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Voluntary Emotion Regulation in Anorexia Nervosa: A Preliminary Emotion-Modulated Startle Investigation

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Abstract

Emotion regulation difficulties are implicated in the development and maintenance of anorexia nervosa (AN). However, research has been limited by an almost exclusive reliance on self-report. This study is the first to use the emotion-modulated startle paradigm (EMSP) to investigate emotional reactivity and voluntary emotion regulation in individuals with AN. Twenty women with AN viewed negative, positive, neutral, and food images and were asked to enhance, suppress, or maintain their emotional responses mid-way through picture presentation. Startle eyeblink magnitudes in response to startle probes administered prior, and subsequent, to regulation instructions indexed emotional reactivity and regulation, respectively. On emotional reactivity trials, startle magnitudes were greater for negative, positive, and food images, compared to neutral images. Participants had difficulty suppressing startle responses to negative and food images, as indicated by non-significant suppress-maintain comparisons. In contrast, startle responses to enhance and suppress cues during presentation of pleasant images were comparable and significantly lower than maintain cues. Findings converge with self-report data to suggest that patients with AN have difficulties with voluntary emotion regulation. The EMSP may be a promising trans-diagnostic method for examining emotion regulation difficulties that underlie risk for eating disorders and other psychiatric conditions.

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Contributors

Dr. Racine contributed to study design, data processing, data collection, data analysis, and manuscript preparation. Drs. Forbush and Wildes contributed to study design, data collection, and manuscript preparation. Ms. Hagan, Ms. Pollack, and Ms. May contributed to data processing and manuscript preparation. All authors have approved the final manuscript.

Introduction

Theoretical models and treatment development efforts have increasingly focused on the role of emotion regulation difficulties in the etiology and maintenance of anorexia nervosa (AN) (Haynos and Fruzzetti, 2011, Schmidt et al., 2012, Treasure and Schmidt, 2013, Wildes et al., 2014). Emotion regulation can be defined as the process of intensifying, weakening, altering, or maintaining emotions (both positive and negative) according to one's goals (Gross, 2007). AN is associated with broad impairments in emotion regulation (Lavender et al., 2015, Oldershaw et al., 2015), and emotion dysregulation prospectively predicts the maintenance of AN symptoms (Racine and Wildes, 2015). However, almost all studies in this area assess emotion regulation using self-report questionnaires. This is potentially problematic because data suggest that individuals with AN have problems with emotion recognition, awareness, and avoidance (Oldershaw et al., 2011, Oldershaw et al., 2015, Wildes et al., 2010). Moreover, several studies have found discrepancies between self-reported emotional and physiologic reactivity to emotional events (Nandrino et al., 2012, Zonneville-Bender et al., 2005). Thus, individuals with AN may have difficulty accurately reporting on their emotion regulation skills. Employing psychophysiological methods to more objectively assess emotion regulation has the potential to significantly contribute to our understanding of emotion dysregulation in patients with AN.

The emotion-modulated startle paradigm (EMSP) is a well-validated psychophysiological method that has been used extensively to study emotional reactivity (Grillon and Baas, 2003, Lang et al., 1990) and, more recently, voluntary emotion regulation (Conzelmann, McGregor, & Pauli, 2015; Dillon and LaBar, 2005, Jackson et al., 2000, Piper and Curtin, 2006). Typically in this paradigm, participants are presented with images that vary on valence (i.e., positive vs. negative) and arousal (i.e., low vs. high). The magnitude of the eyeblink response when participants are presented with a startle-inducing stimulus (e.g., acoustic probe) is potentiated (strengthened) in response to fearful or aversive stimuli and inhibited (weakened) in response to pleasant stimuli, relative to neutral stimuli (Lang et al., 1990). Voluntary emotion regulation can be assessed by providing participants with a regulation cue (e.g., enhance, suppress, maintain) and examining startle responses during the period of instructed emotion regulation (Jackson et al., 2000). The neural circuitry that mediates the startle response has been mapped in rodents, with the central and basolateral nuclei of the amygdala underlying startle potentiation during acute negative emotional states (Davis, 1998, Davis et al., 1997, Lang et al., 1990) and the nucleus accumbens underlying startle attenuation during positive emotional states (Koch et al., 1996, 2000). Recently, the EMSP has been proposed as a key biomarker to aid in the classification of psychiatric conditions (Vaidyanathan et al., 2012, Vaidyanathan et al., 2009), consistent with the Research Domain Criteria (RDoC) approach (Insel et al., 2010).

To our knowledge, only two published studies have administered the EMSP to patients with AN. Friederich et al. (2006) examined motivational responses to emotional images as well as food and thin-body images in 13 patients with AN, 15 patients with bulimia nervosa (BN), and 25 control participants. Both individuals with AN and BN showed potentiated startle responses to pleasant relative to neutral images, unlike the (typical) attenuated response seen in controls. Further, patients with AN had a greater startle response to food images than

patients with BN, supporting the premise that food is experienced as aversive among persons with AN (Friederich et al., 2006). More recently, both patients with AN and controls ($N = 36$ in each group) exhibited attenuated startle to pleasant images, but differed substantially in their responses to emaciated body pictures (Reichel et al., 2014). Startle findings suggested that patients with AN found emaciated body images pleasant, whereas control participants perceived these images as aversive, despite non-significant group differences for self-reported valence and arousal. Importantly, no study has examined voluntary emotion regulation in patients with AN using the EMSP.

The aim of this preliminary study was to use the EMSP to test emotional reactivity and voluntary emotion regulation in patients with AN. Using a within-subjects design, we compared startle responses to disorder-neutral (i.e., positive, negative, neutral) and disorder-specific (i.e., food) images both before and after receiving an emotion regulation cue. We predicted that patients with AN would show: 1) enhanced emotional reactivity, as indicated by a potentiated startle response, to negative and food images (compared to neutral images), and 2) difficulty suppressing emotional responses to negative and food images, as indicated by similar startle responses when receiving suppress and maintain regulation cues. Given inconsistent findings for positive images between the two previous EMSP studies in AN (Friederich et al., 2006, Reichel et al., 2014), we did not have a priori hypotheses regarding within-subject differences for positive images.

Material and Methods

This study was approved by the University of Pittsburgh Institutional Review Board and carried out in accordance with the latest version of the declaration of Helsinki. Informed consent was obtained from all participants after procedures were explained.

Participants

Nineteen participants with a medical chart diagnosis of AN were recruited from a specialty eating disorders treatment facility located in the Eastern United States.¹ Most participants were currently receiving treatment at the facility; two participants recently completed an intake for treatment (see Table 1). Eligibility criteria were as follows: 1) *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (American Psychiatric Association, 2013) diagnosis of AN; 2) female; 3) age ≥ 18 years; 4) no hearing or uncorrected vision problems; 5) no current use of anticonvulsant, stimulant, or narcotic medications. Participants taking anti-anxiety medications (26.3%), antihistamines (10.5%), or other sedatives (21.0%) were required to stop these medications for at least 24 hours prior to study participation, given known effects of these medications on startle response (Grillon and Baas, 2003, Treit et al., 2010). Antidepressants (52.6%) and antipsychotic medications (21.0%) were commonly prescribed to participants and were not considered exclusion criteria based on several studies examining the effects of these medications on startle response in clinical samples (Dichter et al., 2004, Wynn et al., 2007). AN diagnoses were confirmed using the *Structured Clinical Interview for DSM-IV-TR Axis I Disorders* (First et

¹Twenty participants were recruited for the current study, but a technical error rendered data from one participant unavailable

al., 2007) adjusted for *DSM-5* criteria; this modified interview demonstrated excellent inter-rater reliability for eating disorder diagnoses in previous work (Conger's $\kappa = .89-.90$; Forbush et al., under review). The behavioral items from the *Eating Disorder Examination 16.0* (Fairburn, 2008) were administered to further characterize the sample and establish AN-restricting and AN-binge-eating/purging subtypes. Demographic and clinical characteristics of the sample are presented in Table 1.

Images

Ninety-eight color images (28 negative; 28 positive; 28 food; 14 neutral) were selected from the International Affective Picture System (IAPS; Lang et al., 2008) based on normative ratings in females.² Given the limited number of food images in the IAPS, and our desire to present foods typically consumed during binge eating episodes, 43% (12/28) of our food images were taken from the internet. Our experimental design was based on previous studies testing voluntary emotion regulation using the EMSP in healthy controls (Dillon and LaBar, 2005, Jackson et al., 2000, Lissek et al., 2007). Images were presented on the computer screen for a total of 8 seconds. At 4 seconds post-stimulus onset, the word “enhance,” “suppress,” or “maintain” was presented on the screen for 2 seconds before the image returned. A 6-second black screen followed image offset, and trials ended with a 4-second presentation of the word “Relax” (see Figure 1 for depiction of experimental design). Images were crossed with regulation cue (suppress, enhance, maintain) and startle probe time (3-second, 8-second, 12-second) according to the data provided in Table 2 (n.b., neutral images only appeared with the “maintain” cue). Given the onset of the regulation cue at 4 seconds, trials with 3-second probes were used to examine emotional reactivity, and trials with 8-second and 12-second probes were used to examine emotion regulation. Images were divided into two blocks that were administered in a counter-balanced order and separated by a rest period. Image order was quasi-random, such that no more than three pictures of the same image category, with the same regulation cue, or with the same startle probe time, could be administered consecutively.

Procedure

Experimental sessions were scheduled at least one hour after meal or snack times for participants receiving treatment. Participants not receiving treatment were asked to eat a meal two hours prior, and not to eat in the hour prior, to the session. Participants were seated 1.8 meters in front of a 15-inch laptop connected to a commercial startle monitoring system (SR-HLab EMG; San Diego Instruments, San Diego, CA). The startle system controlled the presentation of the acoustic probes and recorded electromyography (EMG) activity. Acoustic startle probes consisted of 50ms 95dB white noise bursts with near instantaneous rise- and fall-time presented binaurally through calibrated headphones (Sony MDRV6 Studio Monitor Headphones; Sony, Tokyo, Japan). Two EMG electrodes filled with

²Selected IAPS pictures: Negative: 1052, 1120, 1201, 1220, 1271, 1300, 2120, 2141, 2205, 2683, 2691, 2703, 3000, 3010, 3030, 3130, 3150, 3300, 3530, 6020, 6212, 6230, 6240, 9187, 9300, 9400, 9471, 9910; Positive: 1340, 1440, 1463, 1710, 1722, 1750, 2040, 2045, 2050, 2070, 2080, 2091, 2156, 2158, 2165, 2274, 2347, 2395, 2550, 2655, 4525, 4532, 4572, 4597, 4599, 5270, 5831, 7502; Neutral: 7000, 7010, 7012, 7050, 7052, 7090, 7100, 7130, 7140, 7150, 7175, 7179, 7491, 7900; Food: 7220, 7220, 7230, 7260, 7270, 7330, 7340, 7350, 7400, 7405, 7410, 7430, 7450, 7460, 7470, 7480.

electrolyte gel (Signa Gel; Parker Laboratories, Fairfield, NJ) were attached over the lower left orbicularis oculi muscle, and the reference electrode was attached over the left mastoid.

Participants were told that the study would involve viewing pictures and regulating emotional responses to these pictures (see Supplementary Material for full experimental instructions). Participants were asked to increase the intensity of their emotion in response to “enhance” cues, decrease the intensity of their emotion in response to “suppress” cues, and keep their emotion at the same level in response to “maintain” cues. Participants were told that they could use whatever emotion regulation strategies they found effective, but they were not to generate a different emotion or think of something unrelated to the picture. Participants were asked about their emotion regulation strategies mid-way through the experiment and at the end of the study (see Results for description of self-reported strategies). Our emotion regulation instructions were identical to those described in Jackson et al. (2000), with two exceptions. First, joy was used as an example instead of disgust because we included positive images, whereas Jackson et al. did not. Second, after instructions regarding what strategies not to use, participants were told that they could use whatever cognitive strategies they found effective.

Prior to the EMSP, 12 practice images (3 per valence) paired with each regulation cue were presented to familiarize participants with the startle probes and emotion regulation procedure. Participants who reported difficulty generating regulation strategies were provided with suggestions by the experimenter (e.g., suppress: depersonalize the picture, focus on least negative/positive aspect of picture; enhance: personalize picture, focus on most negative/positive aspect of picture). After the EMSP, participants viewed each image for 12 seconds and completed self-reported valence and arousal ratings using the Self-Assessment Manikin (SAM; Bradley and Lang, 1994).

EMG Data Reduction and Statistical Analyses

EMG data reduction and statistical analyses were conducted in accordance with guidelines for human startle eyeblink EMG studies (Blumenthal et al., 2005). EMG activity was filtered using a 30 Hz high pass filter, a 300 Hz low pass filter, and a 60 Hz notch filter, and was digitized at 1000 Hz. EMG signals were smoothed using a 5-ms moving average and scored for peak EMG activity 20–150 ms post-stimulus onset using the SDI-HLAB software. Startle response was calculated as the peak EMG activity relative to baseline EMG activity, defined as the average EMG activity during the first 20 ms post-stimulus onset. Each trial was visually inspected for artifact and non-responding. Trials with movement artifact, spontaneous blinks, or excessive baseline activity were excluded from analyses (15%), and trials with no blink during the 20–150 ms scoring window were scored as 0 (10%).³ Given significant between-participant differences in baseline startle magnitude, within-subject T-scores were calculated based on each participant’s startle mean and standard deviation across all trials.

³Startle magnitudes were coded as missing or 0 on greater than one third (31–39%) of trials for three of the 19 participants. Analyses were re-run after excluding these three participants, and the pattern of results was identical (data available upon request).

Mixed linear models (MLMs) were used to analyze both startle-blink T-scores and affective rating data, given the within-subjects nature of the experimental design. For emotion reactivity trials and SAM ratings, picture type was entered as the only fixed effect. For emotion regulation trials, picture type, regulation cue, and the picture type X regulation cue interaction were entered as fixed effects.⁴ Neutral pictures were not included in the emotion regulation MLM, given that neutral images only were paired with maintain regulation cues. Startle, but not SAM analyses, controlled for order of block presentation. Repeated effects were specified using a diagonal matrix that allowed for the estimation of variances, but not covariances.

Results

Affective Ratings

Mean valence and arousal ratings for the four picture categories are presented in Table 3. There were significant main effects of picture type on both valence ($F(3, 404) = 2288.59$; $p < .001$) and arousal ($F(3, 522) = 431.22$; $p < .001$) ratings. All image categories significantly differed on valence: valence ratings for standard emotional images followed the expected pattern (negative > neutral > positive), with food image valence ratings lying between negative and neutral images. Negative images and food images received the highest arousal ratings and did not significantly differ from one another. Arousal ratings for positive images were significantly lower than negative and food images but significantly higher than neutral images.

Emotion Reactivity

Mean startle responses elicited by the 3-second startle probe were compared to examine emotional reactivity and are presented in Table 3. There was a significant main effect of picture type ($F(3, 129) = 4.02$; $p = .009$). Startle responses were larger when viewing negative, positive, and food images, compared to neutral images ($t_s = 2.66$ – 3.02 ; $p_s = .003$ – $.009$). No significant differences emerged in comparisons among valenced and food images ($t_s = 0.25$ – $.31$; $p_s = .76$ – $.90$).

Emotion Regulation

There were significant main effects of both picture type ($F(2, 318) = 4.18$; $p = .02$) and regulation cue ($F(2, 346) = 6.77$; $p < .001$) on startle magnitude to 8-second and 12-second probes. On regulation trials, startle magnitudes were significantly larger when viewing negative images ($M(SE) = 50.17 (.57)$) than when viewing positive images ($M(SE) = 48.33 (.47)$; $p = .01$), and food images ($M(SE) = 48.16 (.48)$; $p = .008$), which did not differ from one another ($p = .80$). Startle responses to regulation cues followed the expected pattern (enhance > maintain > suppress). Significantly smaller startle magnitudes were observed in response to suppress regulation cues ($M(SE) = 47.60 (.41)$) compared to maintain cues

⁴Initial models also included probe time (i.e., 8-second or 12-second) as a fixed effect. The probe time main effect and picture type x probe time interaction were non-significant ($p_s > .14$). Despite a significant interaction between regulation cue x probe time ($p = .048$; enhance 8s > enhance 12s), we chose to present results collapsed across probe time in order to increase the number of trials per condition (6 vs. 3; see Table 2) and thus the stability of the estimates.

($M(SE) = 48.92 (.53)$; $p = .05$) and enhance cues ($M(SE) = 50.15 (.58)$; $p < .001$), which did not statistically differ from one another ($p = .12$).

A significant picture type X regulation cue interaction also was found ($F(4, 265) = 6.67$; $p < .001$); mean startle magnitudes across picture types and regulation cues are presented in Figure 2. Participants demonstrated the ability to enhance, but not suppress, their emotional responses to negative and food pictures. Specifically, significant enhance-suppress ($p = .01$) and trend-level significant enhance-maintain ($p = .08$) differences were detected for negative images, but suppress-maintain differences were non-significant ($p = .56$). This same pattern was observed for food images: enhance-suppress ($p < .001$), enhance-maintain ($p < .001$), suppress-maintain ($p = .75$). In contrast, both enhance and suppress instructions were associated with smaller startle magnitudes in response to positive images than maintain instructions ($p = .003-.02$), and startle responses on enhance and suppress trials did not differ ($p = .34$).⁵

Emotion Regulation Strategies

According to participant self-report, two categories of emotion regulation strategies were most commonly used: cognitive reappraisal and attentional deployment (n.b. participants could endorse using more than one strategy). When asked to enhance emotional responses, participants were more likely to employ cognitive reappraisal strategies (e.g., imagine self or family member as subject of picture; imagine having to eat food in picture; $n = 17/19$; 89.4%) than attentional deployment strategies (e.g., focusing on blood in the picture; focusing on highest calorie food item; $n = 8/19$; 42.1%). In contrast, cognitive reappraisal and attentional deployment were used almost equally when participants were presented with suppress cues: cognitive reappraisal (e.g., remind self it is only a picture or not real; think of food images as advertisements), $n = 12/19$; 63.1%; attentional deployment (e.g., focus on background details or colors/shapes: $n = 13/19$; 68.4%). Post-hoc analyses revealed that there were no significant effects of self-reported regulation strategy on the pattern of startle-blink modulation. Specifically, strategy type did not interact with picture type, regulation cue, or the picture type X regulation cue interaction to predict startle magnitude. Further, simple effects tests revealed that startle magnitudes to enhance and suppress cues did not differ for any picture category based on strategies used to enhance and suppress emotional responses, respectively.

Discussion

Despite well-established associations between self-reported emotion regulation difficulties and AN, research using psychophysiological methods to assess emotion regulation is scarce. The current study is the first to objectively test voluntary emotion regulation, as indexed by startle-blink modulation, to disorder-specific (i.e., food) and disorder-neutral (i.e., negative, positive) images in patients with AN. Unlike previous studies in healthy populations

⁵Given that depression has been associated with poor emotion regulation and blunted startle responses, we conducted a post-hoc analysis controlling for depressive symptoms, as measured by the Inventory of Depression and Anxiety Symptoms-II General Depression subscale (Watson et al., 2012). Startle-blink modulation remained unchanged when including depressive symptoms as a covariate (data available upon request).

(Conzelmann et al., 2015; Dillon and LaBar, 2005, Driscoll et al., 2009, Jackson et al., 2000), startle response patterns in women with AN indexed difficulty suppressing emotional responses to negative and food images, and difficulty enhancing emotional responses to positive images. These results are consistent with self-report questionnaire studies and bolster theoretical models that posit emotion dysregulation as a risk and maintenance factor for AN (Haynos and Fruzzetti, 2011).

Below, the conclusions that can be drawn from this preliminary study are examined within the context of past research on AN and are discussed with regard to directions for future mechanistic and treatment research. First, food appears to activate the defensive motivational system in a manner similar to aversive (e.g., personal threat, disgust) stimuli in women with AN. Both image types were associated with potentiated startle responses, relative to neutral images, as well as non-significant differences in startle responses on maintain and suppress regulation trials. Despite one conflicting result (Friederich et al., 2006), most studies examining clinical and analog samples of women with BN also report potentiated startle responses to food images (Altman et al., 2013, Drobles et al., 2001, Mauler et al., 2006), suggesting implicit emotional reactivity to food is disturbed across eating disorders. In contrast, healthy control participants typically experience startle inhibition when viewing food images in non-deprived states (Drobles et al., 2001, Ferreira de Sá et al., 2014, Mauler et al., 2006). Increased emotional reactivity to food images in persons with AN has been documented across studies using a variety of methodologies (Giel et al., 2011, Joos et al., 2011, Zhu et al., 2012). However, relatively few studies have directly compared reactivity to disorder-specific and disorder-neutral stimuli, especially stimuli with specific affective content (e.g., fear- vs. disgust-eliciting). This type of research may shed light on exactly how individuals with AN process food stimuli, which has implications for the identification of treatment targets (e.g., disgust conditioning; Hildebrandt et al., 2015).

Second, our findings point to a dysfunction in positive emotional reactivity in AN. In contrast to previous work in healthy individuals (Ferreira de Sá et al., 2014), positive images resulted in potentiated, rather than inhibited, startle magnitudes relative to neutral images in our sample. Further, participants did not successfully enhance their startle responses to pleasant images. A lack of startle inhibition across picture types led Friederich et al. (2006) to conclude that AN may be associated with an overall deficit in the appetitive system. Additional support for this premise comes from a recent study that reported less zygomatic EMG activity (reflective of less smiling) in participants with AN versus controls when viewing food and pleasant non-food images (Soussignan et al., 2011). However, emerging theories argue against generalized reward deficits in AN (O'Hara et al., 2015, Wierenga et al., 2014). Indeed, recent data indicate that reward processing is enhanced in the presence of illness-compatible cues (e.g., emaciated bodies) and behaviors (e.g., physical activity) in individuals with AN (Giel et al., 2013, O'Hara et al., 2015, Reichel et al., 2014). Enhanced reward processing of certain stimuli, rather than an overall inability to experience reward, suggests that treatments should focus on shifting appetitive reactivity away from illness-compatible cues and towards stimuli associated with positive emotions in the general population.

Third, and most importantly, patients with AN were unsuccessful at employing emotion regulation strategies when they were asked to *improve* their affective experiences, but they did not demonstrate impairment when instructed to *worsen* their affect. Specifically, emotional responses to images rated as aversive (negative and food) could successfully be enhanced, but not suppressed. In contrast, positive images, which were rated as pleasant by participants despite potentiated startle responses, were successfully suppressed but not enhanced. Clinically, these findings point to the importance of targeting the ability to enhance positive affect, in addition to decrease negative affect, in treatments for AN. Further, these findings map on well with results from a recent meta-analysis of questionnaire studies, which suggested that patients with AN endorse less habitual use of adaptive emotion regulation strategies (e.g., cognitive reappraisal) than controls (Oldershaw et al., 2015). Future research should examine whether less habitual use of strategies such as cognitive reappraisal and attentional deployment is associated with increased difficulty employing these strategies in experimental contexts, such as during the EMSP. In addition, although reported emotion regulation strategy did not influence our results, it will be important for future studies to more carefully consider whether participants with AN choose different strategies to regulate emotions depending on picture content and/or associated arousal (see Sheppes et al., 2011 for a study in healthy controls), and whether strategy choice influences startle-blink modulation.

In conclusion, our results suggest that the EMSP can be successfully used to test emotional reactivity and regulation in patients with AN. Findings are consistent with past research regarding startle-blink magnitude among individuals with AN to disorder-specific and disorder-neutral stimuli, as well as the ability of patients with AN to regulate their emotional responses. Nonetheless, the small number of participants and lack of control group are limitations of the study. The sample size did not provide adequate power to investigate illness-related factors (e.g., AN subtype, BMI, duration of illness) that might moderate voluntary emotion regulation abilities. In addition, emotion- and regulation cue-modulated startle patterns were not examined in comparison to healthy control participants. Although we have noted differences between our findings and past studies that have included healthy controls, methodological differences (e.g., chosen IAPS pictures; no food images in prior regulation studies) do not permit a direct comparison of results. Further, without a control group, we cannot rule out the possibility that comorbid psychiatric symptoms (e.g., depression), rather than AN-specific pathology, account for differences between our findings in AN and those previously reported in healthy controls. Thus, despite the strength of the within-subjects design used in the current study, future EMSP research must confirm that individuals with AN have more difficulty regulating their emotions than healthy controls and identify the psychological factors associated with these difficulties.

An additional limitation was that there were certain restrictions placed on the types of emotion regulation strategies suggested to participants. Specifically, participants were instructed not to generate a different emotion or think of something unrelated to the picture to suppress emotional responses. Although recent treatment approaches for AN have focused on experiencing, rather than avoiding, emotional experiences, distraction may be a helpful emotion regulation strategy in the context of highly arousing stimuli (Sheppes et al. 2011). Further, a recent study in AN and BN found that, unlike rumination, the use of distraction

after a sad mood induction did not result in increases in sadness, drive to abstain from eating, or drive to binge eat (Naumann et al., 2015). Future psychophysiological studies that permit true free-choice of emotion regulation strategies may help clarify the strategies that are most effective for patients with AN.

An intriguing direction for future research would be to identify similarities and differences in voluntary emotion regulation across eating disorders and other psychiatric diagnoses. Emotion regulation difficulties are considered to be trans-diagnostic (Aldao and Nolen-Hoeksema, 2010, Kring and Sloan, 2010), in that they are associated with multiple forms of psychopathology across the internalizing and externalizing spectrums. The EMSP may be a promising methodology for mechanistic research that aims to identify facets of emotion regulation that contribute to both comorbidity and divergent trajectories among psychiatric conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Aldao A, Nolen-Hoeksema S. Specificity of cognitive emotion regulation strategies: A transdiagnostic examination. *Behav Res Ther.* 2010; 48:974–983. [PubMed: 20591413]
- Altman SE, Campbell ML, Nelson BD, Faust JP, Shankman SA. The relation between symptoms of bulimia nervosa and obsessive-compulsive disorder: A startle investigation. *J Abnorm Psychol.* 2013; 122:1132–1141. [PubMed: 24364616]
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders : DSM-5.* 5th. Washington, DC: American Psychiatric Association; 2013.
- Blumenthal TD, Cuthbert BN, Filion DL, Hackley S, Lipp OV, van Boxtel A. Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology.* 2005; 42:1–15. [PubMed: 15720576]
- Bradley MM, Lang PJ. Measuring emotion: The Self-Assessment Manikin and the semantic differential. *J Behav Ther Exp Psychiatry.* 1994; 25:49–59. [PubMed: 7962581]
- Conzelmann A, McGregor V, Pauli P. Emotion regulation of the affect-modulated startle reflex during different picture categories. *Psychophysiology.* 2015; 52:1257–1262. [PubMed: 26061976]
- Davis M. Are different parts of the extended amygdala involved in fear versus anxiety? *Biol Psychiatry.* 1998; 44:1239–1247. [PubMed: 9861467]
- Davis, M.; Walker, DL.; Lee, Y. Roles of the amygdala and bed nucleus of the stria terminalis in fear and anxiety measured with the acoustic startle reflex. Possible relevance to PTSD. In: Yehuda, R.; McFarlane, AC., editors. *Psychobiology of Posttraumatic Stress Disorder.* New York, NY: New York Academy of Sciences; 1997. p. 305–331.
- Dichter GS, Tomarken AJ, Shelton RC, Sutton SK. Early- and late-onset startle modulation in unipolar depression. *Psychophysiology.* 2004; 41:433–440. [PubMed: 15102129]
- Dillon DG, LaBar KS. Startle modulation during conscious emotion regulation is arousal-dependent. *Behav Neurosci.* 2005; 119:1118–1124. [PubMed: 16187839]

- Driscoll D, Tranel D, Anderson SW. The effects of voluntary regulation of positive and negative emotion on psychophysiological responsiveness. *Int J Psychophysiol.* 2009; 72:61–66. [PubMed: 18845192]
- Drobes DJ, Miller EJ, Hillman CH, Bradley MM, Cuthbert BN, Lang PJ. Food deprivation and emotional reactions to food cues: Implications for eating disorders. *Biol Psychol.* 2001; 57:153–177. [PubMed: 11454438]
- Fairburn, CG.; Cooper, Z.; O'Connor, ME. Eating Disorders Examination (Edition 16.0D). In: Fairburn, CG., editor. *Cognitive Behavior Therapy and Eating Disorders*. New York, NY: Guilford Press; 2008. p. 265-308.
- Ferreira de Sá DS, Plein DE, Schulz A, Oitzl MS, Blumenthal TD, Schächinger H. Acoustic startle reactivity while processing reward-related food cues during food deprivation: Evidence from women in different menstrual cycle phases and men. *Psychophysiology.* 2014; 51:159–167. [PubMed: 24354658]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, J. Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition with Psychotic Screen. New York, NY: Biometrics Research Department; 2007.
- Friederich HC, Kumari V, Uher R, Riga M, Schmidt U, Campbell IC, et al. Differential motivational responses to food and pleasurable cues in anorexia and bulimia nervosa: A startle reflex paradigm. *Psychol Med.* 2006; 36:1327–1335. [PubMed: 16790080]
- Giel KE, Kullmann S, Preissl H, Bischoff SC, Thiel A, Schmidt U, et al. Understanding the reward system functioning in anorexia nervosa: Crucial role of physical activity. *Biol Psychol.* 2013; 94:575–581. [PubMed: 24161801]
- Giel KE, Teufel M, Friederich HC, Hautzinger M, Enck P, Zipfel S. Processing of pictorial food stimuli in patients with eating disorders—a systematic review. *Int J Eat Disord.* 2011; 44:105–117. [PubMed: 20127931]
- Grillon C, Baas J. A review of the modulation of the startle reflex by affective states and its application in psychiatry. *Clin Neurophysiol.* 2003; 114:1557–1579. [PubMed: 12948786]
- Gross JJ, John OP. Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *J Pers Soc Psychol.* 2003; 85:348–362. [PubMed: 12916575]
- Gross, JJ.; Thompson, RA. Emotion regulation: Conceptual foundations. In: Gross, JJ., editor. *Handbook of Emotion Regulation*. New York, NY: Guilford Press; 2007. p. 3-20.
- Haynos AF, Fruzzetti AE. Anorexia nervosa as a disorder of emotion dysregulation: Evidence and treatment implications. *Clin Psychol-Sci Pr.* 2011; 18:183–202.
- Hildebrandt T, Grotzinger A, Reddan M, Greif R, Levy I, Goodman W, et al. Testing the disgust conditioning theory of food-avoidance in adolescents with recent onset anorexia nervosa. *Behav Res Ther.* 2015; 71:131–138. [PubMed: 26131915]
- Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, et al. Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. *American J Psychiatry.* 2010; 167:748–751.
- Jackson DC, Malmstadt JR, Larson CL, Davidson RJ. Suppression and enhancement of emotional responses to unpleasant pictures. *Psychophysiology.* 2000; 37:515–522. [PubMed: 10934910]
- Joos AAB, Saum B, van Elst LT, Perlov E, Glauche V, Hartmann A, et al. Amygdala hyperreactivity in restrictive anorexia nervosa. *Psychiatry Res: Neuroimaging.* 2011; 191:189–195. [PubMed: 21316204]
- Koch M, Schmid A, Schnitzler HU. Pleasure-attenuation of startle is disrupted by lesions of the nucleus accumbens. *Neuroreport.* 1996; 7:1442–1446. [PubMed: 8856694]
- Koch M, Schmid A, Schnitzler HU. Role of nucleus accumbens dopamine D1 and D2 receptors in instrumental and Pavlovian paradigms of conditioned reward. *Psychopharmacology.* 2000; 152:67–73. [PubMed: 11041317]
- Kring, AM.; Sloan, DM. Emotion Regulation and Psychopathology : A Transdiagnostic Approach to Etiology and Treatment. New York, NY: Guilford Press; 2010.
- Lang, P.; Bradley, M.; Cuthbert, B.; Gainesville, FL. Technical report A-8. Gainesville, FL: University of Florida; 2008. International Affective Picture System (IAPS): Affective ratings of pictures and instruction manual.

- Lang PJ, Bradley MM, Cuthbert BN. Emotion, attention, and the startle reflex. *Psychol Rev.* 1990; 97:377–395. [PubMed: 2200076]
- Lavender JM, Wonderlich SA, Engel SG, Gordon KH, Kaye WH, Mitchell JE. Dimensions of emotion dysregulation in anorexia nervosa and bulimia nervosa: A conceptual review of the empirical literature. *Clin Psychol Rev.* 2015; 40:111–122. [PubMed: 26112760]
- Lissek S, Orme K, McDowell DJ, Johnson LL, Luckenbaugh DA, Baas JM, et al. Emotion regulation and potentiated startle across affective picture and threat-of-shock paradigms. *Biol Psychol.* 2007; 76:124–133. [PubMed: 17692453]
- Mauler BI, Hamm AO, Weike AI, Tuschen-Caffier B. Affect regulation and food intake in bulimia nervosa: Emotional responding to food cues after deprivation and subsequent eating. *J Abnorm Psychol.* 2006; 115:567–579. [PubMed: 16866597]
- Nandrino J-L, Berna G, Hot P, Dodin V, Latrée J, Decharles S, et al. Cognitive and physiological dissociations in response to emotional pictures in patients with anorexia. *J Psychosom Res.* 2012; 72:58–64. [PubMed: 22200524]
- Naumann E, Tuschen-Caffier B, Voderholzer U, Caffier D, Svaldi J. Rumination but not distraction increases eating-related symptoms in anorexia and bulimia nervosa. *J Abnorm Psychol.* 2015; 124:412–420. [PubMed: 25730516]
- O'Hara CB, Campbell IC, Schmidt U. A reward-centred model of anorexia nervosa: A focussed narrative review of the neurological and psychophysiological literature. *Neurosci Biobehav Rev.* 2015; 52:131–152. [PubMed: 25735957]
- Oldershaw A, Hambrook D, Stahl D, Tchanturia K, Treasure J, Schmidt U. The socio-emotional processing stream in anorexia nervosa. *Neurosci Biobehav Rev.* 2011; 35:970–988. [PubMed: 21070808]
- Oldershaw A, Lavender T, Sallis H, Stahl D, Schmidt U. Emotion generation and regulation in anorexia nervosa: A systematic review and meta-analysis of self-report data. *Clinical Psychol Rev.* 2015; 39:83–95. [PubMed: 26043394]
- Piper ME, Curtin JJ. Tobacco withdrawal and negative affect: An analysis of initial emotional response intensity and voluntary emotion regulation. *J Abnorm Psychol.* 2006; 115:96–102. [PubMed: 16492100]
- Racine SE, Wildes JE. Dynamic longitudinal relations between emotion regulation difficulties and anorexia nervosa symptoms over the year following intensive treatment. *J Consult Clin Psychol.* 2015; 83:785–795. [PubMed: 25181027]
- Reichel VA, Schneider N, Grunewald B, Kienast T, Pfeiffer E, Lehmkuhl U, et al. "Glass fairies" and "bone children": Adolescents and young adults with anorexia nervosa show positive reactions towards extremely emaciated body pictures measured by the startle reflex paradigm. *Psychophysiology.* 2014; 51:168–177. [PubMed: 24423135]
- Schmidt U, Oldershaw A, Jichi F, Sternheim L, Startup H, McIntosh V, et al. Out-patient psychological therapies for adults with anorexia nervosa: Randomised controlled trial. *The Br J Psychiatry.* 2012; 201:392–399. [PubMed: 22995632]
- Sheppes G, Scheibe S, Suri G, Gross JJ. Emotion-regulation choice. *Psychol Sci.* 2011; 22:1391–1396. [PubMed: 21960251]
- Soussignan R, Schaal B, Rigaud D, Royet J-P, Jiang T. Hedonic reactivity to visual and olfactory cues: Rapid facial electromyographic reactions are altered in anorexia nervosa. *Biol Psychol.* 2011; 86:265–272. [PubMed: 21185351]
- Treasure J, Schmidt U. The cognitive-interpersonal maintenance model of anorexia nervosa revisited: A summary of the evidence for cognitive, socio-emotional and interpersonal predisposing and perpetuating factors. *J Eat Disord.* 2013; 1:13. [PubMed: 24999394]
- Treit, D.; Engin, E.; McEown, K. Animal models of anxiety and anxiolytic drug action. In: Stein, MB.; Steckler, T., editors. *Behavioral Neurobiology of Anxiety and its Treatment*. New York, NY: Springer; 2010. p. 21-160.
- Vaidyanathan U, Nelson LD, Patrick CJ. Clarifying domains of internalizing psychopathology using neurophysiology. *Psychol Med.* 2012; 42:447–459. [PubMed: 21854683]

- Vaidyanathan U, Patrick CJ, Cuthbert BN. Linking dimensional models of internalizing psychopathology to neurobiological systems: Affect-modulated startle as an indicator of fear and distress disorders and affiliated traits. *Psychol Bull.* 2009; 135:909–942. [PubMed: 19883142]
- Wierenga CE, Ely A, Bischoff-Grethe A, Bailer UF, Simmons AN, Kaye WH. Are extremes of consumption in eating disorders related to an altered balance between reward and inhibition? *Front Behav Neurosci.* 2014; 8:410. [PubMed: 25538579]
- Wildes JE, Marcus MD, Cheng Y, McCabe EB, Gaskill JA. Emotion acceptance behavior therapy for anorexia nervosa: A pilot study. *Int J Eat Disord.* 2014; 47:870–873. [PubMed: 24407934]
- Wildes JE, Ringham RM, Marcus MD. Emotion avoidance in patients with anorexia nervosa: Initial test of a functional model. *Int J Eat Disord.* 2010; 43:398–404. [PubMed: 19670226]
- Wynn JK, Green MF, Sprock J, Light GA, Widmark C, Reist C, et al. Effects of olanzapine, risperidone and haloperidol on prepulse inhibition in schizophrenia patients: A double-blind, randomized controlled trial. *Schizophr Res.* 2007; 95:134–142. [PubMed: 17662577]
- Zhu Y, Hu X, Wang J, Chen J, Guo Q, Li C, et al. Processing of food, body and emotional stimuli in anorexia nervosa: A systematic review and meta-analysis of functional magnetic resonance imaging studies. *Eur Eat Disord Rev.* 2012; 20:439–450. [PubMed: 22945872]
- Zonneville-Bender MJ, van Goozen SH, Cohen-Kettenis PT, Jansen LM, van Elburg A, Engeland H. Adolescent anorexia nervosa patients have a discrepancy between neurophysiological responses and self-reported emotional arousal to psychosocial stress. *Psychiatry Res.* 2005; 135:45–52. [PubMed: 15893382]

Highlights

- Used objective physiological method to test emotion regulation in anorexia nervosa
- Examined startle-blink magnitudes to images crossed with emotion regulation cues
- Difficulty suppressing emotions to negative and food images was indicated
- Difficulty enhancing emotions to positive images was observed
- Physiology findings converge with self-reported emotion regulation difficulties

Figure 1.

Illustration of the experimental design, including onset of images, regulation cue, and startle probes. Sup = suppress, Main = maintain, Enh = enhance.

Figure 2.

Mean startle-blink responses as a function of picture type (negative, positive, food, neutral) and emotion regulation cues (suppress, enhance, maintain). Error bars reflect the standard error of the mean. Neutral images were only paired with maintain cues.

Table 1

Demographic and Clinical Characteristics (N = 19)

Characteristic	M (SD)	N (%)
Age	25.11 (9.13)	
Duration of illness (years)	6.94 (6.09)	
BMI at admission	16.72 (1.63)	
BMI at time of study	17.30 (1.73)	
Anorexia nervosa subtype		
Restricting		7 (36.8)
Binge eating/purging		12 (63.1)
Level of care at time of study		
Inpatient		13 (68.4)
Partial hospitalization		2 (10.5)
Intensive outpatient		2 (10.5)
No current treatment		2 (10.5)

BMI = body mass index. Participants not currently receiving treatment had completed an intake assessment, but had not begun treatment at the time of the study ($n = 2$).

Table 2

Summary of startle paradigm including regulation cues (enhance, suppress, maintain) crossed with image type (negative, positive, food, neutral) and probe onset times (3-second, 8-second, 12-second)

Image Type	3-second probe	8-second probe	12-second probe
Negative	2 Enhance	3 Enhance	3 Enhance
	2 Suppress	3 Suppress	3 Suppress
	2 Maintain	3 Maintain	3 Maintain
Positive	2 Enhance	3 Enhance	3 Enhance
	2 Suppress	3 Suppress	3 Suppress
	2 Maintain	3 Maintain	3 Maintain
Food	2 Enhance	3 Enhance	3 Enhance
	2 Suppress	3 Suppress	3 Suppress
	2 Maintain	3 Maintain	3 Maintain
Neutral	6 Maintain	3 Maintain	3 Maintain

Table 3

Self-assessment manikin valence and arousal ratings and startle-blink T-scores in response to 3-second probes (emotional reactivity)

Picture Type	SAM Valence <i>M (SE)</i>	SAM Arousal <i>M (SE)</i>	Startle-blink <i>M (SE)</i>
Negative	8.31 (.05)	3.70 (.22)	49.12 (.84)
Positive	2.78 (.06)	5.38 (.22)	49.48 (.81)
Food	6.63 (.10)	3.78 (.21)	49.25 (.69)
Neutral	5.00 (.01)	7.65 (.23)	45.89 (.87)

SAM = self-assessment manikin. SAM Valence ratings range from 1 (very happy) to 9 (very sad). SAM arousal ratings range from 1 (very excited) to 9 (very calm).