



Processing and regulation of negative emotions in anorexia nervosa: An fMRI study

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ABSTRACT

Theoretical models and recent advances in the treatment of anorexia nervosa (AN) have increasingly focused on the role of alterations in the processing and regulation of emotions. To date, however, our understanding of these changes is still limited and reports of emotional dysregulation in AN have been based largely on self-report data, and there is a relative lack of objective experimental evidence or neurobiological data.

The current functional magnetic resonance imaging (fMRI) study investigated the hemodynamic correlates of passive viewing and voluntary downregulation of negative emotions by means of the reappraisal strategy detachment in AN patients. Detachment is regarded as adaptive regulation strategy associated with a reduction in emotion-related amygdala activity and increased recruitment of prefrontal brain regions associated with cognitive control processes. Emotion regulation efficacy was assessed via behavioral arousal ratings and fMRI activation elicited by an established experimental paradigm including negative images. Participants were instructed to either simply view emotional pictures or detach themselves from feelings triggered by the stimuli.

The sample consisted of 36 predominantly adolescent female AN patients and a pairwise age-matched healthy control group. Behavioral and neuroimaging data analyses indicated a reduction of arousal and amygdala activity during the regulation condition for both patients and controls. However, compared with controls, individuals with AN showed increased activation in the amygdala as well as in the right dorsolateral prefrontal cortex (dlPFC) during the passive viewing of aversive compared with neutral pictures.

These results extend previous findings indicative of altered processing of salient emotional stimuli in AN, but do not point to a general deficit in the voluntary regulation of negative emotions. Increased dlPFC activation in AN during passive viewing of negative stimuli is in line with the hypothesis that the disorder may be characterized by excessive self-control. Taken together, the data seem to suggest that reappraisal via detachment may be an effective strategy to reduce negative arousal for individuals with AN.

1. Introduction

How we process and regulate emotions has important consequences for our physical and mental well-being (Gross and Muñoz, 1995). Emotion regulation refers to the processing, intensifying, weakening, altering or maintaining of emotions in a goal-directed manner (Gross & Thompson, 2007). According to contemporary theories of anorexia

nervosa [AN; Haynos and Fruzzetti, 2011] and bulimia nervosa [BN; Fairburn et al., 2003] altered emotion processing and regulation mechanisms are thought to play an important role in the development and maintenance of the disorders (Haynos and Fruzzetti, 2011; Racine and Wildes, 2015; Schmidt and Treasure, 2006; Treasure and Schmidt, 2013; Wildes et al., 2014).

Clinical observations of AN patients are also suggestive of relatively

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elevated self-control (e.g. ability to abstain from food intake and regulation of hunger) and perseverative, obsessive and rigid thinking styles (Danner et al., 2012; Tenconi et al., 2010). Consistent with these observations, functional magnetic resonance imaging (fMRI) studies have found alterations in fronto-parietal networks indicative of increased cognitive control and self-control (Boehm et al., 2014; Ehrlich et al., 2015; King et al., 2016; Lee et al., 2014; Zastrow et al., 2009). As research has placed self-control as an important mechanism within emotion regulation functioning (Paschke et al., 2016), one might expect superior emotion regulation capacities in AN patients.

At the same time, AN appears to be characterized by alterations in general aspects of emotion processing, such as emotional awareness and emotion recognition (Harrison et al., 2009; Kolar et al., 2017; Parling et al., 2010). Unsurprisingly, increased emotional reactivity to disorder-relevant (food and body) stimuli has been observed (Zhu et al., 2012). Broader impairments in emotion regulation have also been reported (Lavender et al., 2015; Oldershaw et al., 2015) which may entail increased usage of maladaptive emotion regulation strategies such as suppression or rumination (Aldao et al., 2010). These self-reported deficits in emotion regulation are assumed to persist even after recovery (Haynos et al., 2014). To date, almost all studies assessing processing and regulation of emotions in AN used classical self-report questionnaires. This is potentially problematic not only because individuals with AN often have difficulties with emotion awareness and recognition, but also a tendency towards emotional avoidance (Oldershaw et al., 2015; Wildes et al., 2010). Moreover, several studies have found discrepancies between self-reported emotional and physiological reactivity to emotional events (Nandrino et al., 2012; Zonneville-Bender et al., 2005). Thus, individuals with AN may have difficulties accurately reporting their emotions and judging their emotion regulation skills. Employing experimental methods to assess processing and regulation of negative emotions and the underlying neural mechanisms might overcome the disadvantages of self-report measures and have the potential to significantly contribute to our understanding of over- or dysregulation of negative emotions in patients with AN.

Overall, functional neuroimaging studies support behavioral findings of altered processing of emotions in AN. Group differences in neural responses to food and body stimuli have been found in visual, limbic as well as frontal brain regions (Zhu et al., 2012). Previous findings in voluntary regulation of positive emotions during the same paradigm in AN patients did not uncover any group differences between passive viewing and distancing in the ventral striatum, a region associated with reward processing (Seidel et al., *in press*). However, altered emotion processing in AN (based on self-reports) has been most frequently reported specifically with regards to negative emotions (Engel et al., 2013). To our knowledge, the neural mechanisms underlying voluntary regulation of negative emotions in patients with AN have not been investigated.

The majority of experimental studies investigating voluntary emotion regulation in healthy populations have focused on reappraisal. Reappraisal involves either the reinterpretation of or the detachment (e.g. by adopting the perspective of a distanced and uninvolved observer) from an emotionally valenced event (Gross, 1998, 2013; Ochsner et al., 2012). Models of the neural circuitry underlying reappraisal include prefrontal and cingulate brain regions which have been implicated in cognitive control (Dosenbach et al., 2008; Paschke et al., 2016). It is generally assumed that these brain regions [e.g. the dorsolateral prefrontal cortex (dlPFC)] modulate activity in posterior and subcortical systems that generate emotional responses. These notions have largely been supported by experimental findings (Goldin et al., 2008; Kanske et al., 2011; McRae et al., 2012; Ochsner & Gross, 2013; Ochsner et al., 2012).

The aim of the current study therefore was to use an established emotion regulation paradigm (Eippert et al., 2007; Ochsner et al., 2002; Walter et al., 2009) to investigate the neural correlates of reappraisal via detachment (distancing) as a voluntary emotion regulation strategy

to reduce arousal in AN. Given the aforementioned heterogeneous findings suggesting deficits in the processing and regulation of emotion as well as increased cognitive control in AN, the current study sought to shed more light on these processes in the context of negative, but disorder-unrelated, visual stimuli. Using subjective (arousal ratings) and objective (fMRI) data, we were interested not only in whether patients would show increased sensitivity to negative (disorder-irrelevant) stimuli presented in our task, but also altered voluntary regulation of emotions triggered by the aversive images.

2. Method

2.1. Participants

The sample in the current study consisted of a total of 72 female volunteers: 36 patients diagnosed with acute AN according to DSM-V (12.1–29.2 years old) and 36 pair-wise age-matched healthy controls (HC; 12.1–29.0 years old). The sample was identical to that included in our recent investigation focused on positive emotion regulation (Seidel et al., *in press*) with the exception of one additional AN patient and her matched HC counterpart. AN patients were admitted to an eating disorder (ED) treatment program at a university child and adolescent psychiatry or psychosomatic medicine department and underwent all assessments within 96 h after beginning a behaviorally-oriented nutritional rehabilitation program. Since only three AN patients (8.3%) were of the binge-purge subtype, no statistical analyses investigated potential differences between AN subtypes. To be included in the HC group, participants had to be of normal weight and eumenorrhoeic. Normal weight was defined as body-mass index (BMI) equal or above the 10th age percentile (if 18 years or younger)/BMI equal or above 18.5 kg/m² (if older than 18 years) or below the 94th age percentile (if 18 years or younger)/BMI below 28 kg/m² (if older than 18 years). HCs were recruited through advertisement among middle school, high school and university students. Exclusion criteria and possible confounding variables for both groups were obtained using a semi-structured research interview the SIAB-EX (Fichter and Quadflieg, 2001) and our own semi-structured interview (for further details please see Supplementary material 1.1). Study data were collected and managed using secure, web-based electronic data capture tools REDCap [Research Electronic Data Capture (Harris et al., 2009)]. This study was approved by the local Institutional Review Board, and all participants (and if underage their guardians) gave written informed consent.

2.2. Clinical, endocrinological and psychometric data

To complement the information obtained with the clinical interviews, we assessed ED-specific psychopathology using the Eating Disorder Inventory [EDI-2 (Thiel et al., 1997)], depressive symptoms using the Beck Depression Inventory [BDI-II (Hautzinger et al., 2009; Teri, 1982)] and anxiety levels using the State-and-Trait-Inventory [STAI/K (Spielberger, 2010)]. To assess habitual emotion regulation, we used the German version of the Emotion Regulation Questionnaire [ERQ (Ablar and Kessler, 2009)]. For BMI measures, we used the gender and age corrected BMI-standard deviation score [BMI-SDS (Kromeyer-Hauschild et al., 2001)]. Plasma samples were collected immediately prior to scanning and leptin concentration was measured using a commercially available Enzyme Linked Immunoassay (ELISA; BioVendor; for details refer to Supplementary material 1.2).

2.3. Emotion regulation task

During fMRI, we used a modified version of an established emotion regulation paradigm (Diers et al., 2014; Ochsner et al., 2002; Walter et al., 2009) during which participants were cued to either passively view a set of negative, positive and neutral pictures or to actively downregulate any emotions arising in response to the negative and

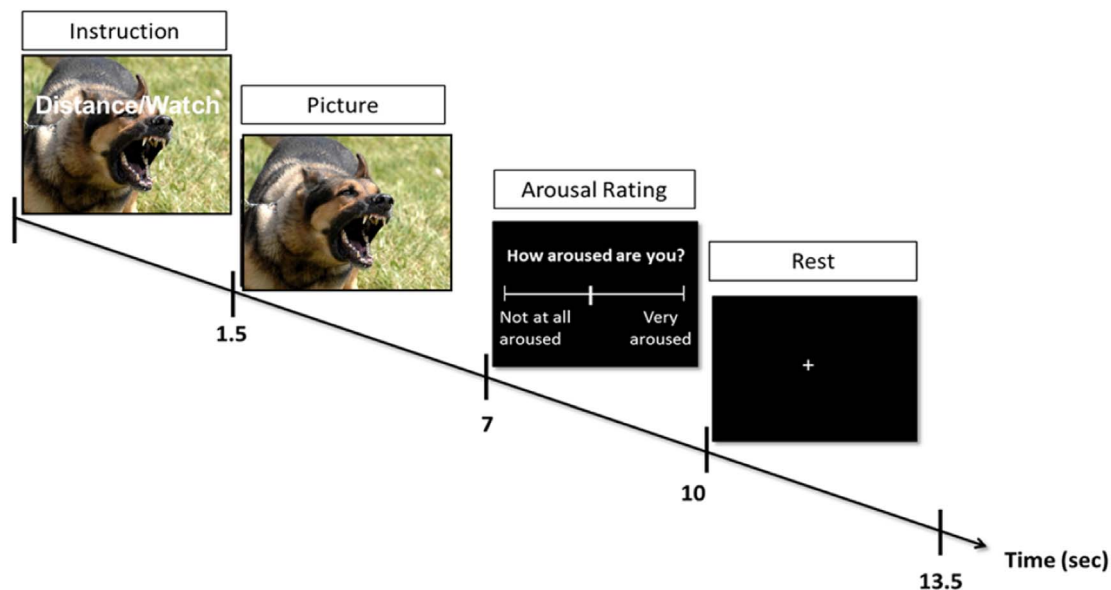


Fig. 1. Design of emotion regulation task. Stimulus was shown for 6.5 s with overlaid instruction (1.5 s) ‘watch’ or ‘distance’. Each stimulus was followed by the arousal rating (3 s) and a jittered (average 3.5 s) fixation cross. Time is shown in seconds.

positive pictures. During the passively viewing condition participants were instructed to simply view the picture without trying to modulate any associated feelings. In the regulation condition they were instructed to downregulate their feeling via the reappraisal strategy ‘detachment’ (distancing), by trying to take the position of a noninvolved observer. The instruction for each condition was given by presenting a cue word laid over the stimulus for 1.5 s stating either ‘view’ or ‘distance’. Image presentation was completely randomized and the order of the respective conditions was pseudorandomized so that the same condition (neutral watch, negative watch, negative distance, positive watch, positive distance) did not occur more than twice in a row. We did not include a ‘regulate neutral’ condition in the experiment since we assumed no initial emotional reaction that could be downregulated. After each picture presentation (6 s) participants were asked to rate how aroused they were at the current moment on a visual analogue scale (3 s) ranging from ‘very aroused’ (200) to ‘not aroused at all’ (–200; for detailed trial setup see Fig. 1). After a practice session (17 trials) participants were asked if they had any difficulties applying the instructions and to explain how they complied with the regulation instruction. The complete fMRI task consisted of 100 trials (20 per condition) and lasted approximately 23 min. For a more detailed description, please refer to Seidel et al. (in press) or the supplementary material which also includes the results of an a priori power analysis (1.3).

2.4. Image acquisition and processing

Structural T1- and functional EPI-Images were acquired between 8 and 9 AM following an overnight fast using standard sequences with a 3T whole-body MRI scanner (TRIO, Siemens) equipped with a standard head coil (see also Supplementary material 1.4 for scanning parameters).

Imaging data were processed using SPM8 (www.fil.ion.ucl.ac.uk/spm) within the Nipype framework (<http://nipype.sourceforge.net/nipype/>). Functional images were slice time corrected, realigned and registered to their mean. The preprocessed images were coregistered to the participant’s structural T1-image. A DARTEL template (Ashburner, 2007) was created using the structural images from all participants. The functional volumes were normalized to Montreal Neurological Institute (MNI) space using the group template. The resulting data were smoothed with an isotropic Gaussian kernel (8 mm FWHM). Prior to

statistical analysis, we evaluated data quality by manual inspection and using artifact detection tools (ART; www.nitrc.org/projects/artifact_detect/) to identify volumes with intensity outliers ($> 3SD$ from the mean of the time series) and excessive movement (> 2 mm in any direction). Participants were excluded if they showed outliers in $> 25\%$ of frames, which was not the case. Groups did not differ regarding the number of motion ($AN_{\text{mean}} = 2.08$ (3.64), $HC_{\text{mean}} = 2.47$ (4.92), $p \geq 0.05$) and intensity outliers ($AN_{\text{mean}} = 6.3$ (4.09), $HC_{\text{mean}} = 5.9$ (5.06), $p \geq 0.05$).

2.5. Statistical analysis

2.5.1. Self-report data

To test for group differences in the response elicited by the different conditions (negative watch, negative distance, neutral), we conducted a 3(task condition) \times 2(group) repeated measures ANOVA on the arousal ratings. Post-hoc Bonferroni-corrected tests were used to investigate differences between the single conditions. To test for possible relationships with psychometric measures, we calculated an arousal regulation score (negative watch–negative distance of arousal ratings). Associations between the calculated score and age, BMI-SDS, measures of ED symptoms (EDI-2), depression levels (BDI-II) and habitual emotion regulation (ERQ) were calculated using Pearson’s correlations or Spearman’s rho, if normal distribution was not given. Analyses of behavioral data and extracted values were carried out in SPSS 23.

2.5.2. Imaging data

Statistical analysis of the fMRI data involved fitting a general linear model (GLM) separately for each participant on a voxelwise basis to model the hemodynamic response to each of the five conditions (neutral, positive/negative watch, positive/negative distance). We modeled the picture presentation phase as boxcar function with a duration of 6 s and the subsequent rating as a stick-function (zero duration). Additional regressors included six motion parameters and one regressor for each motion or intensity outlier volume as nuisance regressors of no interest. All events were modeled using a canonical hemodynamic response function. Based on previous studies of negative emotion regulation (Ochsner et al., 2012; Walter et al., 2009) and our research question of possibly altered emotional reactions to aversive pictures in AN, we focused on the analysis of the negative pictures [for results of the regulation of positive images please refer to Seidel et al., (in press)].

To confirm that the emotion induction worked as intended, we first examined specific activation patterns within the watch conditions by calculating the contrasts negative watch > neutral watch. To address the main research question of this study regarding potential group differences during the regulation condition, we examined the contrasts negative watch > negative distance and negative watch < negative distance. At the second level, we conducted independent two-sample *t*-tests to assess group differences between these individual contrasts within a priori anatomically defined regions of interest (ROIs): the bilateral amygdala and dlPFC, as defined by the AAL atlas (Maldjian et al., 2003; Tzourio-Mazoyer et al., 2002) and implemented in the WFU PickAtlas toolbox for SPM (Maldjian et al., 2003) using MarsBaR toolbox for SPM (Brett et al., 2002). To control for false positives, familywise error correction was performed using 3DClustSim (version from 3rd of July 2017; http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html). Specifically, the program was used to run 10,000 Monte Carlo simulations to estimate the cluster size above which the false positive probability is below a given α -level ($\alpha = 0.05$) for a given voxel-wise *p* value, which was set at 0.001. At this voxel-wise threshold (two-sided), clusters with more than six voxels for the left and right amygdala and 34 voxels for the left and right dlPFC each corresponded to a combined threshold of $p < 0.05$ [familywise error (FWE) corrected] in the respective ROI. The details of supplemental exploratory whole-brain analyses are provided in the supplementary material (Fig. S1).

To calculate associations between neural activation in the different conditions and psychometric measures, we extracted parameter estimates (betas) for the bilateral amygdala and bilateral dlPFC from clusters within each ROI in the respective contrasts (negative watch > neutral, negative watch > negative distance, negative watch < negative distance). The extent of the clusters for extraction of betas was defined with an uncorrected voxelwise threshold of $p < 0.001$.

Similar to the arousal regulation score, we calculated a neural voluntary regulation score by subtracting betas of the negative distance condition from betas of the negative watch condition for the bilateral amygdala (extracted from the cluster revealed by the negative watch > negative distance contrast) and dlPFC (extracted from the cluster revealed by the negative watch < negative distance contrast).

3. Results

3.1. Demographic and clinical variables, self-report data

As displayed in Table 1, group comparisons revealed the following

Table 1

Results of independent-samples *t*-tests. AN = Acute anorexia nervosa patients, HC = Healthy controls, BMI = Body-mass-index, BMI-SDS = Body-mass-index standard deviation score, IQ = Intelligence quotient, EDI-2 = Eating Disorder Inventory (total score), BDI-II = Beck Depression Inventory, STAI = State-Trait-Anxiety Inventory, ERQ = Emotion Regulation Questionnaire. Age is given in years, BMI in kg/m².

| | AN (n = 36) | HC (n = 36) |
|----------------------|----------------|------------------|
| Age | 16.63 (3.85) | 16.90 (3.82) |
| BMI | 14.65 (1.25) | 20.72 (2.40)*** |
| BMI-SDS | - 3.21 (1.07) | - 0.05 (0.63)*** |
| Leptin | 1.58 (2.35) | 12.98 (8.66)*** |
| IQ | 113.78 (10.87) | 112.92 (7.2) |
| EDI-2 | 216.23 (45.30) | 142.23 (25.8)*** |
| BDI-II | 23.11 (10.6) | 5.74 (4.67)*** |
| STAI-state | 48.23 (11.94) | 33.97 (8.37)*** |
| STAI-trait | 46.67 (11.62) | 33.61 (7.67)*** |
| ERQ-Reinterpretation | 23.6 (6.99) | 27.75 (6.37)* |
| ERQ-Suppression | 14.26 (4.97) | 13.80 (5.01) |

* $p < 0.05$.

*** $p < 0.001$.

results in basic demographic and clinical variables: AN patients did not differ from their HC counterparts in age, but BMI and leptin values were significantly lower and both ED symptoms as well as depressive symptoms were considerably elevated. Patients and HC reported equal use of the emotion regulation strategy suppression (ERQ). However, AN reported significantly less use of the reappraisal strategy reinterpretation compared to HC.

An expected main effect of condition in reported arousal was evident [$F(2140) = 158.53$, $p \leq 0.001$, $\eta^2 = 0.85$] and post-hoc tests confirmed that arousal in the negative watch condition was higher as compared to neutral watch ($p < 0.001$, Fig. 2). The data also showed a significant decrease in arousal during the negative distance condition compared to negative watch ($p < 0.001$, Fig. 2). Surprisingly, however, there were no group differences in arousal ratings in any of the three conditions [$F(2140) = 1.41$, $p \geq 0.05$, $\eta^2 = 0.02$]. No associations between the arousal regulation score and age, BMI-SDS, EDI-total, BDI or STAI emerged.

3.2. Imaging data - emotion induction

Confirming that the fMRI task elicited an expected activation pattern, exploratory analysis of the main effect of emotion induction (contrast: negative watch > neutral watch) over both groups revealed increased hemodynamic activity in the bilateral amygdala (left amygdala [- 24 - 6 - 16], $k = 215$, $t_{\text{peak}} = 9.94$; right amygdala [22 - 6 - 14], $k = 248$, $t_{\text{peak}} = 9.56$, for whole brain results see also Fig. S1). An independent-samples *t*-test showed significant differences between the groups within both a priori-specified ROIs (amygdala and dlPFC). Specifically, compared to HC, AN patients showed increased activity in the right amygdala (Fig. 3) in response to passively viewing negative pictures as compared to passively viewing neutral ones. Furthermore, group differences in two clusters within the right dlPFC and two in the left dlPFC were found in the same contrast (Fig. 3, Fig. S2). An additional GLM with age as covariate confirmed the initial results (see Supplementary material Table S1). No correlations between EDI-total, BDI or BMI-SDS with neural responses during the viewing of negative stimuli in either group were significant after correcting for multiple testing (supplementary material Table S2).

3.3. Imaging data - volitional emotion regulation

A significant main effect of regulation (contrast: negative watch > negative distance) was evident in the bilateral amygdala [left amygdala (- 26 - 4 - 18), $k = 104$, $t_{\text{peak}} = 4.07$; right amygdala (22 - 6 - 12), $k = 16$, $t_{\text{peak}} = 3.72$], with a decrease in activity during distance as compared to watch (for whole brain results see also Fig. S1). Increased activation during distancing (contrast: negative watch < negative distance) was found in two clusters within the right dlPFC [dlPFC (16 26 56), $k = 129$, $t_{\text{peak}} = 5.1$; dlPFC (40 24 46), $k = 64$, $t_{\text{peak}} = 4.46$]. No group differences were visible in either ROI or contrast during explicit emotion regulation (or in an additional GLM with age as covariate).

The neural voluntary regulation score of the averaged bilateral amygdala correlated positively with the arousal regulation score ($\rho = 0.31$, $p = 0.008$) over all participants, providing further support that paradigm and analysis strategy produced the expected effects (Fig. 4). Neither the amygdala nor the dlPFC neural voluntary regulation scores were correlated with age, BMI-SDS, EDI-total or BDI-II scores.

4. Discussion

The current study is, to our knowledge, the first to examine the processing and voluntary regulation of negative emotions using fMRI in patients with AN. In line with the notion of altered emotion processing in AN (Oldershaw et al., 2011), patients displayed elevated amygdala

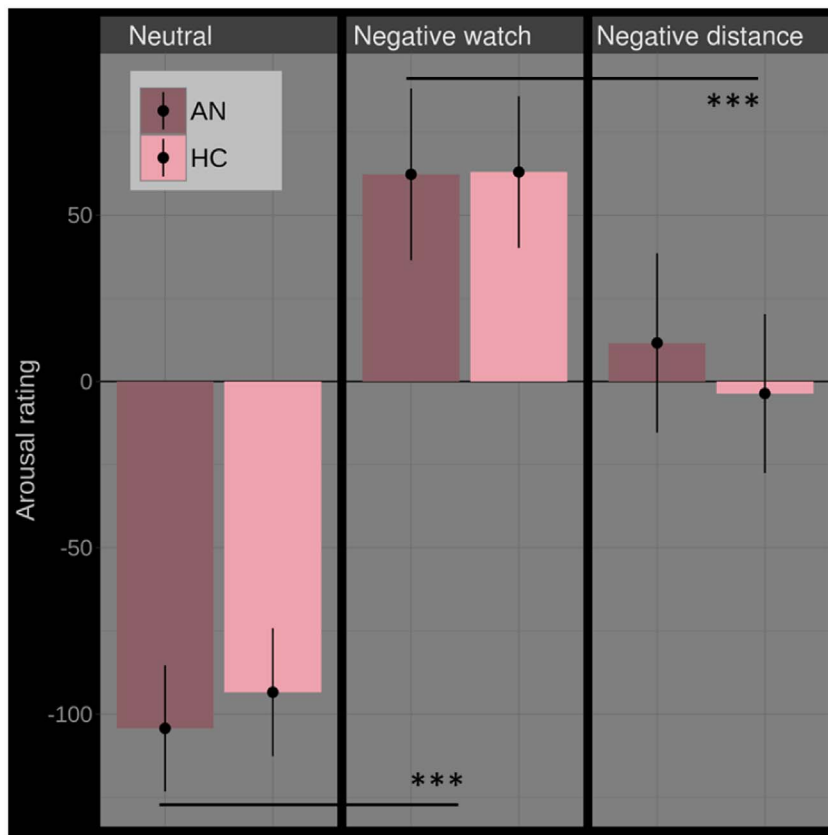


Fig. 2. Arousal Ratings displaying mean and standard error for each group during the emotion regulation task for the conditions neutral watch, negative watch and negative distance. Possible range of rating was -200 (not aroused) to 200 (very aroused). AN = Anorexia nervosa patients, HC = Healthy controls. *** = $p < 0.001$.

reactivity to aversive pictures during the baseline condition of simply watching negative pictures compared to neutral ones. Furthermore, supporting previous indications of increased and sustained self-control in AN (Boehm et al., in press, 2014; Brooks et al., 2011; Ehrlich et al., 2015; Wierenga et al., 2014) we also observed increased dlPFC responses in this contrast in AN. Confirming the validity of the voluntary emotion regulation task, patients and HC displayed down-regulation of subjective arousal and neural responses in the a priori-defined ROI amygdala via distancing in response to aversive disorder-unrelated pictures. However, no group differences were visible during the regulation condition in the amygdala (associated with bottom up processing) or dlPFC [associated with top-down control processes (Banks et al., 2007; Kalisch, 2009; Ochsner et al., 2012)].

The majority of research suggestive of functional alterations within emotion circuits in AN employed paradigms including disorder-related stimuli, such as images of food and bodies. When exposed to such stimuli, patients with AN exhibit greater activation in widespread cortical

and subcortical brain circuits (Zhu et al., 2012), including prefrontal cortices and the amygdala (Ellison et al., 1998; Joos et al., 2011; Miyake et al., 2010; Seeger et al., 2002; Vocks et al., 2011). These hyperactivations, as well as increased amygdala activity in response to disorder-unrelated stimuli in our study, may reflect heightened negative emotional arousal elicited by disorder-related and -unrelated negative visual stimuli. In contrast, studies using emotional (fearful) face stimuli have found amygdala responses to be normal or blunted rather than increased in acute and recovered AN (Bang et al., 2016; Cowdrey et al., 2012; Leppanen et al., 2017). Differences between face and body/food stimuli might be partially explained by slightly impaired recognition of emotions in faces (Kucharska-Pietura et al., 2004; Pollatos et al., 2008), altered processing of facial stimuli (Li et al., 2015; Moody et al., 2015) as well as social anxiety (McAdams and Krawczyk, 2011) in AN.

Increased activation during negative emotion induction was not only found in the amygdala but also found in three clusters within the

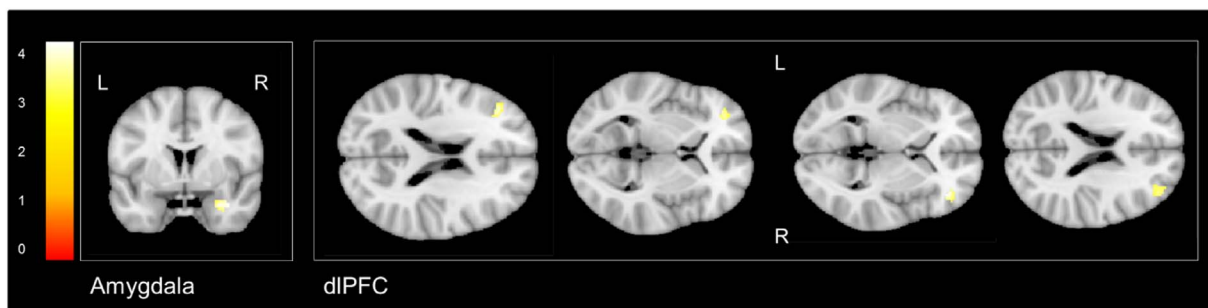


Fig. 3. Group differences (AN > HC, T-map) in the contrast negative watch > neutral. Threshold: $p < 0.001$ at the voxel level with an additional cluster extent threshold of $k > 6$ (amygdala) and $k > 34$ (dlPFC) to achieve FWE correction at $p < 0.05$ (calculated using 3DClustsim). The following locations for peaks were obtained: right amygdala [36 2 -24], $k = 72$, $t_{peak} = 4.38$; left dorsal dlPFC [-36 44 1], $k = 112$, $t_{peak} = 4.1$; left ventral dlPFC [-32 32 14], $k = 78$, $t_{peak} = 4.41$; right ventral dlPFC [38 40 2], $k = 53$, $t_{peak} = 4.24$; right dorsal dlPFC [40 46 22], $k = 62$, $t_{peak} = 3.79$. R = right; L = left. dlPFC = dorsolateral prefrontal cortex.

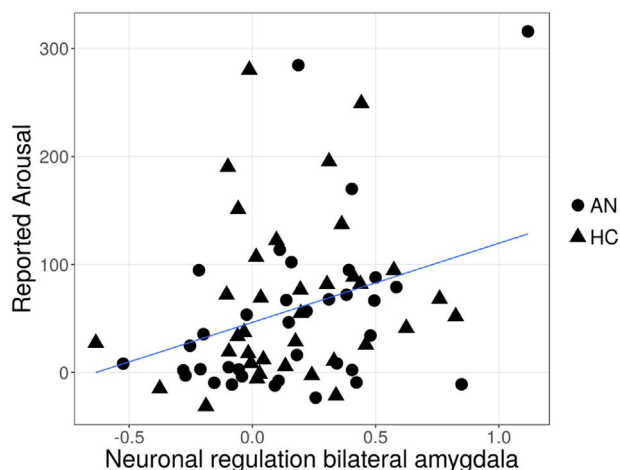


Fig. 4. Pearson's rho for the correlation between arousal regulation score (negative watch-negative distance) and neural voluntary regulation score (negative watch-negative distance) over the averaged bilateral amygdala ($\rho = 0.29, p = 0.014$). AN = Anorexia nervosa patients, HC = Healthy controls.

right and left dlPFC in AN patients. We cautiously suggest these findings to be a possible indicator of active control mechanisms in response to aversive stimuli even though task instructions required none. Further, they might even be an indicator of compensatory control mechanisms mobilized in response to heightened amygdala reactivity. The latter mechanisms, albeit speculative, might also be the reason why we do not find differences in subjective arousal ratings. Studies using resting state and task-based fMRI could also be interpreted in support of the notion of sustained cognitive control processes in AN (Wierenga et al., 2014).

Interestingly, the current task which applies detachment as adaptive reappraisal strategy did not reveal any deviations in downregulation of self-reported negative affect or neural activity during active regulation in our patient group. A speculative interpretation of this finding could be that excessive regulatory control in AN does not directly impact voluntary emotion regulation abilities. Such an interpretation would stand in contrast to studies using questionnaire data in which adult AN patients report difficulties in several domains of emotion regulation (Brockmeyer et al., 2014; Haynos et al., 2014; Merwin et al., 2013; Svaldi et al., 2012). One possible explanation for the discrepancy between the self-report literature and the current results could be that AN patient's answers to their perceived emotion regulation ability are biased by low-self-esteem and a negativity bias (Cardi et al., 2014; Fairburn et al., 1999) that is causing them to underestimate the effectiveness of their emotion regulation ability. Additionally it might be possible that they are lacking access to adaptive regulation strategies such as reappraisal and use maladaptive ones if not explicitly instructed to do otherwise. Reappraisal is considered one of the most effective emotion regulation strategies [successfully regulating negative affect, peripheral physiological measures, and neural responses (Ochsner et al., 2012)], whereas other regulation strategies are assumed to have only short-term effects (Sheppes et al., 2014) or are associated with paradox rebound effects (Abramowitz et al., 2001). The lack of habitual use of cognitive reappraisal in our sample as well as an increased reported usage of spontaneous rumination and suppression (both considered maladaptive) to cope with sad feelings in women with ED [AN;BN; BED (Naumann et al., 2015)] might support this assumption of a preference for or eased access to maladaptive strategies when not explicitly instructed otherwise. This would also explain findings of a recent emotion regulation study using a startle probe paradigm and the extent of pupil dilation, which provides an objective measure of arousal (Racine et al., 2016). During the task, no specific instruction for down-regulation was given to the participants and AN patients were reported to have difficulties in down-regulating negative emotions. As they were free to choose any regulation strategy they might have chosen whatever

was easier to access, which might have included less effective strategies. An alternative explanation may be that patients with the binge-purge subtype of AN show more deficits in emotion regulation [e.g. impulse control, and access to emotion regulation strategies (Brockmeyer et al., 2014; Rowsell et al., 2016; Weinbach et al., 2017)] than patients of the restrictive subtype. As our sample was predominantly restrictive our findings go in line with these notions that individuals with this subtype might have only few deficits in emotion regulation.

The current results have to be interpreted in the light of several limitations. First, although we gave explicit instructions and provided pre-scan training, we cannot be absolutely sure what kind of emotion regulation strategy participants actually used. Second, AN patients are known to act in a socially desirable way and to be perfectionistic (Halimi et al., 2012), which might have biased arousal scores and obfuscated group differences. It might also be possible that deficits in reported emotion regulation previously reported in adults increase with age and chronicity of the disorder and are not visible yet in our on average relatively young, non-chronic sample. However, despite close pairwise age-matching and covarying for age in all analyses, the age range of our sample was broad (12–29 years) and we therefore cannot completely exclude (neuro-) development as a potentially confounding factor to our findings. On a similar note, although the current AN and HC groups did not differ with respect to IQ, future studies should also carefully match according to education which has been shown to impact emotion regulation outcomes (Martin and Ochsner, 2016). Third, although we cannot completely rule out any possible carry over effects from one condition into the other, the randomization of conditions and the jittered inter-trial interval should have kept it to a minimum (Dale, 1999). It is also important to note that the current findings of altered amygdala activation in AN are difficult to dissociate from the acute effects of starvation on the endocrine system and the brain (Kaye et al., 2009; King et al., 2018). Nonetheless, the fact that despite these potent effects there was no group activation differences for the main effect of regulation speaks to the robustness of the results and points to the possible specificity of previously reported effects in fMRI studies using food-specific cues (Phillipou et al., 2014). Indeed, since we carefully filtered the stimulus material to not show any eating-disorder related pictures, increased control mechanisms in AN might be limited to stimuli associated with food or body related content. For future studies, it will be also important to more carefully consider whether AN participants chose different strategies to regulate emotions depending on stimulus content (especially disorder-relevant and irrelevant), AN subtype and/or associated arousal [see Sheppes et al., 2011 for a study in HC], and whether this strategy choice influences neural responses. Also, considering that previous findings did not show increased reactivity to positive pictures (Seidel et al., in press), future studies should first assess valence via ratings as well as carefully distinguish between valences of stimuli when interpreting alterations in emotion processing and regulation. Last but not least future studies should replicate these findings with larger sample sizes to increase statistical power and enable analysis between subtypes.

By showing increased activity in areas associated with the processing (and possibly automatic regulation) of emotion, this study extends previous findings of alterations within brain circuitry associated with emotion generation and cognitive control in patients with AN. As no differences in subjective ratings and neural response during voluntary emotion regulation were visible, the current results may indicate that reappraisal is a feasible strategy to reduce negative arousal in AN patient populations. Therapeutic interventions might integrate these findings by providing training to ease access to these strategies in daily life of patients.

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Conflict of interest

In the last two years, Dr. Roessner has received payment for consulting and writing activities from Lilly, Novartis, and Shire Pharmaceuticals, lecture honoraria from Lilly, Novartis, Shire Pharmaceuticals, and Medice Pharma, and support for research from Shire and Novartis. He has carried out (and is currently carrying out) clinical trials in cooperation with the Novartis, Shire, and Otsuka companies. Henrik Walter has received a speaker honorarium from Servier.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.nicl.2017.12.035>.

References

- Abler, B., Kessler, H., 2009. Emotion Regulation Questionnaire – Eine deutschsprachige Fassung des ERQ von Gross und John. *Diagnostica* 55 (3), 144–152. <http://dx.doi.org/10.1026/0012-1924.55.3.144>.
- Abramowitz, J.S., Tolin, D.F., Street, G.P., 2001. Paradoxical effects of thought suppression: a meta-analysis of controlled studies. *Clin. Psychol. Rev.* 21 (5), 683–703. [http://dx.doi.org/10.1016/S0272-7358\(00\)00057-X](http://dx.doi.org/10.1016/S0272-7358(00)00057-X).
- Aldao, A., Nolen-Hoeksema, S., Schweizer, S., 2010. Emotion-regulation strategies across psychopathology: a meta-analytic review. *Clin. Psychol. Rev.* 30 (2), 217–237. <http://dx.doi.org/10.1016/j.cpr.2009.11.004>.
- Ashburner, J., 2007. A fast diffeomorphic image registration algorithm. *NeuroImage* 38 (1), 95–113. <http://dx.doi.org/10.1016/j.neuroimage.2007.07.007>.
- Bang, L., Rø, Ø., Endestad, T., 2016. Amygdala alterations during an emotional conflict task in women recovered from anorexia nervosa. *Psychiatry Res. Neuroimaging* 248, 126–133. <http://dx.doi.org/10.1016/j.pscychres.2015.12.008>.
- Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Phan, K.L., 2007. Amygdala–frontal connectivity during emotion regulation. *Soc. Cogn. Affect. Neurosci.* 2 (4), 303–312. <http://dx.doi.org/10.1093/scn/nsm029>.
- Boehm, I., Geisler, D., King, J.A., Ritschel, F., Seidel, M., Deza Araujo, Y., ... Ehrlich, S., 2014. Increased resting state functional connectivity in the fronto-parietal and default mode network in anorexia nervosa. *Front. Behav. Neurosci.* 8, 346. <http://dx.doi.org/10.3389/fnbeh.2014.00346>.
- Boehm, I., King, J.A., Bernardoni, F., Geisler, D., Seidel, M., Ritschel, F., Goschke, T., Haynes, J.-D., Roessner, V., Ehrlich, S., 23 August 2017. Subliminal and supraliminal processing of reward-related stimuli in anorexia nervosa. *Psychol. Med.* 1–11. <http://dx.doi.org/10.1017/S003329171700216>.
- Brett, M., Anton, J.-L., Valabregue, R., Poline, J.-B., 2002. Region of interest analysis using the MarsBar toolbox for SPM 99. *NeuroImage* 16 (2), S497.
- Brockmeyer, T., Skunde, M., Wu, M., Bresslein, E., Rudofsky, G., Herzog, W., Friederich, H.-C., 2014. Difficulties in emotion regulation across the spectrum of eating disorders. *Compr. Psychiatry* 55 (3), 565–571. <http://dx.doi.org/10.1016/j.comppsy.2013.12.001>.
- Brooks, S.J., O'Daly, O.G., Uher, R., Friederich, H.-C., Giampietro, V., Brammer, M., ... Campbell, I.C., 2011. Differential neural responses to food images in women with bulimia versus anorexia nervosa. *PLoS One* 6 (7), e22259. <http://dx.doi.org/10.1371/journal.pone.0022259>.
- Cardi, V., Di Matteo, R., Gilbert, P., Treasure, J., 2014. Rank perception and self-evaluation in eating disorders. *Int. J. Eat. Disord.* 47 (5), 543–552. <http://dx.doi.org/10.1002/eat.22261>.
- Cowdrey, F.A., Harmer, C.J., Park, R.J., McCabe, C., 2012. Neural responses to emotional faces in women recovered from anorexia nervosa. *Psychiatry Res.* 201 (3), 190–195. <http://dx.doi.org/10.1016/j.pscychres.2011.08.009>.
- Dale, A.M., 1999. Optimal experimental design for event-related fMRI. *Hum. Brain Mapp.* 8 (2–3), 109–114.
- Danner, U.N., Sanders, N., Smeets, P.A.M., van Meer, F., Adan, R.A.H., Hoek, H.W., van Elburg, A.A., 2012. Neuropsychological weaknesses in anorexia nervosa: set-shifting, central coherence, and decision making in currently ill and recovered women. *Int. J. Eat. Disord.* 45 (5), 685–694. <http://dx.doi.org/10.1002/eat.22007>.
- Diers, K., Weber, F., Brocke, B., Strobel, A., Schönfeld, S., 2014. Instructions matter: a comparison of baseline conditions for cognitive emotion regulation paradigms. *Front. Psychol.* 5.
- Dosenbach, N.U., Fair, D.A., Cohen, A.L., Schlaggar, B.L., Petersen, S.E., 2008. A dual-networks architecture of top-down control. *Trends Cogn. Sci.* 12 (3), 99–105.
- Ehrlich, S., Geisler, D., Ritschel, F., King, J.A., Seidel, M., Boehm, I., ... Kroemer, N.B., 2015. Elevated cognitive control over reward processing in recovered female patients with anorexia nervosa. *J. Psychiatry Neurosci.* 40 (4), 307.
- Eippert, F., Veit, R., Weiskopf, N., Erb, M., Birbaumer, N., Anders, S., 2007. Regulation of emotional responses elicited by threat-related stimuli. *Hum. Brain Mapp.* 28 (5), 409–423.
- Ellison, Z., Foong, J., Howard, R., Bullmore, E., Williams, S., Treasure, J., 1998. Functional anatomy of calorie fear in anorexia nervosa. *Lancet* 352 (9135), 1192.
- Engel, S.G., Wonderlich, S.A., Crosby, R.D., Mitchell, J.E., Crow, S., Peterson, C.B., ... Gordon, K.H., 2013. The role of affect in the maintenance of anorexia nervosa: evidence from a naturalistic assessment of momentary behaviors and emotion. *J. Abnorm. Psychol.* 122 (3), 709–719. <http://dx.doi.org/10.1037/a0034010>.
- Fairburn, C.G., Cooper, Z., Doll, H.A., Welch, S.L., 1999. Risk factors for anorexia nervosa: three integrated case-control comparisons. *Arch. Gen. Psychiatry* 56 (5), 468–476.
- Fairburn, C.G., Cooper, Z., Shafran, R., 2003. Cognitive behaviour therapy for eating disorders: a “transdiagnostic” theory and treatment. *Behav. Res. Ther.* 41 (5), 509–528. [http://dx.doi.org/10.1016/S0005-7967\(02\)00088-8](http://dx.doi.org/10.1016/S0005-7967(02)00088-8).
- Fichter, M., Quadflieg, N., 2001. The structured interview for anorexic and bulimic disorders for DSM-IV and ICD-10 (SIAB-EX): reliability and validity. *Eur. Psychiatry* 16 (1), 38–48.
- Goldin, P.R., McRae, K., Ramel, W., Gross, J.J., 2008. The neural bases of emotion regulation: reappraisal and suppression of negative emotion. *Biol. Psychiatry* 63 (6), 577–586. <http://dx.doi.org/10.1016/j.biopsych.2007.05.031>.
- Gross, J.J., 1998. Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *J. Pers. Soc. Psychol.* 74 (1), 224–237. <http://dx.doi.org/10.1037/0022-3514.74.1.224>.
- Gross, J.J., Thompson, R.A., 2007. Emotion Regulation: Conceptual Foundations. In: *Handbook of Emotion Regulation*. Guilford Press, New York, NY, US, pp. 3–24.
- Gross, J.J., 2013. Emotion regulation: conceptual and empirical foundations. In: *Handbook of Emotion Regulation*.
- Gross, J.J., Muñoz, R.F., 1995. Emotion regulation and mental health. *Clin. Psychol. Sci. Pract.* 2 (2), 151–164. <http://dx.doi.org/10.1111/j.1468-2850.1995.tb00036.x>.
- Halmi, K.A., Bellace, D., Berthod, S., Ghosh, S., Berrettini, W., Brandt, H.A., ... Strober, M., 2012. An examination of early childhood perfectionism across anorexia nervosa subtypes. *Int. J. Eat. Disord.* 45 (6), 800–807. <http://dx.doi.org/10.1002/eat.22019>.
- Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., Conde, J.G., 2009. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* 42 (2), 377–381. <http://dx.doi.org/10.1016/j.jbi.2008.08.010>.
- Harrison, A., Sullivan, S., Tchanturia, K., Treasure, J., 2009. Emotion recognition and regulation in anorexia nervosa. *Clin. Psychol. Psychother.* 16 (4), 348–356.
- Hautzinger, M., Keller, F., Kühner, C., 2009. Beck Depressions Inventar: Revised.
- Haynos, A.F., Fruzzetti, A.E., 2011. Anorexia nervosa as a disorder of emotion dysregulation: evidence and treatment implications: emotion dysregulation in anorexia nervosa. *Clin. Psychol. Sci. Pract.* 18 (3), 183–202. <http://dx.doi.org/10.1111/j.1468-2850.2011.01250.x>.
- Haynos, A.F., Roberto, C.A., Martinez, M.A., Attia, E., Fruzzetti, A.E., 2014. Emotion regulation difficulties in anorexia nervosa before and after inpatient weight restoration. *Int. J. Eat. Disord.* <http://dx.doi.org/10.1002/eat.22265>.
- Joos, A.A.B., Saum, B., van Elst, L.T., Perlov, E., Glauche, V., Hartmann, A., ... Zeeck, A., 2011. Amygdala hyperreactivity in restrictive anorexia nervosa. *Psychiatry Res. Neuroimaging* 191 (3), 189–195.
- Kalisch, R., 2009. The functional neuroanatomy of reappraisal: time matters. *Neurosci. Biobehav. Rev.* 33 (8), 1215–1226.
- Kanske, P., Heissler, J., Schönfelder, S., Bongers, A., Wessa, M., 2011. How to regulate emotion? Neural networks for reappraisal and distraction. *Cereb. Cortex* 21 (6), 1379–1388. <http://dx.doi.org/10.1093/cercor/bhq216>.
- Kaye, W.H., Fudge, J.L., Paulus, M., 2009. New insights into symptoms and neurocircuit function of anorexia nervosa. *Nat. Rev. Neurosci.* 10 (8), 573–584. <http://dx.doi.org/10.1038/nrn2682>.
- King, J.A., Geisler, D., Bernardoni, F., Ritschel, F., Böhm, I., Seidel, M., ... Ehrlich, S., 2016. Altered neural efficiency of decision making during temporal reward discounting in anorexia nervosa. *J. Am. Acad. Child Adolesc. Psychiatry.* <http://dx.doi.org/10.1016/j.jaac.2016.08.005>.
- King, J.A., Frank, G.K., Thompson, P.M., Ehrlich, S., 1 February 2018. Structural neuroimaging of anorexia nervosa: future directions in the quest for mechanisms underlying dynamic alterations. *Biol. Psychiatry* 83 (3), 224–234.
- Kolar, D.R., Huss, M., Preuss, H.M., Jenetzky, E., Haynos, A.F., Bürger, A., Hammerle, F., 2017. Momentary emotion identification in female adolescents with and without anorexia nervosa. *Psychiatry Res.* 255, 394–398. <http://dx.doi.org/10.1016/j.pscychres.2017.06.075>.
- Kromeyer-Hauschild, K., Wabitsch, M., Kunze, D., Geller, F., Geiß, H.C., Hesse, V., ... Hebebrand, J., 2001. Perzentile für den Body-mass-Index für das Kindes- und Jugendalter unter Heranziehung verschiedener deutscher Stichproben. *Monatsschr. Kinderheilkd.* 149 (8), 807–818. <http://dx.doi.org/10.1007/s001120170107>.
- Kucharska-Pietura, K., Nikolaou, V., Masiak, M., Treasure, J., 2004. The recognition of emotion in the faces and voice of anorexia nervosa. *Int. J. Eat. Disord.* 35 (1), 42–47. <http://dx.doi.org/10.1002/eat.10219>.
- Lavender, J.M., Wonderlich, S.A., Engel, S.G., Gordon, K.H., Kaye, W.H., Mitchell, J.E., 2015. Dimensions of emotion dysregulation in anorexia nervosa and bulimia nervosa:

- a conceptual review of the empirical literature. *Clin. Psychol. Rev.* 40, 111–122. <http://dx.doi.org/10.1016/j.cpr.2015.05.010>.
- Lee, S., Ran Kim, K., Ku, J., Lee, J.-H., Namkoong, K., Jung, Y.-C., 2014. Resting-state synchrony between anterior cingulate cortex and precuneus relates to body shape concern in anorexia nervosa and bulimia nervosa. *Psychiatry Res. Neuroimaging* 221 (1), 43–48. <http://dx.doi.org/10.1016/j.pscychresns.2013.11.004>.
- Leppanen, J., Cardí, V., Paloyelis, Y., Simmons, A., Tchanturia, K., Treasure, J., 2017. Blunted neural response to implicit negative facial affect in anorexia nervosa. *Biol. Psychol.* <http://dx.doi.org/10.1016/j.biopsycho.2017.07.010>.
- Li, W., Lai, T.M., Bohon, C., Loo, S.K., McCurdy, D., Strober, M., ... Feusner, J., 2015. Anorexia nervosa and body dysmorphic disorder are associated with abnormalities in processing visual information. *Psychol. Med.* 45 (10), 2111–2122. <http://dx.doi.org/10.1017/S0033291715000045>.
- Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage* 19 (3), 1233–1239. [http://dx.doi.org/10.1016/S1053-8119\(03\)00169-1](http://dx.doi.org/10.1016/S1053-8119(03)00169-1).
- Martin, R.E., Ochsner, K.N., 2016. The neuroscience of emotion regulation development: implications for education. *Curr. Opin. Behav. Sci.* 10 (Supplement C), 142–148. <http://dx.doi.org/10.1016/j.cobeha.2016.06.006>.
- McAdams, C.J., Krawczyk, D.C., 2011. Impaired neural processing of social attribution in anorexia nervosa. *Psychiatry Res. Neuroimaging* 194 (1), 54–63. <http://dx.doi.org/10.1016/j.pscychresns.2011.06.016>.
- McRae, K., Gross, J.J., Weber, J., Robertson, E.R., Sokol-Hessner, P., Ray, R.D., ... Ochsner, K.N., 2012. The development of emotion regulation: an fMRI study of cognitive reappraisal in children, adolescents and young adults. *Soc. Cogn. Affect. Neurosci.* 7 (1), 11–22. <http://dx.doi.org/10.1093/scan/nsr093>.
- Merwin, R.M., Moskovich, A.A., Wagner, H.R., Ritschel, L.A., Craighead, L.W., Zucker, N.L., 2013. Emotion regulation difficulties in anorexia nervosa: relationship to self-perceived sensory sensitivity. *Cognit. Emot.* 27 (3), 441–452. <http://dx.doi.org/10.1080/02699931.2012.719003>.
- Miyake, Y., Okamoto, Y., Onoda, K., Shirao, N., Okamoto, Y., Otagaki, Y., Yamawaki, S., 2010. Neural processing of negative word stimuli concerning body image in patients with eating disorders: an fMRI study. *NeuroImage* 50 (3), 1333–1339. <http://dx.doi.org/10.1016/j.neuroimage.2009.12.095>.
- Moody, T.D., Sasaki, M.A., Bohon, C., Strober, M.A., Bookheimer, S.Y., Sheen, C.L., Feusner, J.D., 2015. Functional connectivity for face processing in individuals with body dysmorphic disorder and anorexia nervosa. *Psychol. Med.* 45 (16), 3491–3503. <http://dx.doi.org/10.1017/S0033291715001397>.
- Nandrino, J.-L., Berna, G., Hot, P., Dodin, V., Latrée, J., Decharles, S., Sequeira, H., 2012. Cognitive and physiological dissociations in response to emotional pictures in patients with anorexia. *J. Psychosom. Res.* 72 (1), 58–64. <http://dx.doi.org/10.1016/j.jpsychores.2011.11.003>.
- Naumann, E., Tuschien-Caffier, B., Voderholzer, U., Svaldi, J., 2015. Spontaneous emotion regulation in anorexia and bulimia nervosa. *Cogn. Ther. Res.* 40 (3), 304–313. <http://dx.doi.org/10.1007/s10608-015-9723-3>.
- Ochsner, K.N., Bunge, S.A., Gross, J.J., Gabrieli, J.D.E., 2002. Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *J. Cogn. Neurosci.* 14 (8), 1215–1229. <http://dx.doi.org/10.1162/089892902760807212>.
- Ochsner, K.N., Silvers, J.A., Buhle, J.T., 2012. Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Ann. N. Y. Acad. Sci.* 1251, E1–24. <http://dx.doi.org/10.1111/j.1749-6632.2012.06751.x>.
- Oldershaw, A., Hambrook, D., Stahl, D., Tchanturia, K., Treasure, J., Schmidt, U., 2011. The socio-emotional processing stream in anorexia nervosa. *Neurosci. Biobehav. Rev.* 35 (3), 970–988. <http://dx.doi.org/10.1016/j.neubiorev.2010.11.001>.
- Oldershaw, A., Lavender, T., Sallis, H., Stahl, D., Schmidt, U., 2015. Emotion generation and regulation in anorexia nervosa: a systematic review and meta-analysis of self-report data. *Clin. Psychol. Rev.* 39, 83–95. <http://dx.doi.org/10.1016/j.cpr.2015.04.005>.
- Parling, T., Mortazavi, M., Ghaderi, A., 2010. Alexithymia and emotional awareness in anorexia nervosa: time for a shift in the measurement of the concept? *Eat. Behav.* 11 (4), 205–210. <http://dx.doi.org/10.1016/j.eatbeh.2010.04.001>.
- Paschke, L.M., Dörfel, D., Steimke, R., Trempler, I., Magrabi, A., Ludwig, V.U., ... Walter, H., 2016. Individual differences in self-reported self-control predict successful emotion regulation. *Soc. Cogn. Affect. Neurosci.* <http://dx.doi.org/10.1093/scan/nsw036>.
- Phillipou, A., Rossell, S.L., Castle, D.J., 2014. The neurobiology of anorexia nervosa: a systematic review. *Aust. N. Z. J. Psychiatry* 48 (2), 128–152. <http://dx.doi.org/10.1177/0004867413509693>.
- Pollatos, O., Herbert, B.M., Schandry, R., Gramann, K., 2008. Impaired central processing of emotional faces in anorexia nervosa. *Psychosom. Med.* 70 (6), 701–708.
- Racine, S.E., Wildes, J.E., 2015. Dynamic longitudinal relations between emotion regulation difficulties and anorexia nervosa symptoms over the year following intensive treatment. *J. Consult. Clin. Psychol.* 83 (4), 785.
- Racine, S.E., Forbush, K.T., Wildes, J.E., Hagan, K.E., Pollack, L.O., May, C., 2016. Voluntary emotion regulation in anorexia nervosa: a preliminary emotion-modulated startle investigation. *J. Psychiatr. Res.* 77, 1–7. <http://dx.doi.org/10.1016/j.jpsychores.2016.02.014>.
- Rowell, M., MacDonald, D.E., Carter, J.C., 2016. Emotion regulation difficulties in anorexia nervosa: associations with improvements in eating psychopathology. *J. Eat. Disord.* 4, 17. <http://dx.doi.org/10.1186/s40337-016-0108-0>.
- Schmidt, U., Treasure, J., 2006. Anorexia nervosa: valued and visible. A cognitive-interpersonal maintenance model and its implications for research and practice. *Br. J. Clin. Psychol.* 45 (Pt 3), 343–366.
- Seeger, G., Braus, D.F., Ruf, M., Goldberger, U., Schmidt, M.H., 2002. Body image distortion reveals amygdala activation in patients with anorexia nervosa—a functional magnetic resonance imaging study. *Neurosci. Lett.* 326 (1), 25–28.
- Seidel, M., King, J.A., Ritschel, F., Boehm, I., Geisler, D., Bernardoni, F., ... Ehrlich, S., 2017. The real-life costs of emotion regulation in anorexia nervosa: a combined ecological momentary assessment and fMRI study. *Transl. Psychiatry* (in press).
- Sheppes, G., Scheibe, S., Suri, G., Gross, J.J., 2011. Emotion-regulation choice. *Psychol. Sci.* 22 (11), 1391–1396.
- Sheppes, G., Scheibe, S., Suri, G., Radu, P., Blechert, J., Gross, J.J., 2014. Emotion regulation choice: a conceptual framework and supporting evidence. *J. Exp. Psychol. Gen.* 143 (1), 163.
- Spielberger, C.D., 2010. State-trait anxiety inventory. In: *The Corsini Encyclopedia of Psychology*. John Wiley & Sons, Inc Retrieved from. <http://onlineibrary.wiley.com/doi/10.1002/9780470479216.corpsy0943/abstract>.
- Svaldi, J., Griepenstroh, J., Tuschien-Caffier, B., Ehring, T., 2012. Emotion regulation deficits in eating disorders: a marker of eating pathology or general psychopathology? *Psychiatry Res.* 197 (1–2), 103–111. <http://dx.doi.org/10.1016/j.pscychres.2011.11.009>.
- Tenconi, E., Santonastaso, P., Degortes, D., Bosello, R., Tittton, F., Mapelli, D., Favaro, A., 2010. Set-shifting abilities, central coherence, and handedness in anorexia nervosa patients, their unaffected siblings and healthy controls: exploring putative endophenotypes. *World J. Biol. Psychiatry* 11 (6), 813–823. <http://dx.doi.org/10.3109/15622975.2010.483250>.
- Teri, L., 1982. The use of the beck depression inventory with adolescents. *J. Abnorm. Child Psychol.* 10, 277–284. <http://dx.doi.org/10.1007/BF00915946>.
- Thiel, A., Jacobi, C., Horstmann, S., Paul, T., Nutzinger, D.O., Schüßler, G., 1997. Eine deutschsprachige Version des Eating Disorder Inventory EDI-2. [German translation of the Eating Disorder Inventory EDI-2]. *Psychother. Psychosom. Med. Psychol.* 47 (9–10), 365–376.
- Treasure, J., Schmidt, U., 2013. 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.* 1, 13. <http://dx.doi.org/10.1186/2050-2974-1-13>.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., ... Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage* 15 (1), 273–289. <http://dx.doi.org/10.1006/nimg.2001.0978>.
- Vocks, S., Herpertz, S., Rosenberger, C., Senf, W., Gizewski, E.R., 2011. Effects of gustatory stimulation on brain activity during hunger and satiety in females with restricting-type anorexia nervosa: an fMRI study. *J. Psychiatr. Res.* 45 (3), 395–403. <http://dx.doi.org/10.1016/j.jpsychores.2010.07.012>.
- Walter, H., von Kalckreuth, A., Schardt, D., Stephan, A., Goschke, T., Erk, S., 2009. The temporal dynamics of voluntary emotion regulation. *PLoS One* 4 (8), e6726. <http://dx.doi.org/10.1371/journal.pone.0006726>.
- Weinbach, N., Sher, H., Bohon, C., 2017. Differences in emotion regulation difficulties across types of eating disorders during adolescence. *J. Abnorm. Child Psychol.* 1–8.
- Wierenga, C., Ely, A., Bischoff-Grethe, A., Bailer, U.F., Simmons, A.N., Kaye, W.H., 2014. Are extremes of consumption in eating disorders related to an altered balance between reward and inhibition? *Front. Behav. Neurosci.* 8. <http://dx.doi.org/10.3389/fnbeh.2014.00410>.
- Wildes, J.E., Ringham, R.M., Marcus, M.D., 2010. Emotion avoidance in patients with anorexia nervosa: initial test of a functional model. *Int. J. Eat. Disord.* <http://dx.doi.org/10.1002/eat.20730>. (NA-NA).
- Wildes, J.E., Marcus, M.D., Cheng, Y., McCabe, E.B., Gaskill, J.A., 2014. Emotion acceptance behavior therapy for anorexia nervosa: a pilot study. *Int. J. Eat. Disord.* 47 (8), 870–873.
- Zastrow, A., Kaiser, S., Stippich, C., Walther, S., Herzog, W., Tchanturia, K., ... Friederich, H.-C., 2009. Neural correlates of impaired cognitive-behavioral flexibility in anorexia nervosa. *Am. J. Psychiatry* 166 (5), 608–616. <http://dx.doi.org/10.1176/appi.ajp.2008.08050775>.
- Zhu, Y., Hu, X., Wang, J., Chen, J., Guo, Q., Li, C., Enck, P., 2012. 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.* 20 (6), 439–450. <http://dx.doi.org/10.1002/erv.2197>.
- Zonneville-Bender, M.J., van Goozen, S.H., Cohen-Kettenis, P.T., Jansen, L.M., van Elburg, A., van Engeland, H., 2005. Adolescent anorexia nervosa patients have a discrepancy between neurophysiological responses and self-reported emotional arousal to psychosocial stress. *Psychiatry Res.* 135 (1), 45–52.