambda} \pm \Delta F_{\lambda}$	$F_{\lambda} \pm \Delta F_{\lambda}$	EW (Å)	$R_{max} \pm \Delta R_{max}$	F + AF	$\Delta \mathrm{T}$	N
	(\min)	(max)	(avg)	()	romax = = romax	r var = = r var	(days)	
Mg II	2.55 ± 0.04	1.2 ± 0.04	1.88 ± 0.04	31.24	3.03 ± 0.11	42.57 ± 1.25	54	7

140 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.

144 Participants

The study recruited a total of 40 individuals meeting criteria for DSM-5 145 restricting-type AN and 310 healty volunteers. Individuals with R-AN were recruited from 146 three facilities in Italy, namely the Specchidacqua Institute in Montecatini (Pisa), the Villa 147 dei Pini Institute in Firenze, and the Gruber Center, Outpatient Clinic in Bologna. The 148 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 150 program included various components, such as individual therapy, family therapy, group 151 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. Individuals diagnosed with R-AN (Restrictive 155 Anorexia Nervosa) were included in the study approximately 6 months (± 1 month) after 156 starting treatment for eating disorders at one of the participating facilities. 157

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. The presence of psychiatric co-morbidities was determined by

specialized psychiatrists and psychologists at the treatment centers using a semi-structured

interview based on the Mini International Neuropsychiatric Interview [MINI; Sheehan et al.

(1998)]. Among the 40 individuals with R-AN in our study, comorbidities included anxiety

disorder (n=16), OCD (n=8), social phobia (n=1), and DAP (n=1). Eighteen R-AN

patients were undertaking medication (anxiolytic antidepressants = 10; Selective Serotonin

Reuptake Inhibitors (SSRIs) = 6; benzodiazepines = 1; mood stabilizers (lithium) = 1).

The control group consisted of 310 adolescent or young-adult females recruited through 167 social media or university advertisements. All participants completed the Eating Attitudes 168 Test-26 (EAT-26; Garner et al., 1982) screening tool. Females who scored higher than 20 on 169 the EAT-26 (Dotti & Lazzari, 1998) and did not report any current treatment for eating 170 disorders were classified as "at-risk" for the study's purposes and assigned to the RI 171 (reference/independent) group, resulting in a total of 36 "at-risk" females. From the 172 remaining participants who scored lower than 20 on the EAT-26 and did not report any 173 current treatment for eating disorders, a random sample of 45 females was selected and 174 assigned to the HC group. It was a requirement for both the HC and RI groups that 175 participants have a normal Body Mass Index. 176

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, past or present psychiatric diagnosis, 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.

Procedure Procedure

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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. The study was presented to participants as an evaluation of
cognitive functions through a computer-based "game" accompanied by additional
questionnaires.

We compared the characteristics of the clinical sample with the controls by 197 administering the following scales: the EAT-26, the Body Shape Questionnaire-14 (BSQ-14; 198 Dowson & Henderson, 2001), the Social Interaction Anxiety Scale (SIAS; Mattick & Clarke, 199 1998), the Depression Anxiety Stress Scale-21 (DASS-21; Lovibond & Lovibond, 1995), the 200 Rosenberg Self-Esteem Scale (RSES; Rosenberg, 1965), the Multidimensional Perfectionism 201 Scale (MPS-F; Frost et al., 1990), and the Raven's Standard Progressive Matrices (Raven et 202 al., 2000). The results of these statistical analyses are provided in the Supplementary 203 Information (SI). 204

The participants were told they were going to play a simple computer game with the
objective of accumulating as many "virtual euro" as possible. 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 2.5-second time limit by pressing a key.
Trials were presented in an interleaved manner, with a randomly drawn inter-trial interval
ranging from 0.5 to 1.5 seconds. Following each trial, 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. Feedback was provided for 2 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 image 224 was considered correct. Feedback during the task was probabilistic, with the correct image being rewarded in 70% of the trials, while negative feedback was provided in the remaining 226 30% of the trials. Both blocks of the task included three rule changes in the form of reversal 227 phases. Participants were informed that stimulus-reward contingencies would change, but 228 not the specifics of how or when this would occur. The objective of the participants was to 229 maximize their earnings, which were displayed at the end of each block. Participants 230 underwent a training block consisting of 20 trials prior to the start of the actual experiment. 231 Participants were instructed to rely on their instincts when uncertain. The Psychtoolbox 232 extensions in MATLAB (MathWorks) were used to program the tasks (Brainard, 1997). 233

234 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.

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). This
algorithm represent the state-of-the-art approach for examining performance in the PRL
task. 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).
Hierarchical modeling of reinforcement learning tasks has been demonstrated to yield
superior predictive accuracy compared to alternative methods (Geen & Gerraty, 2021; e.g.,
Gershman, 2016).

We employed a Bayesian approach in 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 model assumes that subjective option values (Q values) are learned through
reward prediction errors (PEs), which measure the disparity between expected and obtained
outcomes (Sutton & Barto, 2018). The update of subjective option values follows a delta

learning rule (Rescorla & Wagner, 1972):

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

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 included in the model different learning rates for positive and negative prediction errors: 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, instead, this second component of decision-making is replaced by a 273 Drift-Diffusion Model [DDM; Ratcliff and McKoon (2008)] which assumes a stochastic 274 accumulation of evidence on each trial. The DDM includes four parameters: A drift rate 275 parameter (v), which describes the rate of (noisy) evidence accumulation; a decision 276 threshold parameter (a), which represents the amount of evidence needed to make a decision; 277 a non-decision time parameter (t), which accounts for the time devoted to sensory processing, 278 motor preparation, and motor output, and a starting point parameter (z), which accounts 270 for any predispositions in the initial decision variable towards either boundary. 280

To assess the presence of context-dependent learning, we conditioned the model's

parameters on two specific 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.

285 Results

286 Demographic and Psychopathology Measures

TODO

Mean age and Body Mass Index (BMI) for each group of participant were as follows: 288 patients with AN, mean age = 21.18 (SD = 2.41), average Body Mass Index (BMI) = 16.88289 (SD = 1.55); patients with BN, mean age = 20.39 (SD = 1.88), average BMI = 30.09 (SD = 290 5.47); HCs, mean age = 19.77 (SD = 1.06), average BMI = 21.62 (SD = 3.03); healthy 291 individuals at risk of developing eating disorders, mean age = 20.36 (SD = 1.44), average 292 BMI = 22.41 (SD = 4.79). Bayesian statistical analysis revealed no credible age differences 293 among the four groups (AN, BN, HC, and RI). AN participants displayed a lower mean BMI 294 than HC participants, while BN participants had a higher mean BMI than HC participants. 295 No noteworthy difference in BMI was observed between HC and RI participants. 296 Furthermore, there is credible evidence that the Rosenberg Self-Esteem Scale scores of all 297 three groups (AN, BN, and RI) are smaller than those of the HC group. We also found 298 credible evidence that individuals with AN, BN, and RI exhibited higher levels of 290 dissatisfaction with their body shape, as measured by the BSQ-14 questionnaire, when 300 compared to the HCs. Individuals with AN displayed higher stress, anxiety, and depression 301 levels (as measured by the DASS-21) than HCs. Additionally, individuals with AN showed credibly higher levels of social interaction anxiety (as measured by the SIAS) than HCs. All three AN, BN, and RI groups exhibited higher levels of Concerns over mistakes and doubts scores of the MPS scale compared to HCs. Individuals with AN also showed higher levels of 305 Personal standard scores of the MPS scale compared to HCs. Moreover, individuals with AN 306 displayed higher values on all three subscales of the EAT-26 questionnaire relative to HCs. 307

- For more detailed information regarding these comparisons, please refer to the Supplementary Information (SI).
- Sixteen individuals with R-AN were diagnosed with a comorbid anxiety disorder, 8 with OCD, 1 with social phobia, and 1 with DAP.

Models selection

- To evaluate context-dependent learning, we compared several RLDDM models that varied in their conditioning of the model's parameters on the group (R-AN, HC, RI) and context (disorder-related choices and disorder-unrelated choices). We used the Deviance Information Criterion (DIC) to balance model fit and complexity, selecting the model with the lowest DIC as the best trade-off. The following RLDDM models were examined:
- 1. Model M1: Standard RLDDM without conditioning. DIC = 39879.444.
- 2. Model M2: Separate learning rates for positive and negative reinforcements. DIC = 39124.890
- 3. Model M3: Group-based α^+ and α^- parameters. DIC = 39194.763.
- 4. Model M4: Group and context-based α^+ and α^- parameters. DIC = 38197.467.
- 5. Model M5: Group and context-based α^+ , α^- , and a parameters. DIC = 36427.448.
- 6. Model M6: Group and context-based α^+ , α^- , a, and drift rate (v) parameters. DIC = 36185.146.
- 7. Model M7: Group and context-based α^+ , α^- , a, v, and non-decision time (t) parameters. DIC = 34904.053.
- 8. Model M8: Group and context-based α^+ , α^- , a, v, t, and starting point (z) parameters. DIC = 34917.762.
- All models were estimated using Bayesian methods with weakly informative priors.

 Among the evaluated models, Model M7 had the lowest DIC, indicating the best trade-off

 between goodness of fit and model complexity. In Model M7, the parameters α^+ , α^- , a, v,

and t (excluding z) were conditioned on both the group and the context.

334 Modelling results

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 2 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 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	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
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

Group	Par.	Neutral choice	Food choice	p	Cohen's d
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 343 comparisons. We found that, on average, individuals in the R-AN group demonstrate a reduced learning rate in response to positive prediction errors (PEs) for disorder-related 345 choices, as compared to disorder-unrelated choices (Cohen's d=1.206, p=0.0098). In 346 contrast, no substantial evidence was found indicating a difference in the learning rate 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 =(0.2349), HC (p = 0.6993), and RI (p = 0.5101) groups. Moreover, we found that both the 351 R-AN (Cohen's d = 0.802, p = 0.0013) and HC (Cohen's d = 0.474, p = 0.0256) groups 352 showed a higher decision threshold for disorder-related choices compared to 353 disorder-unrelated choices. 354

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 PEs compared to RI (p = 0.0085, Cohen's d = 1.209). In contrast, no credible difference in

the learning rate after positive PEs was found between R-AN and HC (p = 0.4325), as well 361 as between R-AN and RI (p = 0.3232), for choices unrelated to disorder information. 362 Concerning the learning rate after negative PEs, we found that R-AN showed a lower 363 learning rate compared to HC, but only for disorder-related choices: (p = 0.0274, Cohen's d)364 = 1.144). Individuals with R-AN showed a higher decision threshold for disorder-related 365 choices compared to both HC (Cohen's d = 0.622, p = 0.0068) and RI (Cohen's d = 0.454, p = 0.454366 = 0.0118) participants. No credible group differences were found for disorder-unrelated 367 choices. Additionally, we observed that both HC (Cohen's d = 0.520, p = 0.0344) and RI (Cohen's d = 0.529, p = 0.0392) participants exhibited a faster accumulation of evidence and 369 more confident decision-making, as indicated by a higher average drift rate parameter, 370 compared to individuals with R-AN. This difference was only evident for disorder-unrelated 371 choices. Finally, no credible differences were found, for both within-group and between-group comparisons, regarding the non-decision time parameter (t).

374 Preferential choices

To investigate the presence of a bias against food choices in individuals with R-AN 375 during the PRL task, regardless of their past action-outcome history, we analyzed the 376 frequency of food choices in PRL blocks where a food image was paired with a neutral image. 377 Our results show that the AN-R group did not exhibit a bias against the food image, with a 378 proportion of food choices estimated at 0.49, 95% CI [0.46, 0.51]. Furthermore, there were no 379 credible differences in food choices between the R-AN group and the HC group (contrast 380 R-AN - HC = -0.007, 95% CI [-0.037, 0.024]) or between the R-AN group and the RI group 381 (contrast R-AN - RI = 0.013, 95% CI [-0.019, 0.046]).382

383 Comorbidity

We conducted a further statistical analysis to investigate whether the conservative learning behavior observed in individuals with R-AN could be explained by comorbid conditions. Using model M7, we categorized individuals with R-AN based on the presence or

absence of diagnosed comorbidities. Our analysis revealed no credible differences in 387 parameters between the two groups. Specifically, for the disorder-related context, the 388 parameter differences were as follows: $\Delta \alpha^- = 2.614$, 95% CI [-3.173, 8.364]; $\Delta \alpha^+ = -0.635$, 389 95% CI [-4.301, 2.449]; $\Delta a = -0.034$, 95% CI [-0.188, 0.124]; $\Delta v = 0.230$, 95% CI [-1.203, 390 1.586]; $\Delta t = 0.002, 95\%$ CI [-0.050, 0.055]. For the disorder-unrelated context, the parameter 391 differences were: $\Delta \alpha^- = -0.768$, 95% CI [-6.570, 4.401]; $\Delta \alpha^+ = -1.739$, 95% CI [-6.184, 392 1.654]; $\Delta a = -0.126, 95\%$ CI [-0.281, 0.025]; $\Delta v = 0.744, 95\%$ CI [-0.453, 1.886]; $\Delta t = -0.003$, 393 95% CI [-0.057, 0.052]. 394

Discussion

Our findings reveal a context-dependent learning asymmetry in individuals with R-AN specifically in the positive learning rate. This asymmetry is observed when comparing the performance in the PRL task for disorder-related choices versus disorder-unrelated choices.

Importantly, no similar difference is found in the two control groups.

The presence of context-dependent learning asymmetry is also supported by group comparisons. Individuals with R-AN exhibited 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 these differences were observed only for disorder-related choices. In contrast, no substantial difference in learning rates was found between the R-AN group and the HC and RI groups for disorder-unrelated choices.

Support for context-dependent learning in R-AN is also provided by the DDM
parameters of the hDDMrl model. Specifically, we observed that the R-AN group exhibited a
higher decision threshold (parameter "a" in the hDDMrl model) compared to the HC and RI
groups, but this difference was only evident in the context of disorder-related choices. This
suggests that individuals with R-AN displayed a more cautious or conservative
decision-making behavior specifically in relation to disorder-related choices (see also Caudek,

Sica, Cerea, Colpizzi, & Stendardi, 2021; Schiff, Testa, Rusconi, Angeli, & Mapelli, 2021).

Further support of context-related learning in R-AN comes from the result which 413 indicate that both healthy control (HC) and at-risk (RI) participants exhibited a faster 414 accumulation of evidence and displayed more confident decision-making, as reflected by a 415 higher average drift rate parameter, compared to individuals with restrictive anorexia 416 nervosa (R-AN). However, this difference was specifically observed for disorder-unrelated 417 choices. It is noteworthy that individuals with R-AN displayed slower evidence accumulation 418 and less confident decision-making specifically in disorder-unrelated contexts, whereas this 419 group difference was not observed for disorder-related choices. This finding further supports 420 the notion of context-dependent learning in individuals with R-AN, particularly in the 421 context of food-related information. 422

Further evidence of context-related learning in R-AN comes from the analysis of the
drift rate parameter. Individuals with R-AN exhibited slower evidence accumulation and less
confident decision-making compared to the control groups, specifically in the context of
disorder-unrelated choices. Conversely, no credible group differences were observed for
food-related choices. These results suggest that individuals with R-AN may allocate greater
cognitive resources to process salient information in the disorder-related context, which leads
to similar evidence accumulation rates in decision-making compared to the control groups.
In contrast, they exhibit a slower evidence accumulation rate when faced with less salient
disorder-unrelated choices.

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.

Geneeral 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 reduced learning rate in the disorder-related context for patients 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. First, there may be a learning impairment, where participants struggle to accurately update the value of the stimuli. Second, there may be a decision impairment, where participants may still select the wrong stimulus despite having intact learning processes. Our results provide evidence that individuals with R-AN may struggle with both accurately updating the 450 value of disorder-related stimuli and making appropriate decisions based on this information. 451 However, we did not observe similar impairments in decision making for disorder-unrelated 452 choices. These findings provide evidence for context-dependent learning in individuals with 453 R-AN, where the inclusion of disorder-related information negatively impacts their RL 454 performance. It is important to note that this effect is specific to the disorder-related context 455 and does not suggest a generalized RL deficit in individuals with R-AN. Thus, our results 456 challenge the notion of a domain-general RL mechanism impairment in this population. 457

Previous studies have demonstrated that reward and punishment processing in individuals with AN is influenced by stimulus properties and contextual factors (Haynos, Lavender, Nelson, Crow, & Peterson, 2020). 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. While these previous studies have primarily focused on the
effect of context on the subjective value assigned to experiences in AN, our study extends
the investigation by examining the impact of context on the learning process itself. We find
that the context also affects the learning process itself (not only the subjective value),
providing further insights into reward and punishment processing in AN.

Other recent studies have focused on investigating context-specific learning in eating 460 disorders. One task specifically designed for this purpose is the two-step Markov decision 470 task, which distinguishes between automatic or habitual (model-free) learning and controlled or goal-directed (model-based) learning. For instance, studies conducted by Foerde et al. (2021) and Onysk and Seriès (2022) employed similar experiments using the two-step task paradigm. Foerde et al. (2021) compared a monetary two-step task and a food-related 474 two-step task, while Onysk and Seriès (2022) utilized stimuli unrelated to food or body 475 images (i.e., pirate ships and treasure chests) with rewards associated with body image 476 dissatisfaction. The results of these studies consistently demonstrated that individuals with 477 AN tend to exhibit a stronger inclination towards habitual control over goal-directed control 478 across different domains compared to healthy controls. However, no significant differences 479 were observed in learning rates as a function of context, nor between AN patients and 480 healthy controls, according to these findings. In contrast, the present study reveals that, in 481 individuals with R-AN, the learning process per se can be influenced by contextual 482 (disorder-related) information, even when such information is not directly relevant to the 483 task outcome. 484

The implications of the present findings, if replicated by future studies, are relevant to
the treatment of AN. Current treatment practices address the issue of cognitive inflexibility
in AN, with Cognitive Remediation Therapy (CRT) being proposed as an adjunct treatment
targeting specific cognitive processes in AN and other eating disorders. CRT involves
cognitive exercises and behavioral interventions aimed at improving central coherence

abilities, reducing cognitive and behavioral inflexibility, and enhancing thinking style
comprehension (Tchanturia et al., 2010). A key aspect of CRT is to avoid focusing on
symptom-related themes and instead utilize neutral stimuli in cognitive and behavioral
exercises. This approach aims to establish a therapeutic alliance and reduce drop-out rates,
particularly among AN patients.

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 few important limitations and questions 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 rewards and punishments were merely symbolic, and it is unclear how the use of concrete, non-symbolic rewards and punishments would impact the findings. Additionally, the subjective value of one euro, or the loss of one euro, may vary among participants. Therefore,

future studies could aim to determine the equivalence of subjective values for rewards and 516 punishments to enhance the understanding of the underlying processes. 2) Our study only 517 included individuals with R-AN who were not in the most severe stage of the illness, as they 518 were recruited from a center for voluntary medical and psychological support. We did not 519 examine R-AN patients who require hospitalization due to the life-threatening nature of 520 their illness. It is possible that at the later stages of the illness, associative learning abilities, 521 which were preserved in the present sample under neutral conditions, may become impaired. 522 Therefore, investigating the impact of illness severity on context-dependent learning in R-AN 523 patients is an important avenue for future research. 3) While we observed no difference in 524 the choice behavior of R-AN patients, as measured by the relative frequency of image choices, 525 when selecting between a neutral image and a food image, we did find a slower learning rate 526 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 528 "salience" of food images compared to neutral images could be better captured by other 529 measures, such as fixation length or the number of fixations, rather than solely relying on the 530 relative frequency of image choices. This warrants further exploration in future studies. 4) It 531 is worth noting that our study excluded women under the age of 18. However, this age range 532 is a critical period as the onset of AN during this stage may have a more profound impact on 533 associative learning, given the ongoing cognitive development and less-developed protective 534 factors. Therefore, future studies should take into consideration the inclusion of participants 535 in this age range to better understand the influence of context-dependent learning in R-AN. 536

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