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

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The authors made the following contributions. Corrado Caudek: Conceptualization, Writing - Original Draft Preparation, Writing - Review & Editing; Ernst-August Doelle: Writing - Review & Editing, Supervision.

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Abstract

One or two sentences providing a **basic introduction** to the field, comprehensible to a scientist in any discipline.

Two to three sentences of **more detailed background**, comprehensible to scientists in related disciplines.

One sentence clearly stating the **general problem** being addressed by this particular study.

One sentence summarizing the main result (with the words "**here we show**" or their equivalent).

Two or three sentences explaining what the **main result** reveals in direct comparison to what was thought to be the case previously, or how the main result adds to previous knowledge.

One or two sentences to put the results into a more **general context**.

Two or three sentences to provide a **broader perspective**, readily comprehensible to a scientist in any discipline.

Keywords: keywords

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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).

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 behavior based on reward probabilities. The task reflects real-life situations where outcomes are uncertain, requiring individuals to make decisions based on probabilities. By presenting uncertain and varying reward probabilities, the task captures the complexities of decision-making under uncertainty and provides insights into how individuals integrate probabilistic information to guide their behavior. The PRL task involves unannounced reversals of contingencies, demanding behavioral adaptation to changing environments. This reversal learning aspect measures cognitive flexibility – i.e., the ability to shift behavior in response to changing environmental demands. The PRL task has been extensively used in neuroscience research and has shown associations with specific brain regions involved in reinforcement learning and cognitive flexibility [ref]. Neuroimaging techniques like fMRI have revealed neural activations and connectivity patterns during the task, corresponding to reward processing, error monitoring, and cognitive control mechanisms.

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

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.

. . .

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 unedrlying RL mechanisms.

Implications for treatment

The hypothesis of contextual maladaptive RL in R-AN has potential implications for treatment. For example, Cognitive Remediation Therapy (CRT) has been proposed as an adjunct treatment targeting specific cognitive processes in AN and other eating disorders. CRT involves cognitive exercises and behavioral interventions aimed at increasing 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 discussing symptom-related themes and instead use neutral stimuli in cognitive and behavioral exercises. This approach aims to develop a therapeutic alliance and to decrease drop-out rates, particularly with AN patients.

However, recent evidence suggests that CRT may not consistently improve central coherence abilities, cognitive flexibility, or symptoms related to eating disorders (Hagan et al., 2020; Tchanturia et al., 2017). In response to this, Trapp et al. (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 et al., 1987).

The proposal put forth by Trapp et al. (2022) aligns with the hypothesis of this study, suggesting that contextual factors play a crucial role in the maladaptive eating behavior observed in individuals with R-AN, beyond deficits in the underlying RL 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.

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.

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 study approximately 6 months (± 1 month) after starting treatment for eating disorders at one of the participating facilities. The assessment of comorbidities in R-AN patients was carried out by specialized psychiatrists and psychologists at the treatment centers using a comprehensive approach. This approach involved regular and ongoing monitoring of psychiatric symptoms and comorbid conditions throughout the treatment process. The assessment process encompassed clinical interviews and the administration of specific symptom inventories and rating scales to obtain a comprehensive evaluation of comorbid psychiatric disorders.

The HC (healthy control) group consisted of 310 adolescent or young-adult females recruited through social media or university advertisements. All participants completed the Eating Attitudes Test-26 (EAT-26; Garner et al., 1982) screening tool. Females who scored higher than 20 on the EAT-26 (Dotti & Lazzari, 1998) and did not report any current 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 any current treatment for eating disorders, a random sample of 45 females was selected and assigned to the HC group. It was a requirement for both the HC and RI groups that participants have a normal Body Mass Index.

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.

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 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 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 30% of the trials. Both blocks of the task included three rule changes in the form 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 experiment. The Psychtoolbox extensions in MATLAB (MathWorks) were used to program the tasks (Brainard, 1997).

Data analysis

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 to employ a Bayesian approach in our study because RLDDM models can currently only be estimated through Markov Chain Monte Carlo (MCMC) procedures. A Bayesian approach offers the advantage of prioritizing estimation over hypothesis testing, allowing us 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 by assessing the proportion of posterior samples (97.5%) that fell above or below zero, indicating the direction of the effect.

By breaking down decision-making task performance into its component processes through cognitive modeling analysis, it becomes possible to identify any deviances in the underlying mechanisms that may not be reflected in the overall task outcome. RLDDM has six basic parameters: positive learning rate ($alpha^{+}$), negative learning rate ($alpha^{-}$), drift rate (v), decision threshold (a), non-decision time (t), and starting point bias (z) parameters. The α parameter quantifies the learning rate in the Rescorla-Wagner delta learning rule (Rescorla & Wagner, 1972); a higher learning rate results in rapid adaptation to reward expectations, while a lower learning rate results in slow adaptation. The parameter α^{+} is computed from reinforcements, whereas α^{+} is computed from punishments. The drift rate v is the average speed of evidence accumulation toward one decision. 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. The non-decision time t is the time spent for stimuli encoding or motor execution (*i.e.*, time not used for evidence accumulation). The starting point parameter z captures a potential initial bias toward one or the other boundary in absence of any stimulus evidence.

Transparency Openness

We report all data exclusion criteria and how the sample size was determined. All measures used in this study are reported. 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.

Results

Demographic and Psychopathology Measures

Mean age and Body Mass Index (BMI) for each group of participant were as follows: patients with AN, mean age = 21.18 (SD = 2.41), average Body Mass Index (BMI) = 16.88 (SD = 1.55); patients with BN, mean age = 20.39 (SD = 1.88), average BMI = 30.09 (SD = 5.47); HCs, mean age = 19.77 (SD = 1.06), average BMI = 21.62 (SD = 3.03); healthy individuals at risk of developing eating disorders, mean age = 20.36 (SD = 1.44), average BMI = 22.41 (SD = 4.79). Bayesian statistical analysis revealed no credible age differences among the four groups (AN, BN, HC, and RI). AN participants displayed a lower mean BMI than HC participants, while BN participants had a higher mean BMI than HC participants. No noteworthy difference in BMI was observed between HC and RI participants. 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 compared to the HCs. Individuals with AN displayed higher stress, anxiety, and depression 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 Personal standard scores of the MPS scale compared to HCs. Moreover, individuals with AN displayed higher values on all three subscales of the EAT-26 questionnaire relative to HCs. 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.

Reinforcement learning and drift diffusion modeling

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. 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 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
HC	a	**1.222** (0.033)	**1.314** (0.034)	0.0256	0.474

Group	Par.	Neutral choice	Food choice	p	Cohen's d
HC	v	2.157 (0.265)	1.790 (0.263)	0.1606	-0.358
HC	t	0.183 (0.009)	0.172 (0.009)	0.8228	-0.280
HC	α^-	2.780 (0.874)	3.442 (0.980)	0.6993	0.298
HC	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

The results reveal that the R-AN group exhibits a decreased learning rate following positive prediction errors (PEs) when making choices associated with disorder-related information, in contrast to choices linked to disorder-unrelated information (Cohen's d = 1.206, p =0.0098). Instead, there were no evidence of a credible difference in the learning rate between disorder-related and disorder-unrelated conditions in the HC and RI groups.

Moreover, we found that both the R-AN (Cohen's $d = 0.802$, $p = 0.0013$) and HC (Cohen's $d = 0.474$, $p = 0.0256$) groups showed a higher decision threshold when making choices related to disorder-related information compared to choices related to disorder-unrelated information. This finding aligns with the results reported in the studies by Caudek et al. (2021) and Schiff, Testa, Rusconi, Angeli, and Mapelli (2021), indicating a general tendency among individuals to adopt a more cautious decision-making approach in the context of food-related choices, as opposed to choices unrelated to food.

Further evidence of context-dependent learning emerges from between-groups comparisons. When confronted with choices related to disorder-related information, 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 as between R-AN and RI ($p = 0.3232$), for choices unrelated to disorder information.

Concerning the learning rate after negative PEs, we found that R-AN showed a lower learning rate compared to HC, but only when making choices related to disorder-related information: ($p = 0.0274$, Cohen's $d = 1.144$).

Individuals with R-AN also showed a higher decision threshold when making choices related to disorder-related information compared to choices compared to both HC (Cohen's $d = 0.622$, $p = 0.0068$) and RI (Cohen's $d = 0.454$, $p = 0.0118$) participants. No credible group differences were found when considering choices unrelated to disorder information.

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 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 choices unrelated to disorder information.

Finally, no credible differences were found, both within-group and between-group, regarding the non-decision time parameter (t).

Biased choices

TODO: correct the statistics.

In order to investigate whether the slower learning rate observed in individuals with

R-AN during the PRL task could be attributed to a bias against food choices, 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. A bias against the food image was observed, with a proportion of food choices equal to 0.484, 95% CI [0.477, 0.492]. However, no group-specific bias was detected, as indicated by the following comparisons: R-AN - HC: proportion = -0.002, 95% CI [-0.029, 0.026]; R-AN - RI: proportion = -0.002, 95% CI [-0.029, 0.026]. These results indicate that there was no credible group-specific bias in food choices among individuals with R-AN compared to the HC and RI groups.

Comorbidity

To explore whether comorbid conditions influence the conservative learning behavior observed in individuals with R-AN when making choices related to disorder information, we applied model M7 to AN patients, categorizing them based on the presence or absence of diagnosed comorbidities. Our statistical analysis, as described in the Supplementary Information (SI), revealed no credible differences in parameters between the two groups.

Discussion

In this within-subjects study, we examined how disorder-related information impacts probabilistic reversal learning in individuals with restrictive anorexia nervosa (R-AN), healthy female participants (HC), and females at-risk of developing eating disorders (RI). Our findings supported our hypotheses, revealing that R-AN patients exhibited slower learning after positive prediction errors (positive outcomes) related to the disorder, compared to when the outcomes were unrelated to the disorder. Instead, we did not find any difference in the learning rate between disorder-related and disorder-unrelated information in the HC and RI groups.

Furthermore, we noticed that individuals with R-AN exhibited lower learning rates for both positive and negative prediction errors in comparison to the HC group. However, this discrepancy was observed only when the choices were related to disorder-related information. When it came to making choices based on images displaying disorder-unrelated information, no substantial difference in learning rates was observed between the R-AN and HC groups. When comparing the RI and R-AN groups, we found that individuals with R-AN exhibited slower learning rates than RI participants when they experienced positive prediction errors associated with the disorder. However, this difference was not found when the choices involved disorder-unrelated information.

We also observed significant contextual effects on 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 when making choices related to disorder-related information. This indicates that individuals with R-AN displayed a more cautious or conservative decision-making behavior than the HC and RI groups specifically in situations involving disorder-related information.

Furthermore, we found that both the R-AN and HC groups showed a higher decision threshold when making choices related to disorder-related information compared to choices related to disorder-unrelated information. This finding aligns with the results reported in the studies by Caudek et al. (2021) and Schiff et al. (2021), indicating a general tendency among individuals to adopt a more cautious decision-making approach in the context of food-related choices, as opposed to choices unrelated to food.

Additionally, we observed 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 choices unrelated to disorder information.

There is a growing consensus that the reward and punishment processes in AN are not a generic process, but instead are influenced by complex interactions between various stimulus properties (such as the type of reward/punishment cue) and contextual factors [such as long-term objectives, personality traits, temperamental dispositions, and physiological states like hunger, etc.). A recent comprehensive review by Haynos, Lavender, Nelson, Crow, and Peterson (2020) showed that the manner in which AN patients perceive their experiences as rewarding or punishing is influenced by factors such as the degree of predictability, controllability, immediacy, and effort. For example, behaviors associated with AN that are predictable, controllable, and immediate (such as calorie counting or purging) may become rewarding to the individual, providing a sense of control and accomplishment. On the other hand, behaviors that are unpredictable and uncontrollable (such as social outcomes) may be perceived as punishing, increasing anxiety and distress.

Most of these previous studies have mainly explored the subjective value assigned to various experiences by AN patients, which can be perceived as either rewarding or punishing, despite not inherently having these properties. In contrast, the current study examine the effect of contextual factors on the learning mechanism that blends past experiences of clearly defined reward and punishment.

The purpose of this study was to examine the impact of symptom-related information (irrelevant to the task outcome) on the performance of AN and BN patients in an associative learning task. Previous research has shown that outcome-irrelevant information can negatively impact reward learning in the general population. Here, we replicated the findings of Shahar et al. (2019) that image/effector response mapping influences associative learning in a PRL task when only image identity predicts the reward, in all our groups of HCs, AN patients, BN patients, and RI patients. More notably, we discovered that AN patients had a slower learning rate from rewards when image identity provided food information. This was shown by a decrease in the α^+ parameter (which measures the rate of learning from positive feedback) of the RLDDM model, compared to HCs (Pedersen & Frank, 2020). Instead, when image identity was unrelated to food, there was no difference in the rate of value update between AN patients and HCs.

The present results are relevant for the current debate on the role of maladaptive reward and punishment processing in AN. Current theories propose that AN is characterized by a combination of reduced sensitivity to reward and increased sensitivity to punishment, leading to an imbalance in reward processing. This imbalance is thought to result in decreased interest in food rewards and increased control over food intake, contributing to the persistence of AN symptoms. Additionally, heightened punishment sensitivity may contribute to AN by promoting avoidance of food and weight gain, which may be perceived as aversive. However, as Haynos et al. (2020) points out, such characterization of AN as having distorted reward and punishment processing, which is a domain-general description, is inadequate because it does not consider the differences in response depending on the particular characteristics of the cues involved. In their literature review, Haynos et al. (2020) show that current evidence does not indicate a universal shortfall in AN reward and punishment processing. Rather, there seem to be an inappropriate interpretation of what constitutes a reward or punishment in various contexts and for different stimuli and decisions. Behaviors that initially may not be considered rewards or punishments can eventually become associated with either positive or negative reactions, leading them to serve as a form of reward or punishment.

For instance, Haynos et al. (2020) posits that restrictive eating cues, a precursor of AN, can be linked to reward responses in AN. This hypothesis is supported by ecological momentary assessment (EMA) studies that examine affective patterns in relation to disordered eating. These studies have shown higher positive affect and lower negative affect before, during, and after restrictive eating episodes in AN compared to normal meals (Fitzsimmons-Craft et al., 2015) and subsequent reductions in guilt in AN and increased self-assurance for individuals with AN-R (Haynos et al., 2017). These findings indicate that restrictive eating is linked to desirable emotional outcomes in AN and, thus, can be understood as rewarding. Although decreased sensitivity to reward in AN has been documented in some contexts, such as individuals with AN scoring lower on sensation-seeking measures that gauge reactions to immediate novel rewards compared to healthy individuals and those with bulimia nervosa (BN) or binge eating disorder (BED; Matton, Goossens, Vervaet, & Braet, 2015; Rotella et al., 2018), this does not indicate that a reduced sensitivity to reward is evident across all contexts. For instance, the rewarding nature of restrictive eating is not reflected in this reduced sensitivity. The review by Haynos et al. (2020) offers several additional examples of cues, contexts, or decisions that may only be associated with reward or punishment if they are viewed in the context of the ultimate objectives of AN (i.e., thinness). This way of thinking is very much in line with the present results. What the present study adds to this previous theoretical proposal is that previous evidence of domain-specificity of reward and punishment processing in AN have only been provided in an indirect form, that is, in terms of the re-interpretation of cues and consequences of actions in the context of an overarching long-term goal; instead, the present study, for the first time, addresses this issue in a direct manner within the context of associative learning in which reward and punishment are direct consequences of choices.

Other recent studies have examined the issue of the domain-specificity of maladaptive associative learning in eating disorders. One task that has been specifically devised for this purpose is the two-step Markov decision task, which differentiates between automatic or habitual (model-free) and controlled or goal-directed (model-based) learning. For example, Foerde et al. (2021) and Onysk and Seriès (2022) both conducted similar experiments using this task, with Foerde et al. (2021) comparing a monetary two-step task and a food two-step task, and Onysk and Seriès (2022) using stimuli unrelated to food or body images (pirate ships and treasure chests) with rewards associated with body image dissatisfaction. The results of these experiments showed that individuals with AN displayed a stronger preference for habitual control over goal-directed control across domains compared to healthy controls, but there were no differences in the learning rate. However, the primary aim of the two-step experiments was to determine whether the participants' decision-making strategy was influenced by the context or solely based on the previous feedback received, regardless of the context. The results showed that AN patients had difficulty adapting to changing contexts compared to healthy controls (HCs). Furthermore, the experiments did not reveal any differences in the impact of the context (food-related or neutral) on decision making in AN. More importantly, the two-step task did not uncover any difference in the learning rate of AN patients compared to healthy controls (HCs), as a function of the context. In contrast, our results indicate that the learning process itself, particularly the rate at which values are updated, is influenced by information related to the disease, even when such information is not relevant to the outcome.

From a translational perspective, our findings suggest that, at the stage of the disease currently examined, AN patients exhibit maladaptive learning only in certain contexts, and this appears to be influenced by extraneous variables. This is particularly evident in the current study, where the experimental variable (the image identity in the PRL task) has no bearing on the outcome. These results imply that clinical interventions at the present stage of the disease should not concentrate on fixing a seemingly faulty associative learning mechanism. Instead, attention should be directed towards reducing the influence of disruptive factors that hinder the performance of intact associative learning capabilities.

There remain questions for future research. (1) For example, we used images of a one euro coin or a barred representation of a one euro coin to symbolize rewards and punishments, respectively. But such rewards and punishments are only symbolic and the question remains as to what happens when the rewards and punishments are concrete and not symbolic. Yet, these rewards and punishments were merely symbolic, and the question remains as to what happens when the rewards and punishments are actual and not symbolic. Moreover, the subjective value of one euro, or the loss of one euro, is not constant for all participants. Furthermore, the subjective worth of one euro or the loss of one euro is not uniform across all participants. Determining the equivalence of subjective values for rewards and punishments could be a worthwhile objective for future studies. (2) Our study only included AN patients who were not in the most severe stage of the illness, as they were recruited from a center for individuals seeking voluntary medical and psychological support. We did not consider AN patients who are hospitalized due to the life-threatening nature of their illness. It is possible that at the later stage of the illness, the associative learning abilities, which were shown to be preserved in the present sample under neutral conditions, may become impaired. (3) We observed no difference in the choice behavior of AN patients (as measured by relative frequency of image choices) when they were asked to select between a neutral image and a food image. However, when compared to the situation where they had to choose between two neutral images, this condition did result in a slower learning rate and lower decision threshold for AN patients, as compared to healthy controls, according to the RLDDM model. It is possible that the higher "salience" of food images compared to neutral images may be better captured by other measures, such as fixation length or number of fixations, rather than just by the relative frequency of image choices. This could be a topic for future exploration. (4) In our study, we 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 that cognitive development is ongoing and protective factors are less developed. Future studies should take this into consideration.

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