1   When Food Becomes a Distraction: The Impact of Food-Related Information on Reward

2   Learning in Anorexia Nervosa

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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

Word count: X

When Food Becomes a Distraction: The Impact of Food-Related Information on Reward

Learning in Anorexia Nervosa

Introduction

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

Executive functions have gained significant attention in the research on understanding 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

84 atypical RL behavior in R-AN may arise from the interference of extraneous contextual

85 factors, even in the presence of intact RL mechanisms (Haynos, Widge, Anderson, & Redish,

86 2022). This hypothesis suggests that contextual factors, encompassing personal

87 characteristics, long-term goals, and situational influences, can exert a negative impact on

88 RL performance, regardless of the presence of an underlying RL deficit. Individuals with

89 R-AN, being particularly susceptible to the influence of symptom-related information such as

90 food, body weight, and social pressure [ref], may experience heightened vulnerability to these

91 interfering contextual factors.

92   To investigate the influence of contextual factors on decision-making in R-AN, we

93 conducted a study using a Probabilistic Reversal Learning (PRL) task. This task measures

94 RL and cognitive flexibility by allowing participants to learn from feedback and adjust their

95 behavior based on reward probabilities. The task reflects real-life situations where outcomes

96 are uncertain, requiring individuals to make decisions based on probabilities. By presenting

97 uncertain and varying reward probabilities, the task captures the complexities of

98 decision-making under uncertainty and provides insights into how individuals integrate

99 probabilistic information to guide their behavior. The PRL task involves unannounced

100 reversals of contingencies, demanding behavioral adaptation to changing environments. This

101 reversal learning aspect measures cognitive flexibility – i.e., the ability to shift behavior in

102 response to changing environmental demands. The PRL task has been extensively used in

103 neuroscience research and has shown associations with specific brain regions involved in

104 reinforcement learning and cognitive flexibility [ref]. Neuroimaging techniques like fMRI have

105 revealed neural activations and connectivity patterns during the task, corresponding to

106 reward processing, error monitoring, and cognitive control mechanisms.

107   In contrast to previous studies that utilized general stimuli (Schaefer & Steinglass,

108 2021), our study implemented the PRL task with two distinct conditions. Participants were

109 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.

135   Based on the evidence suggesting that outcome-irrelevant information can impact PRL

136 performance, the study hypothesized that differences in RL between R-AN patients and the

137 control groups would primarily emerge in the disorder-relevant condition. Conversely, no

138 substantial differences were expected in the disorder-unrelated condition. By incorporating

139 both disorder-relevant and disorder-unrelated stimuli, the study aimed to examine and

140 quantify anomalies in RL performance among individuals with R-AN, thereby shedding light

141 on the role of contextual factors in their decision-making processes.

Evidence of contextual factors on RL learning in AN

143   TODO

144   The almost totality of the studies have used general (rather than disorder-relevant)

145 stimuli (Schaefer & Steinglass, 2021).

Implications for treatment

147   The hypothesis of contextual maladaptive RL in R-AN has potential implications for

148 treatment. For example, Cognitive Remediation Therapy (CRT) has been proposed as an

149 adjunct treatment targeting specific cognitive processes in AN and other eating disorders.

150 CRT involves cognitive exercises and behavioral interventions aimed at increasing central

151 coherence abilities, reducing cognitive and behavioral inflexibility, and enhancing thinking

152 style comprehension (Tchanturia et al., 2010). A key aspect of CRT is to avoid discussing

153 symptom-related themes and instead use neutral stimuli in cognitive and behavioral

154 exercises. This approach aims to develop a therapeutic alliance and to decrease drop-out

155 rates, particularly with AN patients.

156   However, recent evidence suggests that CRT may not consistently improve central

157 coherence abilities, cognitive flexibility, or symptoms related to eating disorders (Hagan et

158 al., 2020; Tchanturia et al., 2017). In response to this, Trapp et al. (2022) have proposed

159 improvements to address practical issues encountered in the application of CRT. They

160 question the use of neutral stimuli and draw support from Beck's cognitive theory of

161 depression (Beck et al., 1987).

162   The proposal put forth by Trapp et al. (2022) aligns with the hypothesis of this study,

163 suggesting that contextual factors play a crucial role in the maladaptive eating behavior

164 observed in individuals with R-AN, beyond deficits in the underlying RL mechanism alone.

165 If abnormal reward learning is indeed identified as a significant anomaly among individuals

166 with R-AN, particularly in relation to disorder-relevant choices, it would imply that

167 treatments focused on enhancing cognitive flexibility and reinforcement learning processes

168 specific to disorder-relevant stimuli could hold significant promise for this population.

Methods

170   We report how we determined our sample size, all data exclusions (if any), all

171 manipulations, and all measures in the study.

Participants

173   The final sample consists of 69 female outpatients (acAN N = 40, recAN N = 10, acBN

174 N = 13, recBN = 6) and 222 healthy female controls (HCs). Outpatients met Diagnostic and

175 Statistical Manual of Mental Disorders-5 (DSM-5) (American Psychiatric Association, 2013)

176 criteria for AN or BN. They were recruited from the Specchidacqua Institute, Montecatini

177 (PT), Italy, specialized in Eating Disorders. Eligibility was evaluated by the Mental Health

178 professionals of the Institute, the exclusion criteria were having neurological illness, suicidal

179 ideation, alcohol or drug addiction, or psychosis. The acAN (mean age = 20.5 years, $SD =$

180 1.13) and acBN (mean age = 23.15 years, $SD = 1.87$) participants were admitted to

181 psychological treatment at Specchidacqua Institute, 45% of them were also taking

182 antidepressant medication (SSRI), and 38% reported comorbidity with other psychiatric

183 illnesses (22% anxiety disorders, 20% obsessive-compulsive disorder, 9% mood disorders).

184 Mean Body Mass Index was considerable lower for acAN patients (BMI mean = 18.29kg/m2

185   ) then acBN (BMI mean = 24.84kg/m2). Recovered outpatients were recruited from the

186   Gruber Residence, Bologna (BO), Italy. To be included in the recovered group, recAN (mean

187   age = 24.1 years, SD = 1.8) and recBN (mean age = 29.3 years, SD = 2.5) outpatients had

188   to (a) not being seriously underweight ($BMI \geq 18.5$ kg/m2), (b) not engage in

189   dysfunctional eating behaviors (*e.g.*, restrictive diet or binging/purging) for at least 6

190   months, and (c) being adherent to the psychological treatment. HC participants were

191   recruited from undergraduate psychology courses at the University of Florence, Italy, or via

192   social networks. To be included in the HC group, participants had to have a normal Body

193   Mass Index (BMI mean = 21.29 kg/m2), have no history of psychiatric illness, and have no

194   diagnosis of Eating Disorders, according to the Eating Attitudes Test-26 [EAT-26; Garner,

195   Olmsted, Bohr, and Garfinkel (1982), Dotti and Lazzari (1998)] score (EAT-26 < 20).

196   However, 28 out of 222 participants exceeded the EAT-26 cut-off (EAT-26 > 20), meaning

197   the presence of a tendency to eating symptoms. Therefore, the final HC group was composed

198   by 194 participants (mean age = 21.5 years, SD = 0.23), and the other 28 were classified as

199   at-risk participants (mean age = 21.28 years, SD = 0.55). All participants were caucasian,

200   right-handed, and were na"ive to the aim of the study.

201   **Material**

202   **Clinical and Demographic Measurements.**   The *Eating Attitude Test-26*

203   (EAT-26, Garner et al., 1982) consists of 26 items assessing levels and types of eating

204   disturbances in the past three mouths. The EAT-26 is characterized by three subscales: the

205   Dieting Scale, the Bulimia and Food Preoccupation Scale and the Oral Control Scale. Scores

206   ≥ 20 point out the presence of an eating disorder. Respondents are required to rate intensity

207   associated with the items on a 6-point Likert scale (0 = never, rarely, sometimes; 3 =

208   always). The Italian version of the EAT-26 demonstrated good psychometric properties

209   (Dotti & Lazzari, 1998). In fact, Cronbach's alpha was high in an undergraduate sample for

210   the Dieting scale (.87), for Bulimia and Food Preoccupation scale (.70), for Oral Control

211 Scale (.62). Cronbach's alpha for the total scores was 0.86.

212   The *Body Shape Questionnaire-14* [BSQ-14; Dowson and Henderson (2001)] is a

213 14-item self-report scale assessing the global body satisfaction in the past two weeks.

214 Respondents are required to rate intensity of concerns about own appearance associated with

215 the items on a 6-point Likert scale (1 = never, 6 = always). The Italian version of the

216 BSQ-14 demonstrated good psychometric properties (Matera, Nerini, & Stefanile, 2013). In

217 the present sample, $\omega = 0.978$. For the 40-item BSQ, a score below 80 is considered "no

218 concern", a score of 80 to 110 is considered "slight concern", a score of 111 to 140 is

219 considered "moderate concern", and a score above 140 is considered "marked concern".

220   The *Social Interaction Anxiety Scale* [SIAS; Mattick and Clarke (1998)] is a 20-item

221 self-report questionnaire assessing social interaction anxiety. Respondents are required to

222 rate intensity associated with the items on a 4-point Likert scale from 0 (not at all true) to 4

223 (extremely true). Higher scores denote greater social interaction anxiety levels. Both original

224 version and the Italian version (Sica, Musoni, Bisi, Lolli, & Sighinolfi, 2007) show acceptable

225 psychometric properties (in the present sample $\omega = 0.938$). Heimberg, Mueller, Holt, Hope,

226 and Liebowitz (1992) have suggested a cut-off of 34 on the 20-item SIAS to denote a clinical

227 level of social anxiety (32.3 for the Italian 19 item version).

228   The *Depression Anxiety Stress Scale-21* [DASS-21; Lovibond and Lovibond (1995)] is a

229 21-item self-report measure assessing depression, anxiety, and stress over the previous week.

230 Items are rated on a 4-point scale ranging from 0 (did not apply to me at all) to 3 (applied

231 to me very much). Both the original and the Italian version (Bottesi et al., 2015)

232 demonstrate adequate reliability. In the present sample $\omega_{\text{anxiety}} = 0.875$, $\omega_{\text{depression}} = 0.914$,

233 $\omega_{\text{stress}} = 0.899$; for the total scale, $\omega = 0.945$.

234   The *Rosenberg Self-Esteem Scale* [RSES; Rosenberg (1965)] is a 10-item scale designed

235 to assess person's overall self-esteem. It comprises five straightforwardly worded and five

236 reverse-worded items each rated on a 4-point Likert scale ranging from 4 (strongly agree) to

237 1 (strongly disagree). Increased values indicate increased self-esteem. In the present sample,

238 $\omega = 0.949$.

239 The *Multidimensional Perfectionism Scale* [MPS-F; Frost, Marten, Lahart, and

240 Rosenblate (1990)] is a 35-item assessing perfectionism tendencies. According to Stöber

241 (1998), MPS-F is composed of four underlying factors: Concerns over Mistakes and Doubts

242 (CMD), Parental Expectations and Criticism (PEC), Personal Standards (PS), and

243 Organization (O). Both the original MPS-F and the Italian version (Lombardo, 2008)

244 demonstrate adequate reliability. In the present sample, $\omega_{\mathrm{CMD}} = 0.919$, $\omega_{\mathrm{PS}} = 0.851$, ω_{PEPC}

245 $= 0.946$, $\omega_{\mathrm{OR}} = 0.931$; for the total scale, $\omega = 0.932$.

246 Height and weight were measured with a stadiometer and a digital scale, respectively.

247 Estimated IQ was assessed with the Progressive Raven's Matrices Intelligence test.

Procedure

249 The study was approved by the Ethical Committee of the University of Florence, and

250 was run in accordance with the Declaration of Helsinki. Each eligible participant signed the

251 informed consent and agreed to be part of the study. Both the HCs group and the patients

252 group completed the same tasks. Data collection started in December, 2020 until June, 2022.

253 We have to deal with COVID-19 restrictions for the most of the time. Thus, we collected

254 data from HCs remotely: we recruited HCs participants by means of social networks or

255 advertisements at the University. Interested people contacted us using the email on the

256 advertisement, then we send them the informed consent, which they had to sign and send it

257 back to us. Individuals that signed the informant consent were tested for eligibility using

258 self-reported measures. Participants who met the inclusion criteria for HCs group, received

259 instructions via email and completed the PRL task remotely. After completing the task,

260 participants had to notify us, so that we can check the correct registration of data. On the

contrary, data collection for the clinical group was in person. We enrolled only eligible patients, selected by the mental health professionals of the Institute. We scheduled two meeting per participants at the Specchidacqua Institute, Montecatini (PT), Italy.

On the first session, participants signed the informed consent form and completed a battery of self-report questionnaires. On the second session, participants were asked to complete the PRL task. Data collection required overall 1 hour of their time.

Participants completed a reinforcement learning bandit task in two conditions: neutral (two neutral images on each trial) and symptom-specific (a symptom-specific and a neutral image on each trial). This design allowed us to examine outcome-irrelevant learning associated to a symptom-specific context.

Participants completed a total of 2 blocks of the reinforcement learning task. Each block included a different set of image stimuli and had XX trials. Participants did not received any bonus at the end of the task based on their performance.

For measuring cognitive flexibility, participants completed a computerized Probabilistic Reversal Learning (PRL) task. There were two blocks of trials including 160 trials each. In one of the two blocks a neutral image (*e.g.*, a lamp) and a symptom-related image (*i.e.*, a piece of cake) were shown together, to test the domain-specificity hypothesis Caudek, Sica, Marchetti, Colpizzi, & Stendardi, 2020). The other block included neutral images only, as a control task. In both blocks we asked participants to choose one of two stimuli presented simultaneously on the left and right side of the center of a screen and made their choice with a keypress. They had 3s response time per trial. An image of a euro coin was provided as a reward and a strikethrough image of a euro coin as a punishment. Feedback was presented for 2 s. The PRL comprises four epochs (*e.g.*, a sequence of trials in which the same image was considered correct) of 40 trials each. The feedback was probabilistic, which means that for each epoch the correct image was rewarded in the 70% of the cases, whereas on 30% of the trials participants received a negative feedback. As a consequence, the other image

provided no-reward 70% of the time. Both blocks consisted of three rule changes (reversal phase). Participants' aim was to earn as much money as possible. They were informed that the stimulus-reward contingencies would change, but they were not told how or when it would happen. Total reward earned was shown at the end of each block. The experiment was controlled by Psytoolkit.

Data analysis

Credible effects were revealed by 95% credible intervals or by 97.5% of posterior samples falling above or below 0 when computing proportion of posterior in direction of effect.

Results

Quality Control

Trials were excluded for extreme RTs (<150 ms, >2500 ms), or if the remaining (log transformed) RT exceeded the participant's mean $\pm$ 3S.D. Participants' datasets were excluded if, in any block, there were more than 20 RT outliers, fewer than 24 rich or 7 lean rewards, a rich-to-lean reward ratio lower than 2.5, or lower than 40% correct accuracy. In Study 1, 258 depressed adults and 36 controls passed the QC criteria. Study 2 data are from participants who passed these QC checks.

Demographic and Psychopathology Measures

Estimating outcome-irrelevant learning

Spatial-motor associations. We start by examining the presence of spatial-motor connections in the participants' choices. We successfully replicated the findings of Shahar et al. (2019) and Ben-Artzi, Luria, and Shahar (2022). Our results showed robust evidence for spatial-motor outcome-irrelevant learning: the probability of choosing 'stay' was higher for 'same' (.427) compared to 'flipped' (.218) response/key mapping when comparing previously

311 rewarded versus unrewarded responses (posterior $\beta = 0.93$, $SE = 0.06$, $HDI_{.95} = [0.81, 1.06]$;

312 probability of direction (pd) 1.0; 0% in ROPE (-0.10, 0.10) and Bayes Factor (BF) of > 100

313 against the null; Fig. 1). There was no group (HC, AN, BN, RI) $\times$ previous outcome $\times$

314 mapping interaction (see Supplementary Materials).

Reinforcement learning and drift diffusion modeling

316   To model the two-choice decision (between image A and image B) over time in the

317 PRL task, we used a hierarchical reinforcement learning drift diffusion model (RLDDM), as

318 described in Pedersen, Frank, and Biele (2017) and Pedersen and Frank (2020). The

319 RLDDM was estimated in a hierarchical Bayesian framework using the `HDDMrl` module of

320 the `HDDM` (version 0.9.7) Python package (Fengler et al., 2021; Wiecki et al., 2013).

321   By breaking down decision-making task performance into its component processes

322 through cognitive modeling analysis, it becomes possible to identify any deviances in the

323 underlying mechanisms that may not be reflected in the overall task outcome. RLDDM has

324 six basic parameters: positive learning rate ($alpha^+$), negative learning rate ($alpha^-$), drift

325 rate (v), decision threshold (a), non-decision time (t), and starting point bias (z) parameters.

326 The α parameter quantifies the learning rate in the Rescorla-Wagner delta learning rule

327 (Rescorla & Wagner, 1972); a higher learning rate results in rapid adaptation to reward

328 expectations, while a lower learning rate results in slow adaptation. The parameter α^+ is

329 computed from reinforcements, whereas α^+ is computed from punishments. The drift rate v

330 is the average speed of evidence accumulation toward one decision. The decision boundary is

331 the distance between two decision thresholds; an increase of a increases the evidence needed

332 to make a decision. The increase of a leads to a slower but more accurate decision; a

333 decrease in a results in a faster but error-prone decision. The non-decision time t is the time

334 spent for stimuli encoding or motor execution (*i.e.*, time not used for evidence accumulation).

335 The starting point parameter z captures a potential initial bias toward one or the other

336 boundary in absence of any stimulus evidence.

To test the interference of disease-related information on the decision process, we built linear models over each RLDDM parameter. We compared models in which we conditioned either none, each or all model's parameters on diagnostic category (group) and image category (neutral, symptom-related). 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 models were examined. Model M1 is a standard RLDDM. Model M2 extends M1 by incorporating separate learning rates for positive and negative reinforcements. In Model M3, the α^+ and α^- parameters are based on the diagnostic group. In Model M4, the α^+ and α^- parameters of M3 are conditioned on both diagnostic group and image category (two neutral images, or one neutral and one symptom-related image). Model M5 expands upon M4 by considering that the a parameter may be influenced by both diagnostic group and image category. Model M6 extends M5 by taking into account the possible influence of diagnostic group and image category on the v parameter. Model M7 builds upon M6 by considering that the t parameter may depend on both diagnostic group and image category. Finally, Model M8 adds to Model M7 the estimation of a potential bias in the z parameter. All models were estimated with Bayesian methods using weakly informative priors. The winning RLDDM (with lowest DIC) is M7. In the Model M7, the parameters α^+, α^-, a, v, t (but not z) are conditioned on both diagnostic group and image category.

Model	DIC
M1	103209.264
M2	101590.157
M3	101613.877
M4	99133.675
M5	96150.581
M6	95434.070

Model	DIC
M7	92808.856
M8	93157.611

356   Convergence of Bayesian model parameters was assessed via the Gelman-Rubin

357   statistic. All parameters had $\hat{R}$ below 1.1 (max $= 1.062$, mean $= 1.002$), which does not

358   suggest convergence issues.

359   To gauge the impact of outcome-irrelevant image category on decision-making, we

360   contrasted the difference in posterior estimates of the RLDDM parameters between the

361   neutral and symptom-related image conditions within each diagnostic group. As predicted

362   by Hypothesis H1, the decision threshold (a) was found to be greater for food information

363   than for neutral information: HC, $p(a_{\text{food}} < a_{\text{neutral}}) = .0002$; AN, $p(a_{\text{food}} < a_{\text{neutral}}) = .0026$;

364   BN, $p(a_{\text{food}} < a_{\text{neutral}}) = .0140$; RI, $p(a_{\text{food}} < a_{\text{neutral}}) = .0139$]. Posterior parameters

365   estimates, standard deviation, and 95% credibility intervals are shown in the following table.

Parameter	Posterior estimate (SD)	95% CI
a(AN food)	1.415 (0.039)	1.339, 1.491
a(AN neutral)	1.260 (0.038)	1.186, 1.334
a(BN food)	1.440 (0.066)	1.309, 1.567
a(BN neutral)	1.229 (0.072)	1.086, 1.368
a(HC food)	1.340 (0.016)	1.308, 1.371
a(HC neutral)	1.258 (0.016)	1.226, 1.291
a(RI food)	1.389 (0.039)	1.312, 1.463
a(RI neutral)	1.264 (0.042)	1.183, 1.345

366   As expected by Hypothesis H2, our findings indicate that compared to neutral

367 outcome-irrelevant information, decision-making regarding food information resulted in a

368 lower estimate of the learning rate, but only for the AN group when evaluating reward-based

369 learning, $\alpha^+ = 0.144$ ($SD = 0.092$), $\alpha^+ = 0.759$ ($SD = 0.142$), $p(\alpha^+_{\text{food}} > \alpha^+_{\text{neutral}}) = 0.0013$,

370 Δ score on a logit scale $= 2.939$, 95% CI [0.870, 4.975]. No other credible differences were

371 found regarding Hypothesis H2 (see the Supplementary Material for details).

Biased choices

373   To determine if the subpar performance of AN patients in the RL task was due to a

374 bias towards non-food choices (independent of past action-outcome history), we examined

375 the frequency of food choices in the PRL blocks where a food image was paired with a

376 neutral image. As anticipated based on Hypothesis H1, a bias against the food image was

377 observed: proportion of food choices $= 0.484$, 95% CI [0.477, 0.492]. However, no

378 group-specific bias was detected, as evidenced by the following three comparisons: AN - HC:

379 prop $= -0.002$, 95% CI [-0.029, 0.026]; BN - HC: prop $= 0.015$, 95% CI [-0.029, 0.056]; BN -

380 AN: prop $= 0.017$, 95% CI [-0.035, 0.064]; RI- HC: prop $= -0.007$, 95% CI [-0.031, 0.016].

Comorbidity

382   Individuals with eating disorders often have comorbid psychiatric conditions, including

383 depression (up to 75%), bipolar disorder (10%), anxiety disorders, obsessive-compulsive

384 disorder (40%), panic disorder (11%), social anxiety disorder/social phobia, post-traumatic

385 stress disorder (prevalence varies with eating disorder), and substance abuse (15-40%) – see

386 Woodside and Staab (2006) for further details. In this study, we included patients with

387 comorbidities in our sample in order to increase the generalizability of our findings to the

388 broader psychiatric population: 16 patients in the AN group were diagnosed with comorbid

389 anxiety disorder, 8 with OCD, 1 with social phobia, and 1 with DAP; in the BN group, 4

390 patients were diagnosed with mood disorder and 1 with OCD. Comorbid diagnoses were

391 determined using the DSM-V criteria during psychiatric evaluations spanning a minimum of

392 one year, while the absence of comorbidities was evaluated using the same methods within a

393 comparable timeframe. To determine if the lower learning rate observed in the AN group

394 could be due to comorbidity, we utilized model M7 on the patient data by separating

395 patients into groups with and without comorbid conditions. No credible differences were

396 identified in the parameters of the models between patients with and without comorbid

397 conditions (see Supplementary Materials for additional information).

Discussion

399 There is a growing consensus that the reward and punishment processes in AN are not

400 a generic process, but instead are influenced by complex interactions between various

401 stimulus properties (such as the type of reward/punishment cue) and contextual factors

402 [such as long-term objectives, personality traits, temperamental dispositions, and

403 physiological states like hunger, etc.). A recent comprehensive review by Haynos, Lavender,

404 Nelson, Crow, and Peterson (2020) showed that the manner in which AN patients perceive

405 their experiences as rewarding or punishing is influenced by factors such as the degree of

406 predictability, controllability, immediacy, and effort. For example, behaviors associated with

407 AN that are predictable, controllable, and immediate (such as calorie counting or purging)

408 may become rewarding to the individual, providing a sense of control and accomplishment.

409 On the other hand, behaviors that are unpredictable and uncontrollable (such as social

410 outcomes) may be perceived as punishing, increasing anxiety and distress.

411 Most of these previous studies have mainly explored the subjective value assigned to

412 various experiences by AN patients, which can be perceived as either rewarding or punishing,

413 despite not inherently having these properties. In contrast, the current study examine the

414 effect of contextual factors on the learning mechanism that blends past experiences of clearly

415 defined reward and punishment.

416 The purpose of this study was to examine the impact of symptom-related information

417 (irrelevant to the task outcome) on the performance of AN and BN patients in an associative

⁴¹⁸ learning task. Previous research has shown that outcome-irrelevant information can

⁴¹⁹ negatively impact reward learning in the general population. Here, we replicated the findings

⁴²⁰ of Shahar et al. (2019) that image/effector response mapping influences associative learning

⁴²¹ in a PRL task when only image identity predicts the reward, in all our groups of HCs, AN

⁴²² patients, BN patients, and RI patients. More notably, we discovered that AN patients had a

⁴²³ slower learning rate from rewards when image identity provided food information. This was

⁴²⁴ shown by a decrease in the α^+ parameter (which measures the rate of learning from positive

⁴²⁵ feedback) of the RLDDM model, compared to HCs (Pedersen & Frank, 2020). Instead, when

⁴²⁶ image identity was unrelated to food, there was no difference in the rate of value update

⁴²⁷ between AN patients and HCs.

⁴²⁸   We also found that AN patients demonstrated a slower rate of learning from positive

⁴²⁹ feedback when food information was provided through image identity, compared to BN

⁴³⁰ patients. Conversely, no significant differences were observed when the image identity was

⁴³¹ unrelated to food. These findings replicate previous reports that AN and BN patients exhibit

⁴³² divergent anomalies in decision making (*e.g.*, Chan et al., 2014), but also emphasize that

⁴³³ these variations are more pronounced when considering the processing of information related

⁴³⁴ to the condition.

⁴³⁵   The present results are relevant for the current debate on the role of maladaptive

⁴³⁶ reward and punishment processing in AN. Current theories propose that AN is characterized

⁴³⁷ by a combination of reduced sensitivity to reward and increased sensitivity to punishment,

⁴³⁸ leading to an imbalance in reward processing. This imbalance is thought to result in

⁴³⁹ decreased interest in food rewards and increased control over food intake, contributing to the

⁴⁴⁰ persistence of AN symptoms. Additionally, heightened punishment sensitivity may

⁴⁴¹ contribute to AN by promoting avoidance of food and weight gain, which may be perceived

⁴⁴² as aversive. However, as Haynos et al. (2020) points out, such characterization of AN as

⁴⁴³ 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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