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Food vs money? Effects of hunger on mood and behavioral reactivity to reward in anorexia nervosa

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ABSTRACT

Background: Previous studies using neuroimaging and behavioral measures reported altered reward processing in anorexia nervosa (AN). In addition, anhedonia states are frequently reported in AN, potentially due to the physiological stress produced by the permanent starvation. We investigated the effect of fasting and satiety on mood and reaction times to monetary rewards in AN patients and healthy controls.

Methods: Twenty-four participants with acute AN (BMI 14.4 (11.9–15.5) Kg/m^2) and 17 age and gender matched healthy, normal weight subjects (HW) (BMI 21.8 (18.9–24.9) Kg/m^2) performed a reward task (the wheel of fortune) involving uncertain (50/50 probability of winning high and low rewards), safe and risky (30/70 and 10/90 probabilities) categories in fasted (after an 8-h fasting period) and fed (after intake of a standardized meal) states. Data analysis was done with linear mixed models.

Results: AN reacted slower than HW when maximum uncertainty (50/50) was involved. Positive mood in response to winning was higher when fasting especially for HW, while negative mood in response to not winning was higher in the fed state for both groups. Still, HW were more reactive than AN to not winning a highly predictable monetary reward (10/90 safe).

Conclusion: The data on the reaction times indicate an impaired motor response to uncertainty in AN. Mood reactivity to winning a monetary reward does not seem to be impaired in AN, however, our results suggest that negative mood in response to not winning is less adaptive in AN. Implications to clinical psychotherapy are discussed.

1. Introduction

Anorexia Nervosa (AN) is an eating disorder, mainly affecting women, with a prevalence of approximately 1% (Mohler-Kuo, Schnyder, Dermota, Wei, & Milos, 2016). AN is the eating disorder with the highest mortality rate (Fichter & Quadflieg, 2016), and its pathophysiology remains mostly unclear. It is important to elucidate the mechanisms involved in the acquisition and maintenance of the disorder, especially those related to what is responsible for triggering disease-maintained behaviors.

Previous studies reported altered reward processing in AN at neural level, showing reduced striatal activation to natural and monetary rewards as well as reduced dopamine (DA) function (Barbato, Fichele, Senatore, Casiello, & Muscettola, 2006; Bergen et al., 2005; Davis & Woodside, 2002; Ehrlich et al., 2014; Piazza et al., 1993; Wagner et al., 2007). As it is well established that DA is involved in the processing of reward, a DA deficiency has been hypothesized in the etiology of AN (Berridge & Robinson, 2016; Martin-Soelch et al., 2011; Schultz, 2000). Furthermore, animal studies showed that DA-deficient rats ingest less food than the least necessary for survival (also one of the characteristic behaviors for AN) (Szczypka et al., 1999). Anhedonia, a lessened ability to experience pleasure from rewards, also greater among patients with AN (Davis & Woodside, 2002), has also been connected to poor DA functioning (Willner, Daquila, Coventry, & Brain, 1995).

Tapper (2005) suggests the importance of controlling hunger for research involving feeding and eating behaviors. With regard to that, a recent study showed that fasting increases the reinforcing potential of food rewards, in particular highly caloric ones in normal weight

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controls (Goldstone et al., 2009). This effect has not been tested in participants with current AN. However, several studies indicated that food reward processing is different in AN patients. For instance, Stoner, Fedoroff, Andersen, and Rolls (1996) reported that preferences for high-fat food is stronger in controls than in AN, both in the acute phase and after weight gain. Nonetheless, hunger was not controlled in their study. Many studies with AN are performed with women remitted from AN in order to avoid the confounding effects of malnutrition (Wagner et al., 2007; Wierenga et al., 2015), since research with food rewards showed similarities between acute and remitted patients (Stoner et al., 1996). However, that might not be completely true when monetary rewards are used. One recent study, for instance, has shown that responses to monetary reward were normalized after weight gain in patients remitted from the disorder (Steinglass, Decker, Figner, Casey, & Walsh, 2014), therefore, studying patients in the acute phase may be essential for understanding specific responses to non-food rewards in the disorder.

Investigating monetary reward in AN patients is particularly relevant, because, on one hand, several studies indicated changes in the neural processing of monetary reward in AN patients; and, on the other hand, fasting resp. hunger was evidenced to influence responses to monetary reward (Briers, Pandelaere, Dewitte, & Warlop, 2006). For instance, behavioral results of a functional Magnetic Resonance Imaging (fMRI) study showed a diminished sensibility to the feedback associated with monetary reward in recovered AN patients that could be associated with increased cognitive control when dealing with monetary rewards (Wagner et al., 2007). A study using a gambling task revealed that individuals with AN showed poorer decision-making performances to reward compared to controls, but not remitted AN (Tchanturia et al., 2007). More specifically, patients with AN insisted on choosing cards from decks which allowed them to win larger amounts of money (but more often losing them too), and did not shift, different than did controls and remitted patients, to decks that represented safer conditions, lower rewards, but the possibility of actually winning money (Tchanturia et al., 2007). Taken together, the findings suggest an impairment in the processing of reward, which might also lead to altered perceptions of hedonic mood in severe AN. Regarding the effect of hunger on responses to money, one previous study reported that hunger increased the rewarding value of money in students, who were less willing to give it up while fasting (Briers et al., 2006). Yet, a recent study in women remitted from AN showed that hunger does not modulate responses to monetary reward in this group compared to healthy women (Wierenga et al., 2015), but, up to this date, no study has investigated its effect in acutely ill AN patients.

In summary, altered responses to monetary rewards were observed in patients with AN. Considering the occurrence of fasting in AN and its influence on responses to reward, it is relevant to investigate the effect of the feeding state on these responses in participants with AN. Therefore, the aim of this study was to investigate the effect of fasted and fed states on mood and behavioral reactivity to monetary rewards in acutely ill patients with AN. We hypothesized that AN would show more negative affect and less mood reactivity to winning and losing a monetary reward than healthy controls during fasting, and this group difference would be less strong during the fed state. Also, according to the results obtained by Tchanturia and colleagues (2007), we expected patients with AN to show less mood reactivity than controls to losing higher amounts of reward, as well as the group difference to be stronger during fasting.

2. Methods & materials

2.1. Ethics

The study was carried out according to Good Clinical Practice and the Declaration of Helsinki. The study protocol was approved by the University of Zurich Ethics Commission (KEK-ZH-No 2009-0115/1) and registered on ClinicalTrials.gov (NCT00946816). All participants provided written informed consent.

2.2. Participants

We recruited 24 women who met the DSM-IV (American Psychiatric Association, 2000) unit criteria for AN and had a BMI < 17.5 kg/m2 from an inpatient psychotherapy unit for patients with severe eating disorders of the Psychiatric Department of the University Hospital to participate in this study. Concomitant collected data on gastric emptying and postprandial symptoms from these subjects was recently published (Bluemel et al., 2017). In brief, recruitment and data collection occurred within the first 2–4 weeks after admission to the rehabilitation, within the so called “orientation phase”, a period to make patients familiar with the inpatient clinic setting, after stabilizing somatic and psychiatric symptoms following to admission, and before patients started to gain weight. They should try to eat regularly, although not with the intention of gaining weight. Normal weight age-matched healthy women (HW), with BMI between 18.9 and 24.9 kg/m^2 (n = 17) were recruited via public announcements. Detailed excluding criteria can be found in Bluemel et al. (2017).

2.3. Procedure

All participants completed the Beck Depression Inventory (BDI), a 21-item self-report inventory used to assess levels of depression (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Hautzinger, Bailer, Worall, & Keller, 1994), and the State-Trait-Anxiety Inventory (STAI), a self-assessment inventory of the presence and severity of symptoms and generalized propensity to anxiety (Laux, Glanzmann, Schaffner, & Spielberger, 1981; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). On the study day, all participants fasted for at least an 8-h period. Details can be found in Bluemel et al. (Bluemel et al., 2017). They were not allowed to have any food or drink other than those made available for them during the study. During fasting, the participants were asked to complete the Positive and Negative Affect Schedule (PANAS, T1) (Watson, Clark, & Tellegen, 1988), a 20-item self-reported measure of positive and negative affect, followed by the Wheel of Fortune (WoF) to measure reward-related responses (Ernst et al., 2004), and a second completion of the PANAS (T2). Four hours later, participants ingested a standardized muffin (430 kcal, 21% fat, 63% carbohydrate, 16% protein) (Bluemel et al., 2017), and this was followed by a second completion of PANAS – WoF – PANAS. The timing for the muffin ingestion was related to MRI measures of the digestive function. At each time point, hunger was measured using a well-validated procedure by asking the patients to score, in a scale ranging from 0 (“not full”, “not hungry”) their hunger (Bluemel et al., 2017).

2.4. The wheel of fortune task (WoF)

The WoF (Ernst et al., 2004) consists of a two-choice, computerized task, involving monetary gratification. Participants were shown probability circles with two potential monetary rewards, in three different possibility settings (10/90; 30/70; and 50/50). Participants were instructed to win as much money as possible. In each setting, there was a circle showing the probability of winning the amount of money indicated in relation to the given probability. For example, under the 10/90 condition, the circle would show a 10% chance of winning an amount opposed to a 90% chance of winning another. The computer randomly selected the winning option. If the participant selected the same option, she won the chosen amount of money. Otherwise, no money was awarded. After each choice, a Visual Analogue Scale (VAS), ranging from 1 (not sure) to 5 (completely sure) measured how sure the participant had been of her answer. In addition, participants were asked to rate their mood according to their previous performance (loss x win) also using an emoji VAS, ranging from 1 (the saddest x neutral) to 5

(neutral x the happiest). After a familiarization practice (50/50 wheels), participants performed a total of 62 trials during two runs of 31 trials (11 10/90 wheels; 8 30/70 wheels; and 12 50/50 wheels) each. Selecting the low-probability/high-reward option (the 10 and 30 parts of the 10/90 and 30/70 respectively) was considered a "risky" choice, while selecting the other parts (90 and 70) was considered a "safe" choice. The 50/50 wheels were included because they reflect decision-making during maximum uncertainty.

2.5. Data analysis and statistics

We used linear mixed model analyses and applied restricted maximum likelihood estimation to compare conditions. The following models were fitted for the cross-sectional comparison of AN patients and HW. For affect and hunger ratings before and after the task, full factorial models were fitted including group (AN; HW), session (fasted; fed), and time (before (T1) and after (T2) the task) as fixed factors. In all models, subjects were treated as a random effect. To best account for correlations between repeated measurements, all models were optimized by the covariance type for the repeated observations which produced the lowest Akaike's Information Criterion (AIC; (West, Welch, & Galech, 2007)). Reaction times during positive mood (after winning trials) and negative mood after (non-winning trials), full factorial models were fitted including: group (AN; HW), session (fasted; fed), and decision category (50/50 high reward, 50/50 low reward, 30/70 risky decision, 30/70 safe decision, 10/90 risky decision, 10/90 safe decision) as fixed factors, and subjects as random effects. A diagonal covariance structure was accommodated for the repeated observations of reaction time. For mood after trials, a first-order autoregressive moving average covariance structure was accommodated for the repeated observations. We further explored significant interactions by investigating post-hoc contrasts and pairwise comparisons by using Bonferroni corrections. Statistical analyses were performed using IBM SPSS Statistics 22 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Demographics and descriptive statistics

Demographic data and descriptions of the investigated study population are summarized in Table 1.

3.2. Self-reported hunger

We found significant main effects of group ($F_{(1,\ 31.6)} = 8.09$, $p < 0.01$), session ($F_{(1,\ 93.5)} = 97.53$, $p < 0.001$), and an interaction of group x session ($F_{(1,\ 93.5)} = 9.78$, $p < 0.01$) for hunger. HW generally reported more hunger (M = 34.3, SE = 4.2) than AN (M = 18.8, SE = 3.5). Across groups, more hunger was reported in the fasted session (M = 42.0, SE = 3.6) than in the fed session (M = 11.1, SE = 2.6).

Table 1
Demographic and descriptive data of study population. Descriptive data are given as mean ± standard deviation.

	HW	AN
# Participants	17	24
Age [years, mean]	23 (18–37)	23 (17–41)
BMI [kg/m2, mean][a]	21.8 (18.9–24.9)	14.4 (11.9–16.0)
BDI[a]	3.5 ± 2.0	26.0 ± 9.6
STAI (state)[a]	45.1 ± 7.6	62.6 ± 8.6
STAI (trait)[a]	45.0 ± 7.2	66.4 ± 10.1

Demographic data are given as mean (range); descriptive data are given as mean ± standard deviation.
[a] indicates a significant different distribution between groups (Kruskal-Wallis, all p values < 0.05).

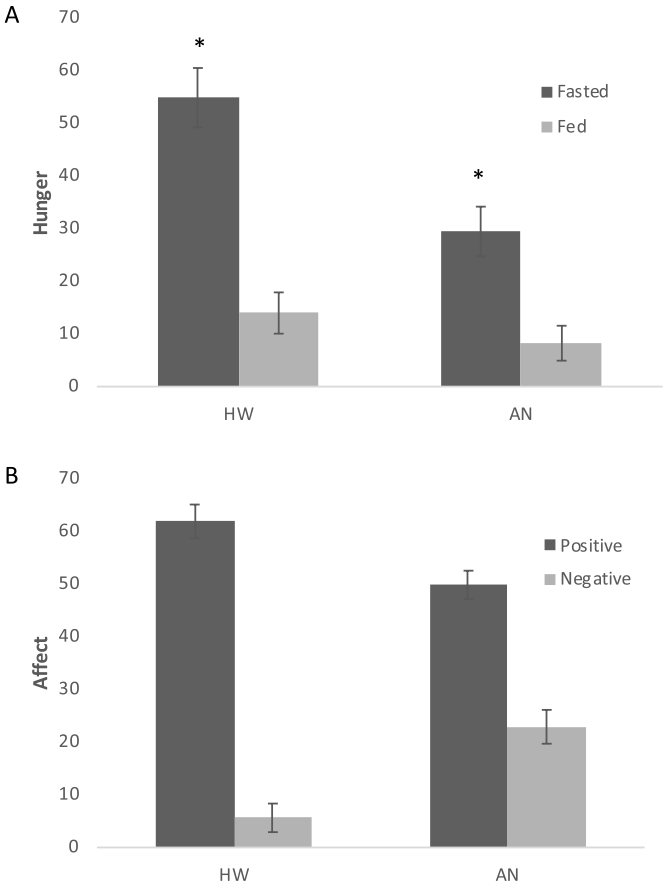

Fig. 1. Means and standard error for self-reported hunger under fasted and fed (**A**) and self-reported affect across time (**B**) in healthy women (HW) and anorexia nervosa (AN). Both HW and AN reported stronger hunger mood under fasted compared to fed, while HW reported more hunger than AN only under fasted. More positive affect was reported among HW, while more negative affect was reported by AN (*p values < 0.05).

The interaction 'group x session' showed that HW only reported more hunger than AN in the fasted session (HW: M = 54.6, SE = 5.6; AN: M = 29.3, SE = 4.7, $p < 0.001$). In the fed session, the group difference for hunger levels was not significant (HW: M = 13.9, SE = 3.9; AN: M = 8.2, SE = 3.3, $p > 0.5$). Results for hunger are shown in Fig. 1A.

3.3. Self-reported affect (PANAS)

We found significant main effects of group ($F_{(1,\ 39.0)} = 8.05$, $p < 0.01$) and time ($F_{(1,\ 57.4)} = 21.75$, $p < 0.001$) on positive affect. With regard to the group effect, HW reported more positive emotions (M = 61.6, SE = 3.2) than AN (M = 49.6, SE = 2.7). For time, participants reported more positive emotions after the task (M = 58.9, SE = 2.3) than before the task (M = 52.2, SE = 2.1) across groups. There was a significant main effect of group on negative emotions ($F_{(1,\ 40.6)} = 16.74$, $p < 0.001$), i.e., AN reported more negative affect (M = 22.8, SE = 2.7) than HW (M = 5.6, SE = 3.2). Means and standard errors for affect are shown in Fig. 1B.

3.4. Responses to reward

The results of the Wheel of Fortune will be presented regarding reaction time and mood following to winning and non-winning trials. Detailed means and standard errors are reported in Table 2 for reaction times and Table 3 for mood.

Table 2
Reaction time in response to reward in the Wheel of Fortune in Anorexia Nervosa (AN) and healthy women (HW) during Fasting and Fed States.

	Session	Decision Category	AN (n = 24), mean ± SE	HW (n = 19), mean ± SE	Fixed Effects	F	P value
Reaction Time	Fasting	50/50 high	2970.30 ± 182.23	2358.56 ± 182.23	Group	1.395	0.245
		50/50 low	2709.07 ± 187.07	2167.58 ± 187.07	Session	190.810	0.000
		30/70 risky	2657.96 ± 207.90	2466.20 ± 207.90	Decision Category	6.163	0.000
		30/70 safe	2410.36 ± 196.63	2449.77 ± 196.63	Group * Session	1.754	0.186
		10/90 risky	2799.29 ± 194.73	2566.44 ± 194.73	Group * Decision Category	5.287	0.000
		10/90 safe	2503.03 ± 182.92	2321.65 ± 182.92	Session * Decision Category	1.518	0.181
	Fed	50/50 high	2295.35 ± 167.75	2025.95 ± 167.75	Group * Session * Decision Category	1.748	0.120
		50/50 low	2213.60 ± 168.45	1658.71 ± 168.45			
		30/70 risky	1933.53 ± 176.60	2133.37 ± 176.60			
		30/70 safe	2123.37 ± 175.64	1973.28 ± 175.64			
		10/90 risky	1943.25 ± 175.93	1973.21 ± 175.93			
		10/90 safe	1930.05 ± 167.46	1586.61 ± 167.46			
	Fasting + Fed	50/50 high	2632.83 ± 138.01	2192.25 ± 162.36			
		50/50 low	2461.34 ± 137.34	1913.15 ± 163.91			
		30/70 risky	2295.75 ± 141.91	2299.79 ± 172.41			
		30/70 safe	2266.86 ± 145.27	2211.52 ± 168.77			
		10/90 risky	2371.27 ± 140.09	2269.82 ± 168.72			
		10/90 safe	2216.54 ± 138.71	1954.13 ± 162.92			

3.4.1. Reaction times

Significant main effects of session ($F_{(1,\ 2828.3)} = 190.81$, $p < 0.001$), decision category ($F_{(5,\ 2789.8)} = 6.16$, $p < 0.001$), and an interaction of group x decision category ($F_{(5,\ 2789.8)} = 5.29$, $p < 0.001$) were found. Across groups, decisions were faster in the fed than during the fasted state. HW reacted faster in 50/50 trials than AN patients, and no group differences were significant in the remaining decision categories.

3.4.2. Mood after winning trials

A main significant effect of decision category ($F_{(5,\ 2311.5)} = 109.01$, $p < 0.001$) as well as interactions of group x session ($F_{(1,\ 142.9)} = 4.73$, $p < 0.05$), group x decision category ($F_{(5,\ 2311.5)} = 9.25$, $p < 0.001$), and session x decision category ($F_{(5,\ 2329.3)} = 3.41$, $p < 0.01$) was found for positive mood after winning trials. . All participants reported higher positive mood after winning trials with 50/50 high reward and winning trials with 10/90 risky compared to the remaining four

Table 3
Mood ratings in response to reward in the Wheel of Fortune in Anorexia Nervosa (AN) and healthy women (HW) during Fasting and Fed States.

	Session	Decision Category	AN (n = 24), mean ± SE	HW (n = 19), mean ± SE	Fixed Effects	F	P value
Positive Mood (to winning)	Fasting	50/50 high	3.68 ± 0.21	3.96 ± 0.25	Group	0.002	0.963
		50/50 low	3.25 ± 0.21	3.27 ± 0.25	Session	1.999	0.160
		30/70 risky	3.61 ± 0.21	3.76 ± 0.26	Decision Category	109.007	0.000
		30/70 safe	3.37 ± 0.22	3.30 ± 0.26	Group * Session	4.733	0.031
		10/90 risky	3.95 ± 0.24	4.42 ± 0.29	Group * Decision Category	9.248	0.000
		10/90 safe	3.33 ± 0.21	3.12 ± 0.25	Session * Decision Category	3.406	0.005
	Fed	50/50 high	3.91 ± 0.21	3.96 ± 0.25	Group * Session * Decision Category	0.816	0.538
		50/50 low	3.37 ± 0.21	3.20 ± 0.25			
		30/70 risky	3.63 ± 0.22	3.54 ± 0.26			
		30/70 safe	3.24 ± 0.22	3.10 ± 0.26			
		10/90 risky	3.97 ± 0.24	3.81 ± 0.29			
		10/90 safe	3.33 ± 0.21	3.01 ± 0.25			
	Fasting + Fed	50/50 high	3.79 ± 0.21	3.96 ± 0.25			
		50/50 low	3.31 ± 0.21	3.23 ± 0.25			
		30/70 risky	3.62 ± 0.21	3.65 ± 0.25			
		30/70 safe	3.30 ± 0.21	3.20 ± 0.25			
		10/90 risky	3.96 ± 0.22	4.11 ± 0.27			
		10/90 safe	3.33 ± 0.21	3.06 ± 0.25			
Negative Mood (to losing)	Fasting	50/50 high	2.61 ± 0.21	2.93 ± 0.25	Group	0.029	0.865
		50/50 low	2.43 ± 0.21	2.50 ± 0.25	Session	7.017	0.009
		30/70 risky	2.39 ± 0.21	2.35 ± 0.26	Decision Category	14.946	0.000
		30/70 safe	2.57 ± 0.22	2.59 ± 0.25	Group * Session	2.709	0.102
		10/90 risky	2.41 ± 0.21	2.45 ± 0.25	Group * Decision Category	2.897	0.013
		10/90 safe	2.67 ± 0.25	2.71 ± 0.30	Session * Decision Category	0.895	0.484
	Fed	50/50 high	3.01 ± 0.21	2.96 ± 0.25	Group * Session * Decision Category	1.067	0.377
		50/50 low	2.75 ± 0.21	2.36 ± 0.25			
		30/70 risky	2.73 ± 0.22	2.51 ± 0.25			
		30/70 safe	2.83 ± 0.22	2.55 ± 0.25			
		10/90 risky	2.89 ± 0.21	2.46 ± 0.25			
		10/90 safe	2.88 ± 0.26	3.17 ± 0.30			
	Fasting + Fed	50/50 high	2.81 ± 0.20	2.95 ± 0.24			
		50/50 low	2.59 ± 0.20	2.43 ± 0.24			
		30/70 risky	2.56 ± 0.20	2.43 ± 0.24			
		30/70 safe	2.70 ± 0.20	2.57 ± 0.24			
		10/90 risky	2.65 ± 0.20	2.46 ± 0.24			
		10/90 safe	2.78 ± 0.23	2.94 ± 0.26			

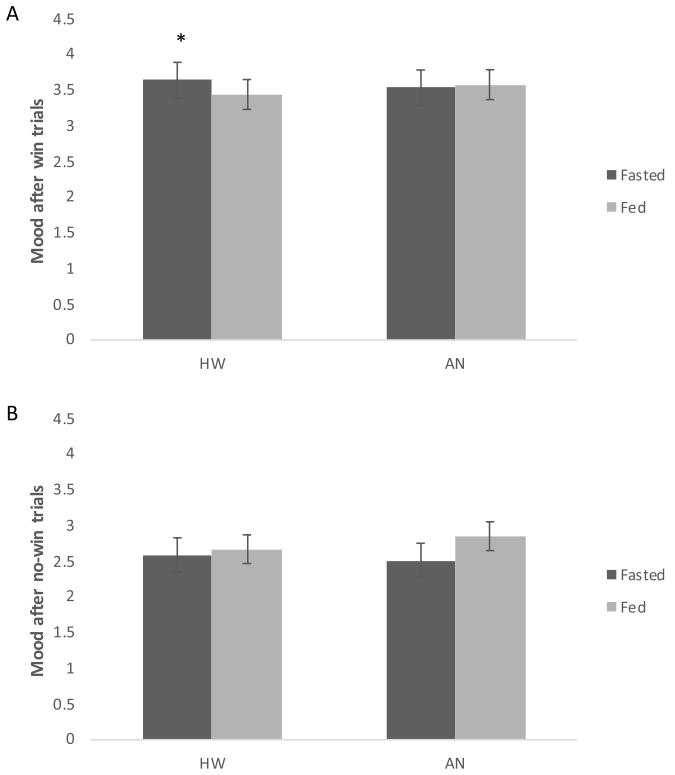

Fig. 2. Positive mood after winning trials (**A**) and negative mood after non-winning trials (**B**) across sessions. Better mood was reported by HW in fasted than in fed (*p < 0.001), while no significant difference between sessions was seen for AN, or negative mood after non-winning trials.

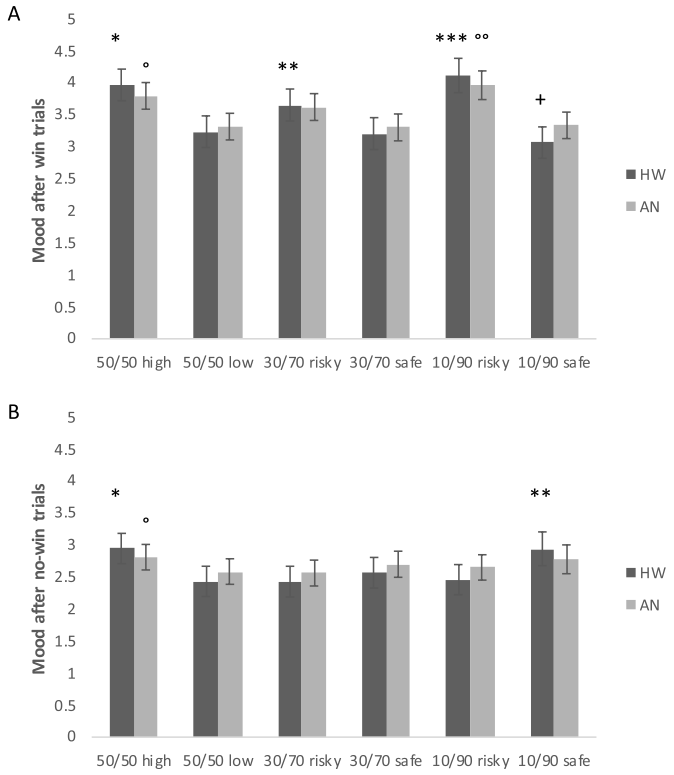

Fig. 3. Positive mood after winning trials (**A**) and negative mood after non-winning trials (**B**) across groups and decision categories. (**A**) In HW, more positive mood was reported after 50/50 high reward conditions in comparison to all other categories, except 10/90 risky (*p values < 0.05). Also, more positive mood was reported after win-trials involving 30/70 risky compared to 50/50 low reward, 30/70 safe and 10/90 safe condition (**p values < 0.05). Still, HW reported more positive mood after winning trials with 10/90 risky conditions compared to other 30/70 and 10/90 conditions (***p values < 0.05), and more positive mood after every category compared to 10/90 safe ($^{+}$p values < 0.05). AN reported more positive mood after 50/50 high reward compared to all but 10/90 risky category (^{o}p values < 0.05). Also, more positive mood was reported by AN in 10/90 risky in comparison to 50/50 low reward, 30/70 risky, 30/70 safe and 10/90 safe conditions (^{oo}p values < 0.05). (**B**) HW and AN reported stronger negative mood after 50/50 low reward and 30/70 risky category compared to 50/50 high reward (*^{o}p values < 0.05). In addition, HW reported stronger negative mood also after 30/70 safe and 10/90 risky categories compared to 50/50 low reward. Moreover, stronger negative mood was reported by HW after 10/90 safe compared to 50/50 low, 30/70 risky and 10/90 risky (**p values < 0.05).

decision categories. Less positive mood was reported after trials with low and safe rewards. Across decision categories, HW reported higher positive mood after winning trials in the fasted than in the fed session, while the difference between sessions was not significant for AN (Fig. 2A). The 'group x decision category' interaction (Fig. 3A) revealed that for HW positive mood was significantly higher after winning trials involving high (50/50) and risky rewards. For AN, higher positive mood after winning was also seen after the higher and riskier reward. After winning trials with 30/70 safe decisions as well as winning trials with 10/90 risky decisions, positive mood was stronger in the fasted state.

3.4.3. Mood after non-winning trials

Significant main effects of session ($F_{(1,\ 176.2)} = 7.02$, $p < 0.01$), decision category ($F_{(5,\ 2188.2)} = 14.95$, $p < 0.001$), and an interaction of group x decision category ($F_{(5,\ 2188.2)} = 2.90$, $p < 0.05$) were found for negative mood after non-winning trials. Across sessions, participants reported more negative mood after non-winning trials in the fed state. Also, higher negative mood was reported after non-winning trials with high and safe rewards (50/50 high reward; 10/90 safe decisions). The 'group x decision category' revealed that in both groups, participants reported more negative mood after non-winning trials with 50/50 high reward compared to low as well as after non-winning trials with 30/70 risky decisions. For AN, these were the only significant comparisons between decision categories. HW additionally reported more negative mood after non-winning trials with that involved high and safe rewards. Means and standard errors for negative mood after non-winning trials are presented in Fig. 3B.

4. Discussion

The aim of this study was to investigate behavioral and affective reactions to monetary reward in AN and healthy women during fed and fasted states. HW reported higher positive and lower negative affect than AN throughout the study. HW's reaction time was faster than AN's when maximum uncertainty was involved, regardless the session. HW reported higher significant positive mood in response to winning during fasting compared to a fed state, while the same difference was not observed in AN. Higher negative mood to not winning a highly predictable reward was only reported among HW, while no significant distinction was seen in AN.

Confirming our hypothesis, reward had a more significant effect on positive mood after winning in the *fasted* state, especially in healthy participants. This is in line with a recent questionnaire study that investigated the effect of hunger in healthy women and stated that their self-reported sense of reward increased proportionally to the fasting time (Watkins & Serpell, 2016). The lack of mood differences between the sessions in reward-related mood in participants with AN could be explained by a general blunted reactivity to reward that could be linked to anhedonia (Davis & Woodside, 2002). This is partly supported by our findings showing more negative and less positive affect in AN as measured by the PANAS, even though AN participants also show an increase

of positive affects measured after the WoF. One explanation for that could be related to a diminished self-awareness of hunger among in AN compared to controls, which may have led to a smaller effect of the session. Davis and Woodside (2002) suggest that the anhedonic state in AN could be connected to hunger and to the physiological stress caused by starvation. Interestingly, a model integrating reward, stress and hunger was proposed in the pathophysiology of AN. Eating less food would be initially rewarding and, therefore, maintained through conditioning learning (Bergh & Södersten, 1996; Södersten, Nergärdh, Bergh, Zandian, & Scheurink, 2008), which could indicate that participants with AN were more under control of the anhedonia than the sensation of hunger, diminishing the positive mood reactivity to winning a monetary reward. Moreover, food deprivation is said to increase the reinforcing effectiveness of food reward in healthy participants (Tapper, 2005). Our findings alongside those from Watkins and Serpell (2016) indicate the same is true regarding monetary reward for healthy women. The effect is not the same in AN, perhaps because anhedonia levels are usually high in the condition, independently of comorbidities like depression (Davis & Woodside, 2002).

We also found interactions of mood and winning/not-winning according to groups and decision categories. For both HW and AN, conditions involving the highest and riskiest rewards evoked stronger increases of positive mood after winning. A reward dysfunction has been reported in AN mostly in relation to aspects proper to the disorder, such as food and body image, and might not be generalized to monetary reward (Keating, Tilbrook, Rossell, Enticott, & Fitzgerald, 2012), but this could be especially when only winning is investigated. In non-winning conditions, AN significantly showed diminished negative mood reactivity in response to more decision categories in comparison to HW, especially those involving the safest condition, i.e. the most predictable reward. Indeed, the most adaptive response to not winning a highly predictable reward would be negative mood (Dollard et al., 1939), as seen in HW, but this is not the case in AN. In line with that are the results obtained by Tchanturia and collaborators (2007), that showed participants with AN kept choosing cards that yielded higher amounts of money (they were sensitive to winning money), even though that also meant losing higher amounts of money. The latest did not control AN's responses, even though it did for recovered patients and healthy controls. Although this aspect has not yet been investigated, and our study specially aimed at behavioral and mood responses, it could be hypothesized that the DA dysfunction may lie behind the lower reactivity to not winning a predictable monetary reward in AN. Increased DA release was seen in animal models in response to unpredictable rewards (Schultz, Dayan, & Montague, 1997), and DA is known to play an important role in motivational behaviors (Berridge & Kringelbach, 2008). Further investigation is necessary to clarify this hypothesis.

Regarding reaction times, shorter time was observed in HW under certain decision categories. Specifically, participants with AN had slower reaction times than HW when a maximum uncertainty decision-making attempt (50/50 conditions) was presented. This leads to the comprehension of an existing impairment connecting uncertainty and motor response in AN. In fact, research has shown motor impairments in patients with eating disorders, and specifically in AN (Green, Elliman, Wakeling, & Rogers, 1996; Hamsher, Halmi, & Benton, 1981), with patients reacting slower than controls in some neuropsychological tests. Our results add to the field suggesting this impairment is stronger in response to trials involving uncertainty. Furthermore, a wide range of research has shown intolerance of uncertainty (IU) among patients with eating disorders (Brown et al., 2017), stating, for instance, that uncertainty is strongly avoided (Sternheim, Konstantellou, Startup, & Schmidt, 2011) in AN. Intolerance to uncertainty (IU), as any broad concept, may have different definitions, depending on the context in which the term is used. Here, in the context of decision-making, IU refers to the propensity to prefer sure outcomes to probabilistic (uncertain) ones. Related to this, research has established two different factors defining IU: 1) desire for predictability and 2) uncertainty paralysis (Berenbaum, Bredemeier, & Thompson, 2008). Accordingly, IU influences affective, cognitive and behavioral responses to uncertain situations (Heimberg, Turk, & Mennin, 2004). IU in anorexia nervosa and other eating disorders has been evidenced mostly by means of self-reported questionnaires (Brown et al., 2017), and not more directly via behavioral measures (Sternheim, Startup, & Schmidt, 2011). Still, compared to healthy controls, AN cared more about being successful in choices with uncertainty (Sternheim, Startup, et al., 2011). Recently, Shihata, McEvoy, Mullan, and Carleton (2016) suggested the use of probability-based decision-making tasks for evaluating this pattern in clinical populations. And, although we have not used the most commonly IU questionnaires, AN's slower reaction time to uncertain conditions could support this hypothesis. Nevertheless, these conditions did not evoke more negative mood in the patients than controls, maybe because the mood rating followed the outcome and was strictly connected to it (winning or losing). Another interpretation could be that IU, in the context of the task, might modulate more closely cognitive than affective responses.

This study is not without limitations. First, it is important to note that these results may not generalize to other types of reward. Second, our hunger scale assessed only one dimension, on a Likert scale. Although it included a measure used in other studies (Marciani et al., 2010, 2012), a more comprehensive psychological evaluation should be done, perhaps using a multidimensional scale. Also, a longer fasting time could also be considered. However, we used a standardized way to manipulate fasting (Bluemel et al., 2017; Watkins & Serpell, 2016), which ensured the avoidance of ethical concerns. Finally, one last point of attention would be the number of participants, which, although very well characterized, was not large. Larger samples could provide further knowledge regarding the intersection between decision-making, illness severity and intolerance to uncertainty.

Future research should focus on elaborating different forms of evaluating hunger in this population and also in larger groups. Something more objective, rather than based on the patients' self-description, especially for AN. That because when it comes to factors related to the disorder, patients' perception may be deceived (Milos et al., 2013). Also, hunger should be an aspect controlled in other trials within AN population, especially those considering food reward. Concerning monetary rewards, other validated tasks should be used in order to further analyze the effect of hunger on mood and affect and on reward itself, both behavioral and by means of functional neuroimaging, since Wagner et al. (2007) report reward-related cerebral activation in AN in response to monetary reward, again, having hunger as an independent variable. Besides that, investigating how DA modulates reward predictability in AN may also bring considerable advances. Finally, another the connection between IU and AN by using the WoF to evaluate behavioral responses and their correlation to the IU questionnaire scores should also be explored.

One of the most remarkable findings of this study was that mood reactivity to winning a monetary reward is higher under fasted compared to fed states, leading to the understanding that fasting alters the reinforcing potential of money in healthy women, but not in acutely ill AN patients. Mood reactivity to winning a monetary reward does not seem to be impaired in AN, however, negative mood in response to not winning is less adaptive in the disorder. Finally, behavioral responses to the WoF strengthen the hypothesis of IU in AN.

These findings could be important for therapeutic treatment targets in AN. For instance, interventions should include coping strategies, with the aim to enhance the patients' decision-making ability. In regard with the positive mood produced by monetary reward, the development and testing of an incentive program could be used to address eating, linking proper eating to winning points (avoiding the use of point loss as punishers, since there seems to be a weaker reactivity to losing money in AN). Using behaviors that are more likely (such as winning points that could be exchanged for some form of reward) as potential reinforcers to those less likely (such as eating) to happen have proved

efficient in enhancing clinical population's repertoire (Mitchell & Stoffelmayr, 1973; Winkler, 1970).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.appet.2018.12.017.

Conflicts of interest

None.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR.* Washington, DC: American Psychiatric Association.

Barbato, G., Fichele, M., Senatore, I., Casiello, M., & Muscettola, G. (2006). Increased dopaminergic activity in restricting-type anorexia nervosa. *Psychiatry Research, 142*, 253–255.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 561–571.

Berenbaum, H., Bredemeier, K., & Thompson, R. J. (2008). Intolerance of uncertainty: Exploring its dimensionality and associations with need for cognitive closure, psychopathology, and personality. *Journal of Anxiety Disorders, 22*(1), 117–125. https://doi.org/10.1016/j.janxdis.2007.01.004.

Bergen, A. W., Yeager, M., Welch, R. A., Haque, K., Ganjei, J. K., van der Bree, M. B. M., et al. (2005). Association of multiple DRD2 polymorphisms with anorexia nervosa. *Neuropsychopharmacology, 30*, 1703–1710.

Bergh, C., & Södersten, P. (1996). Anorexia nervosa, self-starvation and the reward of stress. *Nature Medicine, 2*(1), 21–22.

Berridge, K. C., & Kringelbach, M. L. (2008). Affective neuroscience of pleasure: Reward in humans and animals. *Psychopharmacology, 199*(3), 457–480.

Berridge, K. C., & Robinson, T. E. (2016). Liking, wanting, and the incentive-sensitization theory of addiction. *American Psychologist, 71*(8), 670–679.

Bluemel, S., Menne, D., Milos, G., Goetze, O., Oliver, F., Schwizer, W., et al. (2017). Relationship of body weight with gastrointestinal motor and sensory function: Studies in anorexia nervosa and obesity. *BMC Gastroenterology, 17*(4)https://doi.org/10.1186/s12876-016-0560-y.

Briers, B., Pandelaere, M., Dewitte, S., & Warlop, L. (2006). Hungry for money: The desire for caloric resources increases the desire for financial resources and vice versa. *Psychological Science, 17*(11), 939–943. https://doi.org/10.1111/j.1467-9280.2006.01808.x.

Brown, M., Robinson, L., Campione, G. C., Wuensch, K., Hildebrandt, T., & Micali, N. (2017). Intolerance of uncertainty in eating disorders: A systematic review and meta-analysis. *European Eating Disorders Review, 25*(5), 329–343. https://doi.org/10.1002/erv.2523.

Davis, C., & Woodside, D. B. (2002). Sensitivity to rewarding effects of food and exercises in the eating disorders. *Comprehensive Psychiatry, 43*(3), 189–194.

Dollard, J., Doob, L. W., Miller, N. E., Mowrer, O. H., & Sears, R. R. Yale universityInstitute of human relations. (1939). *Frustration and aggression.* New Haven, London: Pub. for the Institute of human relations by Yale university press; H. Milford, Oxford university press.

Ehrlich, S., Geisler, D., Ritschel, F., King, J. A., Seidel, M., Boehm, I., et al. (2014). Elevated cognitive control over reward processing in recovered female patients with anorexia nervosa. *Journal of Psychiatry & Neuroscience, 40*(5), 307–315.

Ernst, M., Nelson, E. E., McClure, E. B., Monk, C. S., Munson, S., Eshel, N., et al. (2004). Choice selection and reward anticipation: An fMRI study. *Neuropsychologia, 42*, 1585–1597.

Fichter, M. M., & Quadflieg, N. (2016). Mortality in eating disorders - results of a large prospective clinical longitudinal study. *International Journal of Eating Disorders, 49*(4), 391–401.

Goldstone, A. P., Prechtl de Hernandez, C. G., Beaver, J. D., Muhammed, K., Croese, C., Bell, G., et al. (2009). Fasting biases brain reward systems towards high-calorie foods. *European Journal of Neuroscience, 30*(8), 1625–1635. https://doi.org/10.1111/j.1460-9568.2009.06949.x.

Green, M. W., Elliman, N. A., Wakeling, A., & Rogers, P. J. (1996). Cognitive functioning, weight change and therapy in anorexia nervosa. *Journal of Psychiatric Research, 30*(5), 401–410.

Hamsher, K. d. S., Halmi, K. A., & Benton, A. L. (1981). Prediction of outcome in anorexia nervosa from neuropsychological status. *Psychiatry Research, 4*(1), 79–88.

Hautzinger, M., Bailer, M., Worall, H., & Keller, F. (1994). *Beck- Depressions-Inventar (BDI): Bearbeitung der deutschen Ausgabe. Testhandbuch.* Bern: Hans Huber.

Heimberg, R. G., Turk, C. L., & Mennin, D. S. (2004). *Generalized anxiety disorder: Advances in research and practice.* New York: Guilford Press.

Keating, C., Tilbrook, A. J., Rossell, S. L., Enticott, P. G., & Fitzgerald, P. B. (2012). Reward processing in anorexia nervosa. *Neuropsychologia, 50*, 567–575.

Laux, L., Glanzmann, P., Schaffner, P., & Spielberger, C. D. (1981). *Das State-Trait-Angstinventar (Testmappe mit Handanweisung, Fragebogen STAI-G Form X 1 und Fragebogen STAI-G Form X 2).* Weinheim: Beltz.

Marciani, L., Cox, E. F., Hoad, C. L., Pritchard, S., Totman, J. J., Foley, S., et al. (2010). Postprandial changes in small bowel water content in healthy subjects and patients with irritable bowel syndrome. *Gastroenterology, 138*(2), 469–477. https://doi.org/10.1053/j.gastro.2009.10.055 477 e461.

Marciani, L., Hall, N., Pritchard, S. E., Cox, E. F., Totman, J. J., Lad, M., et al. (2012). Preventing gastric sieving by blending a solid/water meal enhances satiation in healthy humans. *Journal of Nutrition, 142*(7), 1253–1258. https://doi.org/10.3945/jn.112.159830.

Martin-Soelch, C., Szczepanik, J., Nugent, A., Barhaghi, K., Rallis, D., Herscovitch, P., et al. (2011). Lateralization and gender differences in the dopaminergic response to unpredictable reward in the human ventral striatum. *European Journal of Neuroscience, 33*(9), 1706–1715.

Milos, G., Kuenzli, C., Martin-Soelch, C., Schumacher, S., Moergeli, H., & Mueller-Pfeiffer, C. (2013). How much should I eat? Estimation of meal portions in anorexia nervosa. *Appetite, 63*, 42–47.

Mitchell, W. S., & Stoffelmayr, B. E. (1973). Application of the Premack principle to the behavioral control of extremely inactive schizrophrenics. *Journal of Applied Behavior Analysis, 6*(3), 419–423.

Mohler-Kuo, M., Schnyder, U., Dermota, P., Wei, W., & Milos, G. (2016). The prevalence, correlates, and help-seeking of eating disorders in Switzerland. *Psychological Medicine, 46*(13), 2749–2758. https://doi.org/10.1017/S0033291716001136.

Piazza, P. V., Deroche, V., Deminière, J.-M., Maccari, S., Le Moal, M., & Simon, H. (1993). Corticosterone in the range of stress-induced levels possesses reinforcing properties: Implications for sensation-seeking behaviors. *Procedures of the National Academy of Science, 90*, 11738–11742.

Schultz, W. (2000). Multiple reward signals in the brain. *Nature Reviews Neuroscience, 1*(3), 199–207.

Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science, 275*(5306), 1593–1599.

Shihata, S., McEvoy, P. M., Mullan, B. A., & Carleton, R. N. (2016). Intolerance of uncertainty in emotional disorders: What uncertainties remain? *Journal of Anxiety Disorders, 41*, 115–124. https://doi.org/10.1016/j.janxdis.2016.05.001.

Södersten, P., Nergärdh, R., Bergh, C., Zandian, M., & Scheurink, A. (2008). Behavioral neuroendocrinology and treatment of anorexia nervosa. *Frontiers in Neuroendocrinology,* (29), 4.

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the state-trait anxiety inventory*. Palo Alto: CA: Consulting Psychologists Press.

Steinglass, J. E., Decker, H., Figner, B., Casey, B. J., & Walsh, T. (2014). Is delay of gratification a stable trait of anorexia nervosa? *Paper presented at the society of biological psychiatry, New York* (New York).

Sternheim, L., Konstantellou, A., Startup, H., & Schmidt, U. (2011a). What does uncertainty mean to women with anorexia nervosa? An interpretative phenomenological analysis. *European Eating Disorders Review, 19*(1), 12–24. https://doi.org/10.1002/erv.1029.

Sternheim, L., Startup, H., & Schmidt, U. (2011b). An experimental exploration of behavioral and cognitive-emotional aspects of intolerance of uncertainty in eating disorder patients. *Journal of Anxiety Disorders, 25*(6), 806–812. https://doi.org/10.1016/j.janxdis.2011.03.020.

Stoner, S. A., Fedoroff, I. C., Andersen, A. E., & Rolls, B. J. (1996). Food preferences and desire to eat in anorexia and bulimia nervosa. *International Journal of Eating Disorders, 19*(1), 13–22 doi:10.1002/(SICI)1098-108X(199601)19:1 < 13::AID-EAT3 > 3.0.CO;2-Z.

Szczypka, M. S., Rainey, M. A., Kim, D. S., Alaynick, W. A., Marck, B. T., Matsumoto, A. M., et al. (1999). Feeding behavior in dopamine-deficient mice. *Proceedings of the National Academy of Sciences, 96*(21), 12138–12143.

Tapper, K. (2005). Motivating operations in appetite research. *Appetite, 45*(2), 95–107.

Tchanturia, K., Liao, P. C., Uher, R., Lawrence, N., Treasure, J., & Campbell, I. C. (2007). An investigation of decision making in anorexia nervosa using the Iowa Gambling Task and skin conductance measurements. *Journal of the International Neuropsychological Society, 13*(4), 635–641.

Wagner, A., Aizenstein, H., Fudge, V., Fudge, J., May, J. C., Mazurkewickz, L., et al.

(2007). Altered reward processing in women recovered from anorexia nervosa. *American Journal of Psychiatry, 164*(12), 1842–1849.

Watkins, E., & Serpell, L. (2016). The psychological effects of short-term fasting in healthy women. *Frontiers in Nutrition, 3*(27), https://doi.org/10.3389/fnut.2016.00027.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 47*, 1063–1070.

West, B. T., Welch, K. B., & Galech, A. T. (2007). *Linear mixed models. A practical guide using statistical software.* Boca Raton, FL: Chapman & Hall/CRC.

Wierenga, C. E., Bischoff-Grethe, A., Melrose, A. J., Irvine, Z., Torres, L., Bailer, U. F., et al. (2015). Hunger does not motivate reward in women remitted from anorexia nervosa. *Biological Psychiatry, 77*(7), 642–652. https://doi.org/10.1016/j.biopsych.2014.09.024.

Willner, P., Daquila, P. S., Coventry, T., & Brain, P. (1995). Loss of social-status - preliminary evaluation of a novel animal-model of depression. *Journal of Psychopharmacology, 9*(3), 207–213.

Winkler, R. C. (1970). Management of chronic psychiatric patients by a token reinforcement system. *Journal of Applied Behavior Analysis, 3*(1), 47–55.