Altered social reward and attention in anorexia nervosa

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Dysfunctional social reward and social attention are present in a variety of neuropsychiatric disorders including autism, schizophrenia, and social anxiety. Here we show that similar social reward and attention dysfunction are present in anorexia nervosa (AN), a disorder defined by avoidance of food and extreme weight loss. We measured the implicit reward value of social stimuli for female participants with ($n = 11$) and without ($n = 11$) AN using an econometric choice task and also tracked gaze patterns during free viewing of images of female faces and bodies. As predicted, the reward value of viewing bodies varied inversely with observed body weight for women with anorexia but not control women, in contrast with their explicit ratings of attractiveness. Surprisingly, women with AN, unlike control women, did not find female faces rewarding and avoided looking at both the face and eyes – independent of observed body weight. These findings suggest comorbid dysfunction in the neural circuits mediating gustatory and social reward in anorexia nervosa.

Keywords: eating disorders, social, bulimia

INTRODUCTION

Eating is a profoundly social experience for humans, and the amount one eats at a meal is modulated by the identity and number of mealtime companions (de Castro and Brewer, 1992; Young et al., 2009). Partaking in a good meal and bonding with a friend are both universally rewarding activities, and indeed, gustatory and social stimuli are known to activate overlapping reward circuitry in the brain (Kringelbach et al., 2003; O'Doherty et al., 2003), suggesting shared neural mechanisms.

Anorexia nervosa (AN), a disease with the highest fatality rate of all the psychiatric disorders (Keel et al., 2003), is notable in that afflicted individuals deprive themselves of the pleasure of food consumption. Moreover, a growing body of clinical evidence suggests that individuals with AN demonstrate impairments in interpersonal behavior as well (Zucker et al., 2007). We hypothesized that these interpersonal impairments are rooted in a fundamental difference in the ways in which individuals with AN process social rewards. If true, disruptions in social reward processing may comprise part of an endophenotype of AN, analogous to the deficits in social reward and cognition in individuals with autism spectrum disorders (ASD) (Zucker et al., 2007; Rastam, 2008), as well as schizophrenia and social anxiety. In addition to shared social deficits in AN and ASD, preoccupation with food and body weight in AN mirrors the intense interests and preoccupations with objects often expressed by people with ASD. Notably, children with autism exhibit more feeding related problems than typically developing children, including restricted food preferences and a significantly higher rate of food refusal (Schreck et al., 2004).

Dysfunctional social reward may thus comprise part of an intermediate phenotype (Insel and Cuthbert, 2009) of AN, analogous to disordered social motivation and attention in ASD. Evidence of dysfunctional social reward processing in AN thus would broaden traditional conceptualizations of the disorder and motivate more direct psychological, neural, and genetic comparisons with other disorders – such as ASD, schizophrenia, and social anxiety – characterized by social dysfunction.

We hypothesized that individuals with AN would show decreased reward for visual images of other individuals, independent of explicit evaluation of such images. To test this hypothesis, we used econometric and eye-tracking techniques to determine whether weight-restored women with AN showed differences in social reward and attention compared with control women. Experiments using eye-tracking methods have consistently identified different patterns of social attention in ASD (e.g., Klin et al., 2002), whereas our econometric choice task has been used in prior studies to quantify the reward value of various types of social imagery (Hayden et al., 2007). The econometric choice task provides a quantitative measure of the tendency to approach or avoid a particular class of images based on the degree to which they add positive or negative reinforcement to a monetary reward. In contrast to having the participants explicitly report the value of the set of images, this task estimates subjects' implicit valuation of the images; in principle, explicit ratings and implicit valuation could differ.

Indeed, we found that weight-restored women with AN were indistinguishable from control women in their explicit ratings of the attractiveness of women in the photos, perhaps reflecting intense cognitive-behavioral therapy. Nonetheless, weight-restored women with AN showed pathological patterns of social reward and attention in the absence of any cues related to food or consumption. Current treatments for AN predominantly focus on food intake and are typically ineffective (Bulik et al., 2007). If, in fact, the etiology of AN arises from a perturbation in reward and decision-making neural circuitry in general, rather than in a specific "labeled line" associated with food intake, this knowledge could have a profound impact on the development of more effective behavioral therapies.

MATERIALS AND METHODS

PARTICIPANTS

Participants were weight-restored females with restrictive anorexia nervosa (AN-WR; $n = 11$, all with BMI in normal range) and control females (CON; $n = 11$, all without history of eating disorders). We chose to study women who were weight-restored from AN to avoid confounding effects of the disorder with those of malnutrition. Thus, our primary criterion for participants in the AN-WR group was to have a past diagnosis of restrictive anorexia but to be currently weight-restored. We note that all participants but one in the AN-WR group had been weight-restored for 9 months or greater, and that analysis with this individual excluded yielded the same pattern of significant results.

AN-WR participants were selected using a two-stage screening process. The first stage consisted of a phone interview conducted by a doctoral level clinical psychologist. The decision to include an individual was based on the consensus of several doctoral level clinical psychologists upon review of the interview data. Diagnosis was confirmed using a second semi-structured interview based on DSM-IV diagnostic criteria (Fairburn and Cooper, 1993) administered by a doctoral level clinical psychologist. Control participants were screened via telephone interview by a trained researcher for the absence of a history of eating disorders. The decision to include an individual in the control group was based on the consensus of the interviewer and at least one doctoral level clinical psychologist. On the day of the experiment, all participants completed an abbreviated eating disorder examination questionnaire (based on Fairburn and Beglin, 1994). *Post hoc* analysis of the participants' eating disorder examination questionnaire scores confirmed that the scores of the AN-WR group were significantly higher than those of the CON group (2.6 ± 1.18 SD AN-WR; 1.3 ± 0.87 SD CON, $t = -2.88$, df = 20, $p = 0.009$). All participants were given a post-experiment interview to confirm that they could discriminate between the three monetary reward levels in the choice task.

STIMULUS SETS

Stimuli depicted either female faces only ("face images") or female body images with head and face visible ("body images"). All face images were drawn from a database consisting of a large (>1000) number of photographs drawn from the dating website Hotornot.com that had been re-sized to uniform dimensions and cropped to include the face only. These images were rated for attractiveness by a separate set of raters for a previous study (Smith et al., 2010). The face images selected for use in the current study were rated within the top 10% or the bottom 10% of the entire distribution, which allowed us to confidently categorize the two image groups as either high attractiveness (60 images) or low attractiveness (60 images).

For the full body stimulus set, we partially drew our images from a database that had been rated for attractiveness in a previous study (Hayden et al., 2007). In order to incorporate a wider range of body weights in our stimulus set, we additionally incorporated photos downloaded from specialty websites targeted toward over- or underweight women. As in our prior study, we eliminated photos which were blurry or small, photos with animals or displays of

wealth, photos in which emotionally salient objects such as guns, snakes or motorcycles were visible, photos with subjects in provocative sexual positions or with nudity and photos in which the subjects appeared to be younger than 18 years old. All full body images clearly depicted the face of the individual in addition to the body of the individual from at least the waist up. Additionally, full body images were cropped to minimize photographic background and were not a standard size.

Full body images fell into one of four weight categories, ranging from extremely underweight to overweight. There were 60 images in each category, for a total of 240 full body images.

All images were balanced for luminance in Matlab.

MONETARY CHOICE TASK

We used an adjusting procedure in a monetary choice task to determine the reward value of seeing these same images for each group of participants (described previously in Hayden et al., 2007). Participants chose between maximizing a cash payout and sacrificing cash for the opportunity to view each image. Participants were given a choice between a constant value target and a target whose value varied across blocks of trials. Choice of the constant target was followed by presentation of a gray square and the sound of coins dispensed from a slot machine for 500 ms. Choice of the variable target was followed by presentation of a photo (image category was changed in 60 trial superblocks) and of the sound of coins for 300, 500, or 700 ms (duration was changed in 20 trial blocks). Participants were instructed that the duration of the coin dispensing sound corresponded to the amount of money they had earned on that trial, with longer sounds corresponding to larger payoffs. The exact relationship between monetary value and sound was not explicitly reported to the participant before the experiment and the difference in payout between each of the three sound durations was equivalent to about one US cent ($0.01). Cumulative money earned and the amount earned for the previously run block was reported to each participant after every block. Compensation for participation in the experiment consisted of the amount earned in this portion of the experiment plus a base hourly rate and was rounded up to the nearest dollar, which resulted in all participants earning the same amount regardless of performance.

Analysis of choices was performed as described previously (Hayden et al., 2007) using Matlab (Mathworks, Natick, MA, USA) and Statistica 6.0 (Statsoft, Tulsa, OK, USA). Briefly, the point of subjective equivalence (PSE) between the constant target and the variable target was calculated by fitting the choice frequencies at each payout level to a cumulative normal function. These fits were performed for each participant and each image category separately. The sign-reversed PSE represents the theoretical monetary compensation required to induce indifference (50% choice probability) between the two options in the choice task. If the displayed images of other individuals have no impact on the reinforcing value of the variable target, then the PSE is 0. A PSE greater than zero indicates that the image set added reinforcing value to the monetary value of the variable target, whereas PSEs significantly less than zero indicate that the image set subtracted reinforcing value from the monetary value associated with the variable target.

IMAGE RATING TASK

Participants were asked to explicitly rate the attractiveness of female face images and the attractiveness and estimated body weight of female full body images on a 9-point Likert scale. Face images were validated in a previous study to be very attractive or very unattractive (Smith et al., 2010).

EYE-TRACKING

We probed whether AN-WR and CON females differed in how they visually inspected the images. In a passive viewing task, participants observed each image for 5 s while the position of the eye was monitored with a ViewPoint® infrared eyetracker at a sample rate of 30 Hz (Arrington Research Inc, Scottsdale, AZ, USA). Image presentation, eye position, and region of interest (ROI) selection were all performed using ViewPoint® 2.8.4 Software (Arrington Research Inc, Scottsdale, AZ, USA) on a Dell desktop (Precision 530 model WHL). The stimuli were displayed on a 1680 × 1050 pixel monitor (Acer AL2216W) that was positioned 44 cm from the participant's eye. In order to reduce task demands, 10 images from each category were presented, for a total of 60 images. The eye tracker was calibrated for each participant using a 9-point fixation routine prior to each viewing session. Gaze position was calculated using ViewPoint's proprietary non-linear algorithm based on the dark pupil method. Participants were instructed to hold their heads as still as possible and to keep their chin and forehead pressed against a head stabilizing chin rest (Headspot, University of Houston College of Optometry, Houston, TX, USA). Before each image presentation, participants fixated on a central point and pressed a button that performed a slip correction (re-centering the calibration grid on the origin). Eye-tracking was performed in two sessions consisting of 30 trials each, with a break taken in the middle to prevent fatigue.

Analysis of the eye-tracking data was performed using Matlab (Mathworks, Natick, MA, USA) and Statistica 6.0 (Statsoft, Tulsa, OK, USA, USA). ROIs were defined by rectangles overlaid on each image. For face pictures, the ROIs were the eyes and mouth, and for the body pictures, the ROIs were the face and body. Eye positions were scored as falling either inside or outside each ROI, with the relevant measure being the percentage of valid samples per trial that fell within each ROI. Eye movement velocity was calculated for each sample by determining the difference between the current and last calculated gaze points. Eye velocity threshold for fixation was determined as follows: Investigators (K. K. Watson and D. M. Werling) used a simplified point fixation protocol, similar to the calibration routine, to gather eyedata in ViewPoint for a series of fixations and saccades. Data were imported into Matlab and eye velocity was plotted. Saccades and fixations were easily distinguishable in this format, and an eye velocity threshold was determined that would separate fixations from saccade. The set threshold of 0.15 (arbitrary Viewpoint distance units) was very close to ViewPoint's default saccade velocity detection threshold of 0.10. Sample velocities that fell below these thresholds were categorized as fixations. The number and placement of fixations, but not of saccades, were analyzed.

For illustration, we plotted a heatmap of eye positions on an example (**Figure 3**) by calculating the x-y coordinates of the first 145 valid eye samples for that image for each participant. For each group, the number of times any sample fell within a given pixel on

the image was averaged across all participants. The resulting two-dimensional histogram was then filtered with a symmetric two-dimensional Gaussian low pass filter with a mean of 100 pixels and standard deviation of 20 pixels. The resulting heatmap was rendered partially transparent and exported into image processing software (Canvas X, ACD Systems, Miami, FL, USA), where it was overlaid onto the image. Warmer colors indicate higher eye position sample counts (and, hence, a greater amount of looking time).

RESULTS

We found that control and AN-WR participants did not differ in their explicit ratings of attractiveness [repeated measures ANOVA, $F(1,21) = 1.5$, $p = 0.238$], and that both groups discriminated between the high- and low-attractiveness face image groups in their ratings [$F(1, 21) = 313.0$, $p < 0.001$; **Figure 1**].

When participants were asked to rate the weights of the full body images, AN-WR participants' weight estimates were significantly heavier than those of control participants for all categories [repeated measures ANOVA, $F(1,21) = 15.1$, $p < 0.01$], consistent with previous reports (Tovee et al., 2000). Both control and AN-WR participants rated the weight of body images as a function of weight class [$F(3,63) = 385.34$, $p < 0.001$; see **Figure S1** in Supplementary Material].

When asked to explicitly rate the attractiveness of each full body image, neither control nor AN-WR participants scaled their assigned ratings with observed body weight. Both control and AN-WR participants rated images of slender-bodied women (within normal limits – thin, WNL-T) as significantly more attractive than those in overweight and underweight image categories (repeated measures ANOVA with *post hoc* LSD *t*-test, $p < 0.001$; **Figure 2**). Thus, overall AN-WR and control females were remarkably similar in their explicit ratings of attractiveness and showed similar bias in relating attractiveness to body weight.

Despite the similarity in explicit ratings of attractiveness between the two study groups, the reward value of body images varied monotonically with body weight for AN-WR females (*t*-test of individual subject *R*-values against zero: $t = 7.08$, df = 10, $p < 0.0001$; Group correlation of body weights against cash value $R = -0.33$, $p = 0.03$; **Figure 2** and **Figure S2** in Supplementary Material) whereas the reward value of body images was uninfluenced by weight for CON females (*t*-test of individual subject *R*-values against zero: $t = -1.52$, df = 10, $p = 0.16$; Group correlation of body weights against cash value $R = 0.14$, $p = 0.36$; **Figure 2** and **Figure S2** in Supplementary Material). It might be argued that differential valuation of bodies by their weight in AN-WR is to be expected given their strong preoccupation with body weight. Despite this effect, we found patterns of differential valuation present even in absence of direct body weight information: the reward value of faces was significantly less for AN-WR females than for CON females [repeated measures ANOVA, $F(1,22) = 4.41$, $p = 0.048$]. Control females consistently sacrificed money to see faces but AN-WR females did not (*t*-test of means against zero: controls, $t = -2.76$, df = 10, $p = 0.02$; AN-WR, $t = 1.04$, df = 10, $p = 0.32$; **Figure 1**).

Together, these data imply diminished reward value for faces and concomitant enhancement in reward value for emaciated and thin bodies in AN-WR. We tested these ideas directly using eye-tracking.
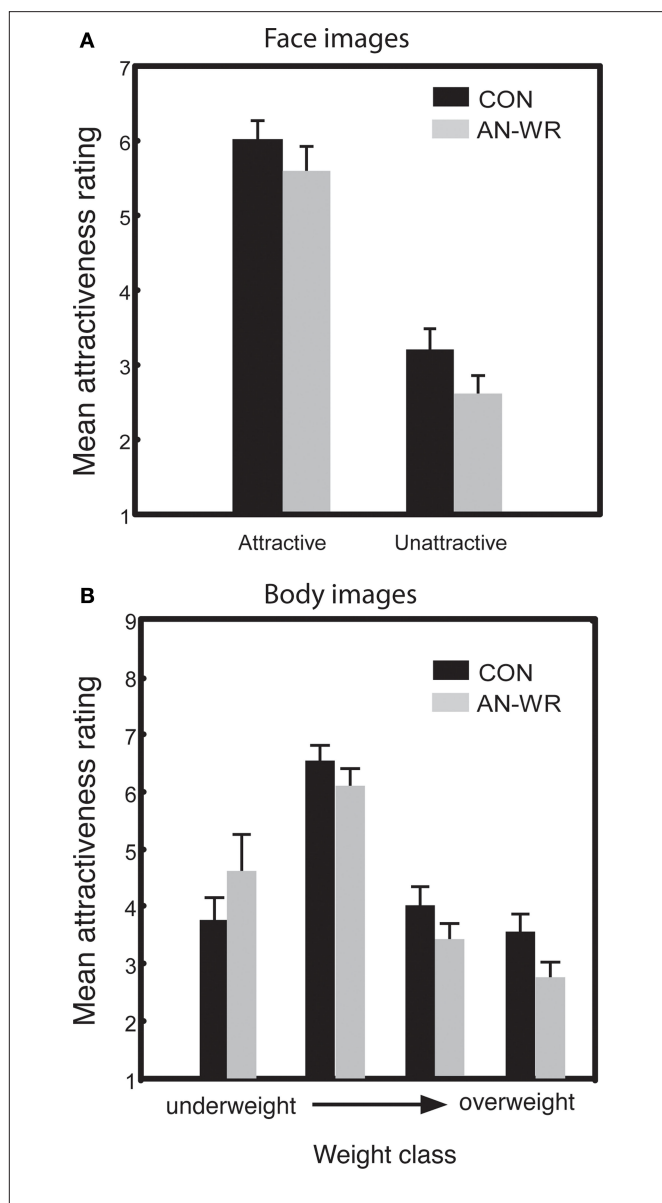
FIGURE 1 | Explicit judgments of attractiveness in anorexia nervosa. (A) Control (CON, black) participants and weight-restored participants with anorexia nervosa (AN-WR, gray) did not differ when asked to rate images of female faces for attractiveness. Canonical "attractive" images were rated higher than "unattractive" images for both groups. **(B)** Both CON and AN-WR participants rated images of slender-bodied women as significantly more attractive than images of either very overweight or very underweight individuals.
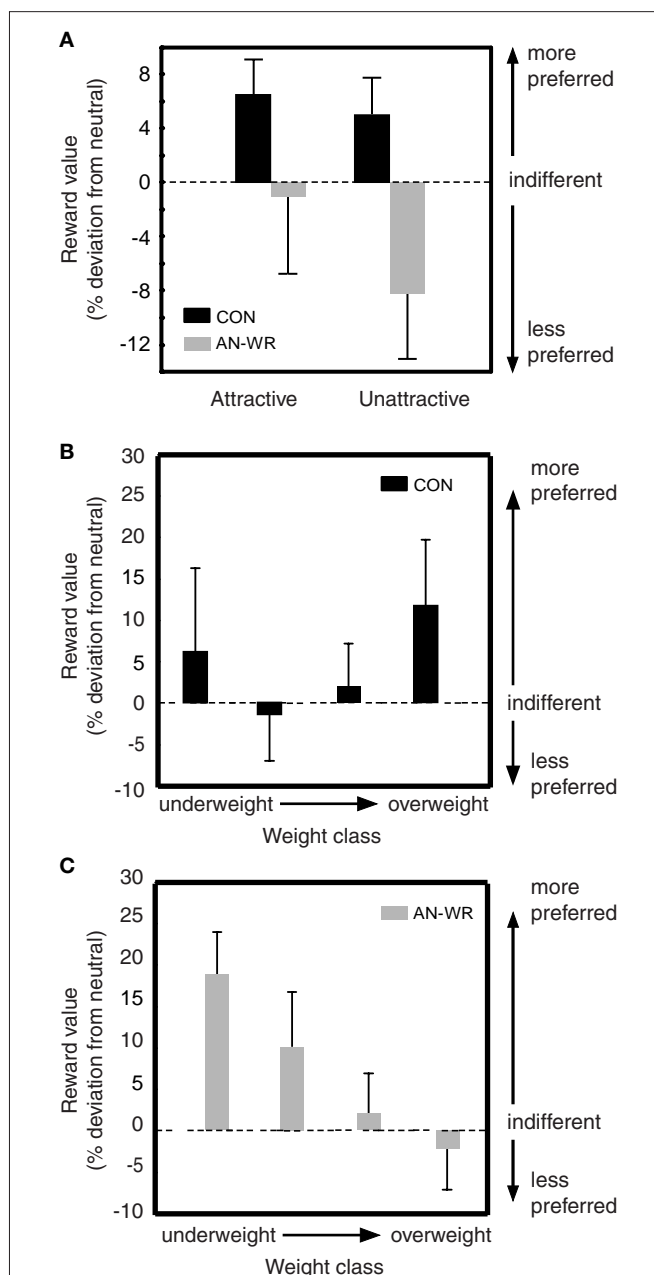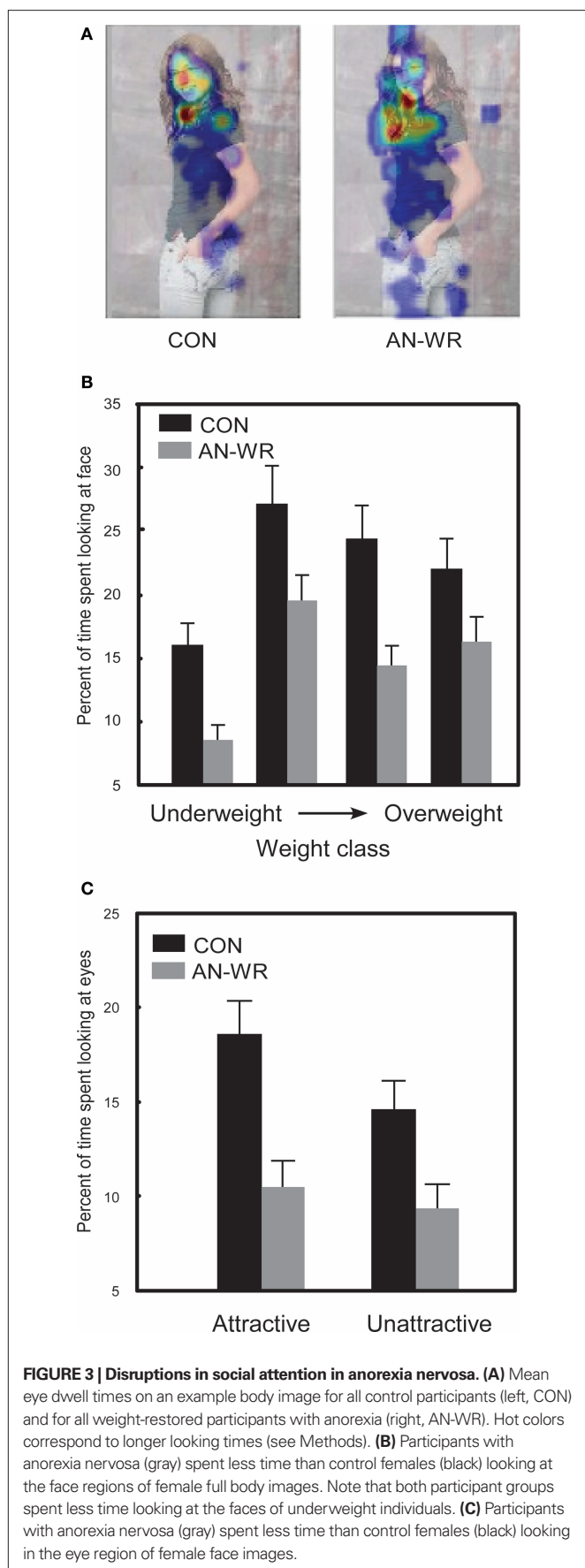

FIGURE 2 | Disruptions in social reward value in anorexia nervosa. (A) In an econometric choice task, control participants (CON, black) paid significantly more than participants with anorexia nervosa (AN-WR, gray) to view both attractive and unattractive face images. **(B)** When given the opportunity to view full body images in the context of the econometric choice task, control participants were indifferent to the weight of the depicted individual. **(C)** In contrast, the amount participants with anorexia nervosa paid to display full body images scaled with the weight of the depicted individual.

When freely viewing the same sets of images, AN-WR females were less likely than control females to look at faces of females when the body was present in the image [factorial ANOVA, main effect for subject group, $F(1,948) = 33.00$, $p < 0.001$, **Figure 2**]. Both AN-WR and control females looked at the faces of extremely thin females to a lesser degree than they looked at the faces of other image classes [factorial ANOVA, main effect for image class, $F(3,948) = 9.56$, $p < 0.001$; Fisher t-test, df = 948, $p < 0.01$]. There was no significant interaction between subject group and image class ($p > 0.75$).

Moreover, when faces alone were presented, AN-WR females spent significantly less time looking in the eye region than did controls [factorial ANOVA, main effect for subject group, $F(1,476) = 18.20$, $p = 0.00002$]. Similar avoidance of the eyes has been reported in ASD (Pelphrey et al., 2002; Dalton et al., 2005), schizophrenia (Gordon et al., 1992), and social anxiety (Horley et al., 2003), and is thought to reflect heightened vigilance to social threat (Ochsner, 2004).

FIGURE 3 | Disruptions in social attention in anorexia nervosa. (A) Mean eye dwell times on an example body image for all control participants (left, CON) and for all weight-restored participants with anorexia (right, AN-WR). Hot colors correspond to longer looking times (see Methods). **(B)** Participants with anorexia nervosa (gray) spent less time than control females (black) looking at the face regions of female full body images. Note that both participant groups spent less time looking at the faces of underweight individuals. **(C)** Participants with anorexia nervosa (gray) spent less time than control females (black) looking in the eye region of female face images.

DISCUSSION

We found that weight-restored females with anorexia differ from otherwise healthy females in implicit measures of social reward despite showing intact cognitive appraisal of physical attractiveness. Specifically, we found that neurotypical females (i.e., those who have never had an eating disorder) implicitly find the faces of other females rewarding, but AN-WR females do not. This result implies that faces elicit approach behavior for neurotypical women but not for AN-WR women, similar to the deficits in social approach and orienting found in ASD, schizophrenia, and social anxiety disorders (Gordon et al., 1992; Pelphrey et al., 2002; Horley et al., 2003; Dalton et al., 2005). This conclusion is further supported by our eye-tracking data showing that neurotypical females direct gaze to the eyes and face, but that women with AN-WR avoid the eyes and hyperscan the body. Thus, while control women will pay to see face images and are drawn to salient social stimuli in a free viewing context, AN-WR women are indifferent to face images and avoid viewing the eyes and faces of others.

Furthermore, for neurotypical females bodies are neither attractive or repulsive as a function of their weight. By contrast, emaciated bodies are highly rewarding for AN-WR females to look at, but overweight bodies are not. We note that this pattern of implicit reward value differs from the explicit ratings of attractiveness, in which both AN-WR and CON explicitly report the underweight body images as being less attractive than body images depicting a healthy body weight. Thus, although the term "attractiveness" implies that the viewer is drawn toward the object, the deviation of explicit ratings from implicit reward value measures derived from our econometric choice task endorses the latter as a better measure of approach behavior and underlying motivation. Our results are consistent with a prior finding of heightened implicit negative valuation of overweight bodies in subjects with AN relative to control subjects using an affective priming task (Cserjesi et al., 2010).

Our data support further study of the differences in social perception and reward circuitry in AN and are consistent with published identifying reward circuitry differences in AN. For example, symptom provocation in AN is associated with heightened activation in medial prefrontal regions, including the medial orbitofrontal cortex and anterior cingulate cortex, which are known to be integral in reward processing (Uher et al., 2004). Another study indicates that individuals weight-restored from AN show altered related activity in response to monetary reward, which suggests a deficit in general reward processing in AN (Wagner et al., 2007). These studies are complementary to the results reported here and suggest that deficits associated with AN are observable across many modalities of reward, not just food.

Patterns of visually guided attention reported in this study, specifically avoidance of the eyes, mirrors similar gaze behavior in ASD and other social disorders (Zucker et al., 2007) in which the typical tendency to attend to the eyes of others is diminished (Klin et al., 2002). Disrupted social attention may underlie some of the more complex social deficits found in ASD, including difficulties deciphering the emotions and intentions of others (Baron-Cohen et al., 1997; Adolphs et al., 2001; Pelphrey et al., 2002). Our data demonstrate that individuals with AN actively avoid the eyes of faces, thus depriving them of a rich source of social information (Walkersmith et al., 1977; Emery, 2000; Henderson et al., 2005). Consistent with these

findings, prior reports indicate that women with AN have difficulty maintaining eye contact with an interviewer (Cipolli et al., 1989) and reading emotions in faces (Kucharska-Pietura et al., 2004).

These observations suggest the hypothesis that both differences in social motivation and visual orienting may contribute to impaired interpersonal function in AN, as in ASD and other social disorders (Adolphs et al., 2001; Pelphrey et al., 2002). It is possible that our results may be explained by comorbidity of a variety of pathologies with AN, as we did not screen our subjects for disorders other than AN. This is especially relevant given that a subgroup of individuals with AN also suffers from ASD (Gillberg and Billstedt, 2000). Future studies should examine the possibility that the alterations in social reward and attentional processing in AN reported here are driven by secondary pathology. Regardless, understanding and treating AN will benefit from further psychological, neural, and genetic comparisons with other disorders – such as ASD, schizophrenia, and social anxiety – characterized by social dysfunction.

A prior study found women with AN score higher than healthy controls on a self-report measure of autistic traits (Hambrook et al., 2008). Through use of the novel choice task and eye-tracking, the latter of which is widely used to characterize variations in social attention in ASD, our results complement prior findings without relying on self-report measures. Measuring social cognitive abilities via self-report is potentially problematic due to a patients' lack of insight regarding social competence, as well as high demand characteristics. Moreover, unlike a prior study that reports reduced eye contact in individuals with AN (Cipolli et al., 1989), our tasks do not rely on subjective scoring and can therefore be implemented in a consistent fashion across laboratories and clinics. Such consistency is crucial for the adaptation of that technique for diagnostic and therapeutic purposes.

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Conflict of Interest Statement: The authors declare that the research was con-ducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

SUPPLEMENTARY MATERIAL

FIGURE S1 | Control subjects (CON, orange) and weight-restored individuals with anorexia (AN-WR, green), show no difference in relative weight estimation between the four image categories when asked to rate images for body weight on a 9-point Likert scale (repeated measures ANOVA, subject group membership X image weight class; interaction term $F = 0.42$, $p = 0.157$). However, there were significant main effects of subject group membership ($F = 15.3$, $p = 0.001$) and image category ($F = 409.8$, $p = 0$). AN-WR subjects assigned significantly higher weight ratings across all image categories. Bars depict means + SEM.

FIGURE S2 | Whereas there is no significant correlation between the body weight of the depicted image and the amount CON subjects will pay to see that image (left), the amount AN-WR subjects will pay in order to see a body image is inversely related to the weight of the depicted image (right). Each data point in the plots above corresponds to a single image weight category for a single subject; hence, there are four data points per subject. Weight rating indicates the mean weight rating assigned to images in that image category as reported by the subject. PSE (point of subjective equality) is the payout subjects will relinquish at a point of equal choice frequency between the image and non-image options (see Methods for details). Units are in US cents.