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Same, same but different - Attention bias for food cues in adults and adolescents with Anorexia Nervosa

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International Journal of Eating Disorders
Title: Same, same but different - Attention bias for food cues in adults and adolescents with Anorexia Nervosa

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Abstract

Objective: Attention processing for food may be biased in people with Anorexia Nervosa (AN). However previous studies have had inconsistent results. This is likely to be due to indirect assessment of attention, which does not inform on the underlying attention processes, and/or the heterogeneity of participants across studies, testing either adults or adolescents with AN, i.e. people at very different developmental and illness stages.

Method: Eye-tracking was employed as a direct assessment of attention during a visual probe task with food versus non-food pictures. Attention bias for food was measured in 39 adults and 34 adolescents with AN and in 53 adults and 31 adolescents without AN.

Results: All participants had a direction bias for food, specifically for high-calorie food. However, adults with AN subsequently avoided maintaining attention on food versus non-food cues, compared to adults without AN. Adolescents with or without AN demonstrated increased attention maintenance on food versus non-food cues, and, contrary to our hypothesis, did not differ in their attention bias for food cues. Accordingly, adults with AN differed significantly from adolescents with AN in attention maintenance for food cues: whilst adolescents with AN showed significantly increased attention maintenance on food stimuli, adults avoided maintaining attention on food cues.

Discussion: Adults with AN may apply attention strategies to facilitate restrictive eating. This strategy is absent in adolescents with AN. This difference in food-related attention bias between adolescents and adults with AN suggests that attention biases develop over time as the illness progresses.

Words: 245

Keywords: anorexia nervosa, attention bias, eye-tracking, food, visual probe
Anorexia Nervosa (AN) is a life-threatening eating disorder (ED), characterised by persistent
restrictive eating and/or other pathological weight loss behaviours (American Psychiatric
Association, 2013), often driven by intense fear of weight gain, food and eating (Murray,
Loeb, & Le Grange, 2016; Steinglass et al., 2012; Steinglass et al., 2011). Whilst in
adolescents with AN, who typically have a short illness duration, treatment outcomes are
excellentmoderate, in adults with a more established form of the illness, outcomes are much
poorer (Brockmeyer, Friederich, & Schmidt, 2017; Schmidt et al., 2016). Thus, novel
treatments which target illness mechanisms contributing to AN pathology and its
maintenance, are needed (Brockmeyer et al., 2017; Murray, Treanor, et al., 2016; Schmidt &
Campbell, 2013).

Cognitive models of AN posit a crucial role of biased attention processes for food-
related information in the development and maintenance of restrictive eating behaviour
(Vitousek & Hollon, 1990; Williamson, White, York-Crowne, & Steward, 2004). Attention
bias for food is defined by aberrant processing of food relative to non-food cues (Faunce,
2002; Williamson et al., 2004). Theoretically, people with AN may show pathological
approach or avoidance attention patterns towards food. Food- and eating related information
may be processed preferentially (i.e. attentional approach), due to either hunger or worry
about intake, or both (Werthmann, Jansen, & Roefs, 2015). Alternatively, processing of food
cues may be avoided (i.e. attentional avoidance) to facilitate restrictive eating (Nijs &
Franken, 2012; Werthmann et al., 2015). To complicate matters, these processes may be
similar or different in early (i.e. orienting) versus late (i.e. maintenance) phases of attention
(Field et al., 2016; Field, Munafò, & Franken, 2009).

Several studies have tested attention for food cues in AN, with mixed findings
(Brooks, Prince, Stahl, Campbell, & Treasure, 2011; Giel, Teufel, et al., 2011). Meta-
analyses suggest that compared to controls, individuals with AN have a food-Stroop based
attention bias with a small effect size (Brooks et al., 2011; Dobson & Dozois, 2004; Faunce, 2002). The Stroop interference effect can be interpreted as an indicator of the strength of attention bias, however, the Stroop paradigm cannot distinguish between specific (approach or avoidance) attention processes. Other studies have applied different paradigms that indirectly (i.e. based on response latencies) assess attention processes, again with inconclusive results (see for reviews, e.g. Giel, Teufel, et al., 2011; Werthmann et al., 2015). In contrast, eye-tracking is a direct measure of overt visual attention and therefore is more informative when studying attention allocation processes (Field et al., 2009), including bias for food cues (Werthmann et al., 2015). So far, to our knowledge, only one previous study used eye-tracking in participants with AN (Giel, Friederich, et al., 2011). Results showed that adults with AN did not differ in early orienting towards food versus non-food pictures from both-fasted and non-fasted healthy controls. However, participants with AN had significantly reduced attention maintenance on food pictures, indicative of attentional avoidance of food cues, compared to healthy controls. This observation suggests an approach-avoidance attention pattern, which may be interpreted in terms of a vigilance-avoidance anxiety reaction (Mogg, Bradley, Miles, & Dixon, 2004) or in terms of motivational ambivalence towards food (Field, et al. 2016).

Thus, inconsistent results may be attributed to the diverse assessment of attention. Another potential reason for the inconsistency of previous results may be that studies differed in whether they tested adolescents or adults with AN. As the peak age of onset of AN is from age 15 to 19 (Micali, Hagberg, Petersen, & Treasure, 2013), studies with adolescent samples predominantly consist of patients with early stage illness of short duration, whereas adult samples will typically consist of patients with a more long-lasting form of the illness. Across different psychiatric disorders it has been recognised that with increasing duration, the illness becomes more entrenched and difficult to change. This is proposed to arise from
‘neuroprogression’, i.e. neurobiological changes that alter the trajectory of illness (Gama, Kunz, Magalhães, & Kapczinski, 2013; Moylan, Maes, Wray, & Berk, 2013). In EDs, converging neuroimaging and cognitive neuroscience data support this idea (Berner & Marsh, 2014; O’Hara, Campbell, & Schmidt, 2015; Steinglass & Walsh, 2016).

So far, only a handful of studies have specifically focused on cognitive and neural processes in adolescents versus adults with AN. A study using a category learning task with corrective feedback found that whilst adolescents and adults with AN were able to learn the task equally well, after a rule change, the adults (but not the adolescents) performed significantly worse than control participants, i.e. displayed greater cognitive rigidity (Shott et al., 2012). Functional neuroimaging studies comparing adolescents and adults with AN reported significant differences in neural processing of food and affective stimuli in adolescents compared to adults in AN (Horndasch, Roesch, et al., 2018) and also in neural processing of body image stimuli (Fladung, Scholze, Schöll, Bauer, & Grön, 2013) in adolescents compared to adults in AN. Similarly, differences in late positive potentials (LLP) as measured during event-related electroencephalography, emerged between adolescents and adults with AN when viewing pictures of bodies (Horndasch, Kratz, et al., 2018). Taken together these findings suggest that AN behaviours may be much more malleable during the early stages of illness.

**Aim and hypotheses**

It is unclear how attention biases in AN develop and whether they remain stable or change over the course of illness. Accordingly, to test if attention bias differs across age (and illness duration), this study compares attention bias for food cues in adult versus adolescent patients with AN and their respective non-ED counterparts using a visual probe task with concurrent eye-tracking and response latency assessment.
We hypothesised an “approach-avoidance” pattern of attention bias for food cues in AN participants, but not controls, in line with previous findings by Giel and colleagues (Giel, Friederich, et al., 2011). This pattern would be manifested in heightened attention capture (direction bias), followed by reduced attention maintenance (duration bias) on food versus non-food cues in participants with AN compared to participants without AN. We further aimed to explore if pathological attention patterns are similar different in adolescents versus adults with AN.

Key characteristics of AN severity, such as ED symptoms, weight suppression and duration of illness were expected to be significantly positively related to attention bias scores (i.e. greater severity would be related to higher bias scores) (e.g., Veenstra & de Jong, 2012), whereas the relation of body mass index (BMI) remained to be explored, as theoretically, a higher BMI (as a sign of lower severity) may be related to either reduced (less bias) as well as increased (more vigilance) bias scores (Jessica Werthmann, Jansen, & Roefs, 2015).

Method

Participants

The study comprised a convenience sample of participants recruited for a study on attention bias manipulation (participants with AN and adolescents without AN) and a study evaluating the test-retest reliability of attention bias within a healthy sample of adults (Van Ens, Schmidt, Campbell, Roefs, & Werthmann, in prep.). These studies involved the same experimental procedure using a visual probe paradigm to assess food-related attention bias at the Centre for Neuroimaging Sciences, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. Testing took place between April 2015 and April 2017.

Within this timeframe, community-dwelling 39 adults with Anorexia Nervosa AN and 34 adolescents with Anorexia Nervosa AN were recruited from Eating Disorder Services of the South London and Maudsley NHS Foundation Trust. Adults with AN were also
recruited via web-advertisements. Inclusion criteria for AN patients were a DSM-5 diagnosis of Anorexia Nervosa and additionally, for adults with AN a BMI below 18.5 kg/m² because the adults with AN subsequently participated in a study that required this inclusion criterion.

Exclusion criteria were a dose of psychotropic medication that had not been stable for 14 days prior to testing, a major psychiatric disorder needing treatment in its own right, acute suicide risk, life-threatening AN, requiring inpatient treatment, learning or developmental impairments and/or severe comorbid medical conditions or alcohol and drug-abuse disorders.

Most (63%) participants with AN were currently in psychological treatment and adolescents with AN did not differ from adults with AN in this regard \[X^2(2, N = 73) = .95, p = .62\].

As comparison group of 61 adults and 35 adolescents without current or past ED diagnoses were recruited. Eye-tracking data of eight adult controls needed to be excluded (see data reduction section), leaving a final sample of 53 adults without EDs. Four adolescent controls were excluded because of a family or personal history of AN \((n = 2)\) or because eye-tracking data were not recorded due to technical problems \((n = 2)\), leaving a final sample of 31 adolescents without AN.

**Materials**

**Visual probe task.** This was used to assess spatial attention for food. During this task, two pictures are presented side by side on the computer screen, followed by a probe, either replacing the left or the right picture. Participants are instructed to indicate the position of the probe by pressing a corresponding key on the keyboard. This task presumes that participants will react faster to the probe replacing the picture that captured their attention than to probes presented on the opposing screen side. Response latencies were assessed as an indirect measure of attention. In addition, concurrent eye-tracking served as a direct measure of attention. A recent study indicated good internal consistency and test-retest reliability of this paradigm (Van Ens et al., in prep.).
**Trial types.** The task consisted of 120 trials in total; with 80 critical and 40 filler trials. Two blocks with 40 critical trials and 20 filler trials each were presented, separated by a brief break. Filler trials showed pairs of non-food items and were used to disguise the purpose of the task. In critical trials food items were paired with non-food items. In one block, high-calorie foods were displayed during critical trials, in the other block low-calorie foods were shown in critical trials. Block order was counterbalanced across participants.

**Trial procedure.** A fixation cross was presented until participants fixated on it for 100ms. Then the picture pairs were presented for 3000ms followed by the presentation of the probe. The position of (food and non-food) pictures and the position of the probe was counterbalanced. Accordingly, the probe replaced equally often food (i.e., congruent trials) and non-food items (i.e., incongruent trials). Trial order was randomised individually per participant.

**Stimuli.** In each block, ten pictures either depicting palatable high-calorie or low-calorie foods paired with non-food items (e.g., musical instruments) were presented, see Figure 1. All picture pairs were matched as closely as possible on visual aspects, such as lightening, brightness, complexity. Each picture pair was presented four times. For filler trials, ten pictures sets depicting two neutral non-food items pairs were presented four times in total. Half of these were presented only in the first block and the other half only in the second block. Picture pairs were selected from a larger picture pair pool piloted within a group of women without eating disorders and were the same as used in a previous study by our group (Van Ens et al., in prep.).

<Insert Figure 1 about here>

**Assessment of attention.** Attention bias was assessed based on recordings of response latencies and eye-movements during critical trials of the visual probe task. To calculate response latency bias scores, correct response latencies were during critical trials were
analysed (i.e. data from error trials and filler trials were discarded, see Field, Mogg, Zetteler, & Bradley, 2004). Response latency bias was calculated, per participant for high-calorie images, low-calorie images and food pictures in general separately, by subtracting the mean response latency in congruent from the mean response latency in incongruent trials. A positive bias score is interpreted as attentional approach towards food and a negative score suggests attentional avoidance.

To calculate attention bias scores based on eye-tracking, eye-movements were recorded by a desktop mounted EyeLink 1000 system (SR Research Ltd., Mississauga, Ontario, Canada). Prior to recording, a 9-point calibration with subsequent validation procedure was executed. Direction and duration bias scores were calculated per participant for low-calorie food, high-calorie food and as an overall score for food images. Direction bias reflects early attention allocation whereas duration bias represents a measure of sustained attention allocation (Field, Mogg, & Bradley, 2004; Werthmann, Jansen, Vreugdenhil, et al., 2015).

*Direction bias.* To calculate direction bias scores, a percentage score indicating the proportion of trials in which initial fixations landed on food cues relative to all trials in which initial fixations towards either cue were made (Castellanos et al., 2009; Werthmann, Vreugdenhil, Jansen, et al., 2015). A score above 50% suggests early attention approach towards food cues, whereas a score below 50% is indicative of early attention avoidance of food cues (Castellanos et al., 2009; Werthmann, Jansen, Vreugdenhil, et al., 2015).

*Duration bias.* This was calculated by subtracting the average total dwell time in ms on non-food stimuli from the average total dwell time in ms on food stimuli (Field, Mogg, & Bradley, 2004; Werthmann, Vreugdenhil, Jansen, et al., 2015). A positive score suggests sustained attentional approach and a negative score indicates sustained attentional avoidance of food cues.
Questionnaires

Eating Disorder Examination Questionnaire – Short Version. This 12-item self-report questionnaire (EDE-QS; Fairburn & Beglin, 1994; Gideon et al., 2016) assesses ED symptom severity (e.g. weight and shape concerns, restrictive eating behaviour) over the last seven days on a four-point Likert scale, from zero (0 days/ not at all) to three (6-7 days/markedly) (Gideon et al., 2016). Higher scores indicate more severe ED symptoms. The internal consistency was high in our study [\( \alpha = 0.93 \)].

Weight suppression. Weight suppression has been defined as the difference between an individual’s current weight and highest past weight (Berner, Shaw, Witt, & Lowe, 2013; Witt et al., 2014). Weight suppression is a significant predictor of ED pathology, treatment response and weight gain in AN (Berner et al., 2013; Witt et al., 2014). To assess weight suppression, participants current weight was subtracted from their highest weight (excluding pregnancy) at their current height (see Witt et al., 2014).

Hunger. This was rated on a seven-point Likert scale ranging from 0 (not hungry at all) to 6 (extremely hungry), completed by participants, when they entered the laboratory.

Demographic information. All participants provided sociodemographic and clinical information.

Procedure

Ethical approval was obtained from the National Health Research Authority (IRAS number 160749) and the local research ethics committee of King’s College London (HR-14/15-0878). Participants received verbal and written descriptions of the study and informed consent was obtained. After screening, eligible participants were invited to the experimental session. To create standardised instructions for attention assessment (e.g. Werthmann et al., 2013), participants were asked not to eat or drink anything except water two hours prior to testing. Upon entering the eye-tracking laboratory, participants indicated their current subjective
hunger. Then attention bias was assessed with the visual probe task. Participants continued with their respective experimental procedures, for approximately a further 20 - 45 minutes. At the end of the session, participants were asked to complete the EDE-Q, provided demographic information, participants with AN were asked to provide additional information about their illness duration and current treatment, and participants’ height and weight was measured to calculate BMI.

Data reduction

For details see online appendix 1. For eye-tracking biases, participants’ gaze fixation were analysed, which were defined as any period that was not a blink or saccade and lasted at least 100ms (Eyelink Dataviewer User’s Manual, 2002-2008, SR Research Ltd.). Eye movements were extracted using Data Viewer (SR Research Ltd., Mississauga, Ontario, Canada). To further analyse fixation data, three interest areas were created (see Werthmann, Jansen, Vreugdenhil, et al., 2015). Following standard procedures, eye movements were discarded if they occurred in filler trials, in the mid area of the screen, and before the presentation of an image pair (i.e. anticipatory fixations, see Christiansen, Mansfield, Duckworth, Field, & Jones, 2015; Werthmann, Jansen, Vreugdenhil, et al., 2015). Participants were excluded from analyses if they were identified as “starers”, meaning that they did not make any eye-movements in more than half of all critical trials (Bradley et al., 2003). Eight adult participants without AN were removed from the analysis on this basis.

Response latency data were trimmed following standard procedures (Christiansen et al., 2015; Werthmann et al., 2013). Response latencies were discarded if they were faster than 200ms, slower than 2000ms, and then if they deviated more than 3 SDs from each participant’s mean (see Christiansen et al., 2015; Field et al., 2004). According to this procedure, 2.1-2.6% of data were discarded in the different participant groups.

Analyses
Based on our theory-driven hypotheses comparing if attention bias indices differ between a.) adults with versus adults without AN, b.) adolescents with versus adolescents without AN and c.) adults with versus adolescents without AN. To test if attention biases differ between groups of participants, independent t-tests were conducted. One sample t-tests were used to test if an attention bias for food within each group was observed. For direction bias, this is tested against the value of 50 (as a score of 50% indicates an equal attention distribution towards food versus non-food cues, that is no attention bias). For duration bias and response latency bias, this is tested against 0 (as a score of 0 indicates an equal attention distribution towards food versus non-food cues, that is no attention bias). To explore if attention bias indices are associated with key characteristics of AN severity, correlation analyses were applied.

**Results**

**Group characteristics**

A univariate analysis of variance (ANOVA) revealed some differences on baseline measures between participant groups: As expected, participants with AN had a significantly lower BMI and reported significantly higher ED symptom levels than participants without AN. In general, adult participants were significantly older than adolescent participants. Adolescents with or without AN did not differ in age, however adults with AN were slightly older than adults without AN. Age was therefore included as covariate in subsequent analyses comparing adults with and without AN. Groups differed with regard to self-reported hunger. Therefore, hunger was added as covariate in subsequent analyses. For description of baseline characteristics, see Table 1.  

<Insert Table 1 about here>

**Direction bias**
Comparison of adolescents with and without AN. Adolescents with AN did not differ from adolescents without AN in initial orientation towards food cues in general \([t(63) = 0.97, p = 0.34]\), nor towards high-calorie foods \([t(63) = 0.98, p = 0.32]\), or low-calorie foods \([t(63) = 0.54, p = 0.59]\), see Figure 2. Both groups directed their initial gaze significantly more often towards food cues in general \([t(30) = 2.43, p = 0.02] \) and \([t(33) = 3.37, p = 0.002]\); in adolescents without and with AN, respectively, and specifically towards high-calorie foods \([t(30) = 4.1, p < 0.001]\) and \([t(33) = 4.55, p < 0.001]\) for adolescents without AN and with AN respectively; but not low-calorie foods \([ts < 0.8, ps > 0.42]\) in both samples.

Comparison of adults with and without AN. Adults with AN did not differ from adults without AN in their initial orientation towards foods \([t(90) = 1.69, p = 0.095]\), see Figure 2. When controlling statistically for baseline differences in age between adults with and without AN (by entering age as covariate in the analysis), the difference in attention bias in initial orientation became significant \([F(1,89) = 4.57, p = 0.035]\). After entering hunger as covariate, to control for differences in hunger at baseline, results remained the same. A one-sample t-test against 50 (signifying no bias) showed that adults with AN oriented significantly more often towards food cues in general \([t(38) = 4.2, p < 0.001]\), and towards high-calorie foods \([t(38) = 4.85, p < 0.001]\), but not low-calorie foods \([t(38) = 0.17, p = 0.87]\). Adults without AN initially oriented only more often towards high-calorie foods \([t(52) = 2.74, p = 0.008]\).
**Duration bias**

**Comparison of adolescents with and without AN.** Adolescents with AN did not differ statistically from adolescents without AN in their gaze duration on food versus non-food cues in general \([-t(63) = 0.74, p = 0.46]\), or for high-calorie foods \([t(63) = 0.78, p = 0.44]\), see Figure 2, or low-calorie foods \([t(63) = 0.49, p = 0.63]\). Both groups looked significantly longer at food cues in general \([t(30) = 2.51, p = 0.018]\) and \([t(33) = 2.69, p = 0.011]\) for adolescents without and adolescents with AN, respectively; and specifically longer at high-calorie food \([t(30) = 3.04, p < 0.01]\) and \([t(33) = 2.49, p = 0.018]\) for adolescents without and adolescents with AN respectively. A significant bias towards low-calorie food was exclusively observed in adolescents with AN \([t(33) = 2.13, p = 0.04]\).

**Comparison of adults with and without AN.** Adults with AN differed significantly from adults without AN in their duration bias for food in general \([t(90) = 2.46, p = 0.016]\), and specifically for high-calorie foods \([-t(90) = 2.7574, p = 0.0071]\), see Figure 2, but not for low-calorie foods \([t(90) = 1.12, p = 0.26]\). Adults without AN showed a significant bias towards food cues in general \([t(52) = 2.71, p = 0.009]\), and towards high-calorie \([t(52) = 2.64, p = 0.011]\), as well as low-calorie foods \([t(52) = 2.28, p = 0.027]\). This bias was absent in adults with AN \([all ts < 1.4, all ps > 0.16]\). The negative bias scores observed on duration bias for high-calorie foods in adults with AN compared to adults without AN suggest attentional avoidance of high-calorie food in adults with AN.

**Response latency bias**

**Comparison of adolescents with and without AN.** No significant differences in response latency bias were observed between adolescents with and without AN, all \([ts(63) < 0.19, all ps > 0.85]\). Neither adolescents with nor adolescents without AN showed significant food-related bias on response latencies bias scores as indicted by a one-sampled t-test against 0 \([all ts < 1.32, all ps > 0.20]\).
Comparison of adults with and without AN. Adults with AN did not differ from adults without AN on response latency bias scores \[\text{all } ts < 0.46, \text{ all } ps > 0.65\]. Results of a one-sampled t-test against 0 (signifying no response latency bias) showed that adults with AN did not show an increased response latency bias towards foods \[\text{all } ts < 1.40, \text{ all } ps > 0.17\]. However, adults without AN did show significantly increased response latency bias for high-calorie foods \[t(52) = 2.20, p = 0.032\], yet not for foods in general or low-calorie foods \[\text{all } ts < 1.6, \text{ all } ps > 0.11\].

Comparison of attention bias indices in adults and adolescents with AN.

Adolescents with AN did not differ from adults with AN on direction bias indices for foods in general \[t(71) = 0.42, p = 0.68\], for high-calorie foods \[t(73) = 0.66, p = 0.51\], and for low-calorie foods \[t(73) = 0.10, p = 0.92\]. However, a significant difference between adults and adolescents with AN emerged regarding their duration bias for food cues in general \[t(71) = 2.64, p = 0.01\], see Figure 2. Whereas adolescents with AN had positive bias scores, indicative of attentional approach, adults with AN had negative bias scores, indicative of attentional avoidance and this difference was most pronounced for high-calorie foods \[t(71) = 2.74, p = 0.008\]. No significant differences emerged with regard to duration bias for low-calorie foods \[t(71) = 1.31, p = 0.19\]. Comparisons based on response latency bias scores yielded no significant differences between groups \[\text{all } ts < .55, \text{ all } ps > 0.58\].

Influence of baseline differences in hunger

For details please refer to online appendix 2.

Correlation analyses

Indices of AN severity and attention bias for food. Pearson correlations were conducted for symptom severity (i.e. EDE-QS scores), illness duration (i.e. years since onset of AN), BMI and weight suppression with direction bias indices (general, high-calorie, low-
calorie), duration bias indices (general, high-calorie, low-calorie) and response latency bias indices (general, high-calorie, low-calorie) within participants with AN. Results yielded significant positive correlations of weight suppression with all bias indices [all $rs(59) > .300$, all $ps < .05$]. No other severity measure correlated significantly with attention bias indices.

Post-hoc exploratory correlation analyses revealed that in adolescents with AN, weight suppression correlated highly with all attention bias indices [$r(21)$ ranging from .51 to .80, all $ps < .05$], and illness duration also correlated moderately to highly with direction bias indices [$r(27)$ range between .53 and .77 with all $ps < .01$], duration bias in general [$r(27) = .43$, $p = .02$], and duration bias for low-calorie foods specifically [$r(27) = .59$, $p < .01$]. BMI correlated moderately positively with direction bias [$r(33) = .40$, $p < .05$] and direction bias for low-calorie food [$r(33) = .41$, $p < .05$]. In contrast, post-hoc correlations in adults with AN, revealed that BMI correlated moderately negatively with direction bias in general [$r(39) = -.35$, $p < .05$], and with direction bias for high-calorie foods [$r(39) = -.42$, $p < .01$]. Note that the reported correlations were not Bonferroni corrected. After applying Bonferroni correction only the correlations of direction bias (general and high-calorie foods) with illness duration and weight suppression and direction bias, duration bias (general and low-calorie foods) remained significant at $p < 0.015$ within the sample of adolescents with AN, see Table 2.

<Insert Table 2 about here>

**Discussion**

The aim of this research was to study attention bias for food in AN, by employing eye-tracking and response latency assessments during a visual-probe paradigm in adults and adolescents with AN compared to their respective non-ED counterparts.

Initial orientation was biased towards food in all participants, specifically when high-calorie food was presented. However, differences in attention bias emerged when duration
bias (i.e. an index for maintained attention) was studied. In adults with AN the hypothesized
approach-avoidance pattern of attention was found: Following increased orientation towards
food, adults with AN showed reduced attention maintenance on food versus non-food cues,
whereas adults without AN maintained attention on food. Contrary to our expectations,
adolescents with AN and adolescents without AN also showed significantly increased
attention maintenance on food cues, particularly on high-calorie foods.

The approach-avoidance attention bias observed in adults with AN replicates earlier
results (Giel, Friederich, et al., 2011), demonstrating pathological food-related attention
patterns in adults with AN. Adults with AN may use attention processes as an implicit
cognitive strategy to vigilantly screen their environment for “threatening” food cues and
avoid looking at foods to resist potential food temptation, thus, and facilitating restrictive
eating (Giel, Friederich, et al., 2011; Jessica Werthmann, Jansen, & Roefs, 2015; Williamson
et al., 2004). Our findings add to previous research demonstrating that when hungry, AN
patients display weaker activation of the right visual occipital cortex than healthy controls
(Santel, Baving, Krauel, Münte, & Rotte, 2006) and observations of hypoconnectivity in
circuitry responsible for modulating responses to food cues in people with AN (Scaife,
Godier, Reinecke, Harmer, & Park, 2016). Importantly, our findings in adults with AN
provide important insights into cognitive mechanisms underlying restrictive eating behaviour
and highlight the potential of “brain-directed” treatments targeting cognitive processes in AN
directly (e.g., Schmidt & Campbell, 2013).

Contrary to our expectations, adolescents with AN did not demonstrate the same
pathological attention pattern as adults with AN and did not differ in their food-related
attention biases from adolescents without AN. The observation that all adolescents displayed
biased attention towards foods in early and late attention phases corroborates previous
research demonstrating increased attention approach towards foods in adolescents with AN
(Neimeijer, Roefs, & de Jong, 2017) and non-clinical groups (Werthmann, Jansen, Vreugdenhil, et al., 2015; Werthmann et al., 2013). The finding that cognitive processes for disorder-relevant cues are less disturbed in adolescents versus adults with AN is also in line with previous research showing differential patterns of cognitive biases in adults versus adolescents with AN (Horndasch, Kratz, et al., 2018; Horndasch, Roesch, et al., 2018). Potentially this finding is good news, suggesting that cognitive processes may still be malleable in early phases of illness (Gama et al., 2013; Moylan et al., 2013; Treasure, Stein, & Maguire, 2015). However, our correlational findings in adolescents with AN, showing moderate to high correlations between indices of AN severity and attention bias scores may highlight the critical role of attention bias in the development and maintenance of persistent, maladaptive eating behaviour in AN pathology.

Overall, several limitations should be noted: satiety was not experimentally controlled, however, the potential influence of self-reported hunger was accounted for in analyses. The potential influence of circadian rhythm was not taken into account, as participants were tested at various time points. Participants with AN varied in whether or not they were currently receiving treatment, however, adults with AN did not differ from adolescents with AN with regard to treatment enrolment. The long stimulus presentation time (3000ms) may have contributed to null findings regarding the response latency attention bias index, because several shifts in attention may have taken place, which may have made response latency bias assessment unreliable. Note that a replication in larger samples is warranted to increase the statistical power of observed results.

More broadly, our results are consistent with the idea of neuroprogression, suggesting that over the course of illness, cognitive and neural processes change in a way that aid the habitual use of maladaptive cognitions and behaviour (Foerde, Steinglass, Shohamy, &
Walsh, 2015; O’Hara et al., 2015). Accordingly, future research should strive to elucidate the role of attention mechanisms for pathological eating behaviour over course of illness in AN.
References


3 https://doi.org/10.3389/fnbeh.2014.00395


5 https://doi.org/10.1037/a0033930


9 https://doi.org/10.1016/j.cpr.2010.09.006


reliability of the alcohol-related visual probe task is increased by utilising personalised stimuli and eye-tracking. Drug Alcohol Depend, 155, 170–174. https://doi.org/10.1016/j.drugalcdep.2015.07.672


RUNNING HEAD: Attention bias for food in Anorexia Nervosa

1 https://doi.org/10.1037/hea0000405
2 Fladung, A. K., Schulze, U. M. E., Schöll, F., Bauer, K., & Grön, G. (2013). Role of the
3 ventral striatum in developing anorexia nervosa. *Translational Psychiatry.*
4 https://doi.org/10.1038/tp.2013.88
6 supporting maladaptive food choices in anorexia nervosa. *Nature Neuroscience.*
7 https://doi.org/10.1038/nn.4136
8 Gama, C. S., Kunz, M., Magalhães, P. V. S., & Kapczinski, F. (2013). Staging and
9 neuroprogression in bipolar disorder: A systematic review of the literature. *Revista
10 Brasileira de Psiquiatria.* https://doi.org/10.1016/j.rbp.2012.09.001
12 Development and psychometric validation of the EDE-QS, a 12 item short form of the
14 https://doi.org/10.1371/journal.pone.0152744
16 Attentional processing of food pictures in individuals with anorexia nervosa - An eye-
18 https://doi.org/10.1016/j.biopsych.2010.09.047
20 Processing of pictorial food stimuli in patients with eating disorders-A systematic
22 https://doi.org/10.1002/eat.20785
23 Horndasch, S., Kratz, O., Van Doren, J., Graap, H., Kramer, R., Moll, G. H., & Heinrich, H.
24 (2018). Cue reactivity towards bodies in anorexia nervosa - Common and differential
RUNNING HEAD: Attention bias for food in Anorexia Nervosa

1. https://doi.org/10.1017/S0033291717001994
3. https://doi.org/http://dx.doi.org/10.1371/journal.pone.0191059
RUNNING HEAD: Attention bias for food in Anorexia Nervosa

1 https://doi.org/10.1007/s13679-012-0011-1
3 nervosa: A focussed narrative review of the neurological and psychophysiological
4 literature. *Neuroscience and Biobehavioral Reviews.*
5 https://doi.org/10.1016/j.neubiorev.2015.02.012
7 anorexia nervosa: fMRI during cognitive processing of food pictures. *Brain Research,*
10 activation of the frontal pole to high vs low calorie foods: The neural basis of food
12 https://doi.org/10.1016/j.pscychresns.2016.10.004
13 Schmidt, U., Adan, R., Böhm, I., Campbell, I. C., Dingemans, A., Ehrlich, S., … Zipfel, S.
17 https://doi.org/10.1002/erv.2257
20 Disorders Review.* https://doi.org/10.1002/erv.2172
22 (2012). Fear of food as a treatment target: exposure and response prevention for
23 anorexia nervosa in an open series. *Int J Eat Disord,* 45(4), 615–621.
25 (2011). Rationale for the application of exposure and response prevention to the
treatment of anorexia nervosa. *Int J Eat Disord, 44*(2), 134–141.


https://doi.org/10.1016/j.eatbeh.2013.06.005


Figure legend

Figure 1. Examples of critical picture pairs with high-calorie food (left panel) and low-calorie food (right panel) used in the visual probe task.

Figure 2. Graphical presentation of mean bias scores with standard errors for direction bias for high-calorie food cues (in %, upper panel) and duration bias for high-calorie food cues (in ms, lower panel), respectively. Graphs are presented separately for comparisons between adolescents with and without AN (column A), adults with and without AN (column B) and adults and adolescents with AN (column C).
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adults (n = 39)</th>
<th>Adolescents (n = 34)</th>
<th>Adults (n = 53)</th>
<th>Adolescents (n = 31)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Age</td>
<td>29.66&lt;sup&gt;a&lt;/sup&gt;&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10.00</td>
<td>15.53&lt;sup&gt;a&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.46</td>
<td>25.96&lt;sup&gt;a&lt;/sup&gt;&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body mass index</td>
<td>15.97&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
<td>1.50</td>
<td>17.12&lt;sup&gt;c&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.34</td>
<td>21.73&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Subjective hunger&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1.59&lt;sup&gt;a&lt;/sup&gt;&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.59</td>
<td>0.68&lt;sup&gt;c&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.32</td>
<td>3.08&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;d&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>EDE - QS total score&lt;sup&gt;4&lt;/sup&gt;</td>
<td>20.33&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
<td>7.15</td>
<td>18.12&lt;sup&gt;c&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
<td>5.71</td>
<td>2.53&lt;sup&gt;b&lt;/sup&gt;&lt;sup&gt;d&lt;/sup&gt;&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Years since onset of ED&lt;sup&gt;5&lt;/sup&gt;</td>
<td>12.72&lt;sup&gt;a&lt;/sup&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
<td>9.95</td>
<td>1.34&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.96</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics of adult and adolescent participants with and without AN.

Note. <sup>M</sup> = Mean; <sup>SD</sup> = Standard deviation.

<sup>a</sup> Significant difference between adults vs. adolescents with AN; <sup>b</sup> significant difference between adults with vs. adults without AN; <sup>c</sup> significant difference between adolescents with vs. adolescents without AN; <sup>d</sup> significant difference between adults vs. adolescents without AN; <sup>e</sup> significant difference between adults with vs. adolescents without AN; <sup>f</sup> significant difference between adolescents with vs. adults without AN.

<sup>†</sup>Subjective hunger was scored on a seven-point Likert scale ranging from 0 (not hungry at all) to 6 (extremely hungry); <sup>‡</sup>EDE - QS =, Eating disorder examination questionnaire - short version (Gideon et al., 2016); <sup>§</sup>ED =, Eating disorder; <sup>¶</sup>Degrees of freedom were adjusted to F(1, 64) due to smaller sample size of subgroup comparison.
<table>
<thead>
<tr>
<th>AN Sample (n = 73)</th>
<th>Bias Index</th>
<th>Years since onset of AN †</th>
<th>Body mass index ‡</th>
<th>EDE-QS §</th>
<th>Weight suppression ¶</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adolescents (n = 34)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direction bias</td>
<td>.774**</td>
<td>.403*</td>
<td>-.127</td>
<td>.666**</td>
<td></td>
</tr>
<tr>
<td>HC-Direction bias</td>
<td>.710**</td>
<td>.257</td>
<td>-.131</td>
<td>.546*</td>
<td></td>
</tr>
<tr>
<td>LC-Direction bias</td>
<td>.529**</td>
<td>.412*</td>
<td>.065</td>
<td>.510*</td>
<td></td>
</tr>
<tr>
<td>Duration bias</td>
<td>.434*</td>
<td>.230</td>
<td>-.041</td>
<td>.801**</td>
<td></td>
</tr>
<tr>
<td>HC-Duration bias</td>
<td>.240</td>
<td>.131</td>
<td>-.110</td>
<td>.644**</td>
<td></td>
</tr>
<tr>
<td>LC-Direction bias</td>
<td>.591**</td>
<td>.314</td>
<td>.087</td>
<td>.730**</td>
<td></td>
</tr>
<tr>
<td><strong>Adults (n = 39)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direction bias</td>
<td>.019</td>
<td>-.346*</td>
<td>-.115</td>
<td>.195</td>
<td></td>
</tr>
<tr>
<td>HC-Direction bias</td>
<td>-.051</td>
<td>-.422**</td>
<td>-.091</td>
<td>.171</td>
<td></td>
</tr>
<tr>
<td>LC-Direction bias</td>
<td>.091</td>
<td>.10</td>
<td>.061</td>
<td>.075</td>
<td></td>
</tr>
<tr>
<td>Duration bias</td>
<td>-.074</td>
<td>-.278</td>
<td>-.179</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>HC-Duration bias</td>
<td>-.030</td>
<td>-.310</td>
<td>-.106</td>
<td>.152</td>
<td></td>
</tr>
<tr>
<td>LC-Direction bias</td>
<td>-.127</td>
<td>-.069</td>
<td>-.238</td>
<td>.306</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Post-hoc correlation analyses of attention bias indices and measures of Anorexia Nervosa severity, conducted separately for adolescents with AN and adults with AN.

*Note. HC = high-calorie; LC = low-calorie; due to missing data, analyses could not be performed on the complete sample as specified † based on n = 27 in adolescent sample, ‡ based on n = 33 in adolescent sample, § EDE-QS = Eating disorder examination questionnaire - short version, ¶ based on n = 21 in adolescents sample.

*p - value < .05, **p - value < .01, correlations printed in bold refer to correlation that would remain significant after applying Bonferroni corrections for multiple testing.
Figure 1. Examples of critical picture pairs with high-calorie food (left panel) and low-calorie food (right panel) used in the visual probe task.

297x209mm (300 x 300 DPI)
Figure 2. Graphical presentation of mean bias scores with standard errors for direction bias for high-calorie food cues (in %, upper panel) and duration bias for high-calorie food cues (in ms, lower panel), respectively. Graphs are presented separately for comparisons between adolescents with and without AN (column A), adults with and without AN (column B) and adults and adolescents with AN (column C).
Online Supplementary File - Appendix 1

Data Reduction

For eye-tracking biases, participants’ gaze fixation were analysed, which were defined as any period that was not a blink or saccade and lasted at least 100ms (Eyelink Dataviewer User’s Manual, 2002-2008, SR Research Ltd.). Eye movements were extracted using Data Viewer (SR Research Ltd., Mississauga, Ontario, Canada). To further analyse fixation data, three interest areas were created (see Werthmann, Jansen, Vreugdenhil, et al., 2015). Following standard procedures, eye movements were discarded if they occurred in filler trials, in the mid area of the screen, and before the presentation of an image pair (i.e. anticipatory fixations, see Christiansen, Mansfield, Duckworth, Field, & Jones, 2015; Werthmann, Jansen, Vreugdenhil, et al., 2015). Participants were excluded from analyses if they were identified as “starers”, meaning that they did not make any eye-movements in more than half of all critical trials (Bradley et al., 2003). Eight adult participants without AN were removed from the analysis on this basis.

Response latency data were trimmed following standard procedures (Christiansen et al., 2015; Werthmann et al., 2013). Response latencies were discarded if they were faster than 200ms, slower than 2000ms, and then if they deviated more than 3 SDs from each participant’s mean (see Christiansen et al., 2015; Field et al., 2004). According to this procedure, 2.1-2.6% of data were discarded in the different participant groups.
Online Supplementary File - Appendix 2

**Influence of baseline differences in hunger**

When controlling statistically for baseline differences in hunger between all groups (see Table 1 for specific differences between groups), all results reported on comparisons of attention bias indices between groups remained largely the same. Entering hunger as covariate did not influence any result in a statistically meaningful way.
Response to reviewers

Reviewer: 1

Page 4, line 4: As the DSM-5 does not include the fear of weight gain as a compulsory criterion anymore and due to the discussion and empirical findings on the non-fat-phobic type of AN, the sentence should be modified. **Reply:** Thank you for pointing out that not all AN patients necessarily have a fear of food. We have adjusted the sentence accordingly. It now reads: “Anorexia Nervosa (AN) is a life-threatening eating disorder (ED), characterised by persistent restrictive eating and/or other pathological weight loss behaviours (American Psychiatric Association, 2013), often driven by intense fear of weight gain, food and eating (Murray, Loeb, & Le Grange, 2016; Steinglass et al., 2012; Steinglass et al., 2011).”

Page 6, line 4: Please correct the last part of the sentence “So far, only a handful of studies have specifically focused on cognitive and neural processes in adolescents versus adults AN”. **Reply:** We have adjusted the sentence, it now reads: “So far, only a handful of studies have specifically focused on cognitive and neural processes in adolescents versus adults with AN.”

Page 6, line 21: The authors write that they hypothesized an “approach-avoidance” pattern of attention bias for food cues. Therefore, I would recommend to describe the approach-avoidance theory as well as corresponding empirical findings in the introduction section in more detail. **Reply:** Due to the word limit and the request of the reviewers to add a limitation section, we were not able to discuss the background of approach-avoidance responses at length. However, we included a sentence referring to approach-avoidance attention patterns observed in previous research. We now state (on page 4, lines 14-16): “This observation suggests an approach-avoidance attention pattern, which may be interpreted in terms of a vigilance-avoidance anxiety reaction (Mogg & Bradley, 2006) or in terms of motivational ambivalence towards food (Field, et al. 2016).”

Page 7, line 2: The authors write that “We further aimed to explore if pathological attention patterns are similar in adolescents versus adults with AN.” However, the authors use statistical tests that are adequate to test for differences. Either, the sentence should be slightly rephrased, focusing on differences (which I would recommend) or the statistical procedures need to be adopted. **Reply:** Thank you. We have adjusted the hypothesis accordingly, it now reads “We further aimed to explore if pathological attention patterns are different in adolescents versus adults with AN.”

Page 7, line 18: Please correct the sentence “Within this timeframe, community –dwelling 39 adults with Anorexia Nervosa and 34 adolescents with Anorexia Nervosa were recruited from Eating Disorder Services of the South London and Maudsley NHS Foundation Trust.” **Reply:** We have simplified this sentence into: “Within this timeframe, 39 adults with Anorexia Nervosa and 34 adolescents with Anorexia Nervosa were recruited from Eating Disorder Services of the South London and Maudsley NHS Foundation Trust.”

Page 7, line 22: Please give reasons why for adults with AN, a BMI below 18.5 kg/m2 was used as an inclusion criterion. **Reply:** The sample of this study comprised a convenience sample, see also page 6 lines 14-21 “The study comprised a convenience sample of participants recruited for a study on attention bias manipulation (participants with AN and adolescents without AN) and a study evaluating the test-retest reliability of attention bias within a healthy sample of adults (Van Ens, Schmidt, Campbell, Roefs, & Werthmann, in prep.). These studies involved the same experimental procedure using a visual probe
paradigm to assess food-related attention bias. Testing took place between April 2015 and April 2017.” Accordingly, the study including adults with AN had slightly different inclusion criteria to the study including adolescents with AN. Following your suggestion, we have now included this information in the participant section: “Inclusion criteria for AN patients were a DSM-5 diagnosis of Anorexia Nervosa and additionally, for adults with AN a BMI below 18.5 kg/m², because the adults with AN subsequently participated in a study that required this inclusion criterion.”

Page 9, line 4: Please correct the sentence “As comparison group of 61 adults and 35 adolescents without current or past ED diagnoses were recruited.” Reply: We have corrected this sentence as requested: “A comparison group of 61 adults and 35 adolescents without current or past ED diagnoses was recruited.”

Page 11, line 11: It might be helpful for the reader to explain in more detail how the duration bias was operationalized and calculated as a measure of attention shift (related to the approach-avoidance theory). Reply: The approach-avoidance pattern previously observed in attention processes does not rely on one bias measure, but on a combined response of increased early orientation (= approach) as measured by direction bias, followed by diminished attention maintenance (= avoidance) as measured by duration bias. In response to the reviewer’s comment, we have included a corresponding sentence in the hypotheses section to clarify. This now reads (page 6, lines 1-4): This pattern would be manifested in heightened attention capture (direction bias), followed by reduced attention maintenance (duration bias) on food versus non-food cues in participants with AN compared to participants without AN.

Page 11, line 15: Please provide Cronbach’s Alpha of the questionnaires used in the present study. Reply: We computed Cronbach’s Alpha for the EDE-QS, as this was the single questionnaire, we reported for the purpose of this study. Accordingly, we now state: “The internal consistency was high in our study [α = 0.93].”

Page 7 and page 18: Please delete the given name from the reference (Jessica Werthmann, Jansen, & Roefs, 2015). Reply: We have corrected the reference accordingly.

Page 14, line 8: Please specify how groups differed with regard to self-reported hunger. Reply: As can be deduced from our Table 1, which summarizes group characteristics, the groups differed significantly on self-reported hunger on a scale running from 0 to 6, with adolescents with AN being the least hungry (Mean = .068), whereas adults with AN and adolescents without AN reported similar hunger levels (Means around 1.6 to 1.8, respectively) and adults without AN were moderately hungry (Mean = 3.08). Accordingly, we added hunger as co-variate to our analyses, see page 12, lines 21-22. However, entering hunger as co-variate did not influence results in a meaningful way. To clarify this additional analysis, we added a corresponding paragraph to the online supplementary materials (Appendix 2), stating:

“ Influence of baseline differences in hunger.
When controlling statistically for baseline differences in hunger between all groups (see Table 1 for specific differences between groups), all results reported on comparisons of attention bias indices between groups remained largely the same. Entering hunger as covariate did not influence any result in a statistically meaningful way.”

Additionally, also in response to a comment of reviewer 2, we have revised our Table 1 in an effort to simplify the visual presentation of group differences by using different letters as superscript signaling significant difference between groups.

Influence of baseline differences in hunger.
When controlling statistically for baseline differences in hunger between all groups (see Table 1 for specific differences between groups), all results reported on comparisons of attention bias indices between groups remained largely the same. Entering hunger as covariate did not influence any result in a statistically meaningful way.”

Additionally, also in response to a comment of reviewer 2, we have revised our Table 1 in an effort to simplify the visual presentation of group differences by using different letters as superscript signaling significant difference between groups.
Page 18: Please be more specific and explain what is meant by “important insights”. Reply: To reduce the length of the paper we have decided to delete this sentence.

Page 19: Please specify what is meant by “critical role” (“highlight the critical role of attention bias in the development and maintenance persistent, maladaptive eating behaviour in AN pathology”). Do the authors have any ideas concerning the specific mechanisms? Reply: We have tried to formulate this sentence tentatively by stating “our correlational findings in adolescents...may highlight the critical role of attention bias...”. With this statement, we aimed to emphasize the striking finding that attention bias indices were related to severity indices in adolescents (but not in adults). A potential explanation for this finding may be that during early stages of AN, attention processes may be (more or less) consciously employed to facilitate restrictive eating behaviour (Williamson et al., 1999; Giel et al., 2011; Werthmann, Jansen and Roefs, 2015). However, after a certain “chronicity” threshold is reached, these processes may have become so habitual, that the association between attention bias and other severity indices becomes meaningless. However, as this is highly speculative, we urge for further research on this matter and have not included these (currently empirically largely unfounded) speculations in our discussion section.

Finally, I would recommend the authors to provide a limitations section. Reply: In accordance with the suggestion of all reviewers we have included a limitation section: “Overall, several limitations should be noted: satiety was not experimentally controlled, however, the potential influence of self-reported hunger was accounted for in analyses. The potential influence of circadian rhythm was not taken into account, as participants were tested at various time points. Participants with AN varied in whether or not they were currently receiving treatment, however, adults with AN did not differ from adolescents with AN with regard to treatment enrolment. The long stimulus presentation time (3000ms) may have contributed to null findings regarding the response latency attention bias index, because several shifts in attention may have taken place, which may have made response latency bias assessment unreliable. Note that a replication in larger samples is warranted to increase the statistical power of observed results.”

Page 29: Please check the graphical quality of the figure. Reply: We have worked on improving the graphical quality of both figures.

Reviewer: 2

Comments to the Author
The article describes an experimental study including adolescent and adult participants with and without anorexia nervosa. The study aim is to investigate attentional engagement and maintenance towards high- and low-caloric food stimuli using a dot-probe paradigm and eye tracking. Attentional bias in anorexia nervosa has been investigated, but former results are ambiguous, wherefore the study at hand asks an important and up-to-date question in eating disorder research. The methodology of the study is sound and the article is well-written and clear. There are only some minor points the authors may address before the article should be published:

-In general: take care of spelling: e.g. picture sets and item pairs on page 9, lines 7-8 and in the description of Figure 1. There are some more orthographical errors the authors should try to fix before publication. Page 8, lines 4-6: the first sentence seems to need rephrasing. In the next sentence, 53 adults should be plural. Reply: Thank you. We have corrected our spelling mistakes accordingly.
Page 4, line 5: The authors state in the introduction that in “adolescents with AN treatment outcomes are excellent”, which does not totally reflect the results stated in the review by Brockmeyer et al., 2017 with 17.5 to 50% recovery. The authors should consider using a more tentative wording here. Reply: We have adjusted our sentence accordingly and it now reads: "Whilst in adolescents with AN, who typically have a short illness duration, treatment outcomes are moderate, in adults with a more established form of the illness, outcomes are much poorer (Brockmeyer, Friederich, & Schmidt, 2017; Schmidt et al., 2016).”

Page 8, task description: it would be helpful to have a short description of the meaning of critical versus filler trials, i.e. what was shown in each of these trial types. Reply: We have inserted a short description of critical versus filler trials: “Trial types. The task consisted of 120 trials in total; with 80 critical and 40 filler trials. Two blocks with 40 critical trials and 20 filler trials each were presented, separated by a brief break. Filler trials showed pairs of non-food items and were used to disguise the purpose of the task. In critical trials food items were paired with non-food items. In one block, high-calorie foods were displayed during critical trials, in the other block low-calorie foods were shown in critical trials.”

Data analysis: the authors calculated independent t-tests for hypothesis testing, which leads to the question how they controlled for multiple comparisons. Another possibility would have been to do an ANOVA with factors age, group and food type, or MANOVA including the different outcome types. What were the considerations leading to this type of analyses, i.e. multiple t-tests? Reply: We appreciate the opportunity to explain our reasoning in our choice of data analyses. We decided for a hypotheses-driven data analysis approach, which led us to conduct nine t-test because according to our hypotheses we aimed to compare: A) adults with and without AN on three different (not necessarily related) attention bias indices, B) adolescents with and without AN on these same three indices and C) adults and adolescents with AN on these three indices. We formulated these theory-based hypotheses prior to our analytic approach. An ANOVA comparing all groups would mean that we would automatically compare adults with AN with adolescents without AN and adolescents with AN with adults without AN and adults and adolescents without AN. This multiple comparison did not seem justified or meaningful considering the theoretical background and aims of the current study. Likewise we did not use a MANOVA, because, similar to the ANOVA model, several non-theory-driven tests would have automatically been conducted. While we agree in general with the importance of applying Bonferroni correction when applying multiple comparisons of the same construct within the same sample and in fact do so (e.g. when conducting multiple correlations, see Table 2), we did not apply Bonferroni corrections on our main hypotheses because this study constitutes a fairly exploratory study on this subject (i.e. it is the first study to compare adults and adolescents with AN on attention bias) and each hypothesis is based on a different “sample” comparison (as it would be normally done in separate studies), we therefore argue that applying Bonferroni in this context may not be a logical decision and may in fact increase the chance of a type 2 error and thus lead to falsely rejecting the null-hypothesis (Feise, 2002; Streiner & Norman, 2011). However, to acknowledge the concern about the multiple comparisons, we have included a corresponding statement in the limitations section of our paper (page 18, lines 11-20): “Note that replication in larger samples is warranted, to increase statistical power of observed results.” Of note, our main findings would remain trend-significant after applying Bonferroni corrections: the difference between adults with or without AN on duration bias for high-calorie food would remain trend-significant after applying Bonferroni correction for multiple testing (p-value = .007; adjusted alpha level = .0055) and, similarly, the difference between adolescents with AN and adults with AN would remain trend-significant (p-value = .008; adjusted alpha level
= .0055). We therefore see this rather as a power issue, as stated in the limitation section, see page 18. In addition, to accommodate the reviewer, we also performed a MANOVA with group (adults with AN, adults without AN, adolescents with AN, adolescents without AN) on all attention bias indices (nine variables) as dependent variables and found that group had a trend-significant influence in the overall multivariate analysis based on Pillai-Spur test statistics \[ F(24,444) = 1.439, p = .083, \text{ partial } \eta^2 = .07 \] and a significant influence of group specifically on duration bias in general \[ F(3,157) = 3.36, p = .02, \text{ partial } \eta^2 = .06 \] and on duration bias for high-calorie food \[ F(3,157) = 4.39, p = .005, \text{ partial } \eta^2 = .08 \].

-Group characteristics: was the EDE-QS-Score of participants with AN significantly different between age groups, i.e. were adult AN participants actually more ill? **Reply:** As can be derived from Table 1 presenting sample characteristics, adults and adolescents with AN did not differ statistically significant on symptom severity (measured by the EDE-QS), however, they differed significantly with regard to chronicity (illness duration). To simplify spotting significant group differences on characteristics at baseline, we have also revised our Table 1 in an effort to simplify the visual presentation of group differences by using different letters as superscript signaling significant difference between groups.

-Assessment of attention, duration bias: the measuring unit should be noted, as well in the text as in the graphics. **Reply:** We have adjusted our manuscript and graphics accordingly, see page 9, lines 19-21 and Figure 2.

-Post-hoc analyses: reading this paragraph, it does not directly become clear, what the reason was for doing these correlational analyses only in adolescents with AN. A short statement would be helpful to the reader to understand the thread. **Reply:** We conducted post-hoc correlation analyses in both, adolescents with AN and adults with AN separately, as stated in the corresponding paragraph on page 16. To highlight this, we have now changed the paragraph slightly: “Post-hoc exploratory correlation analyses revealed that in adolescents with AN, weight suppression correlated highly with all attention bias indices [r(21) ranging from .51 to .80, all ps <.05], and illness duration also correlated moderately to highly with direction bias indices [r(27) range between .53 and .77 with all ps <.01], duration bias in general [r(27) = .43, p = .02], and duration bias for low-calorie foods specifically [r(27) = .59, p < .01]. BMI correlated moderately positively with direction bias [r(33) = .40, p < .05] and direction bias for low-calorie food [r(33) = .41, p < .05]. In contrast, post-hoc correlations in adults with AN revealed that BMI correlated moderately negatively with direction bias in general [r(39) = -.35, p < .05], and with direction bias for high-calorie foods [r(39) = -.42, p < .01]. Note that the reported correlations were not Bonferroni corrected. After applying Bonferroni correction only the correlations of direction bias (general and high-calorie foods) with illness duration and weight suppression and direction bias, duration bias (general and low-calorie foods) remained significant at p < 0.001 within the sample of adolescents with AN.”

-The null results regarding response latencies may be due to the long picture presentation times and that participants changed their gaze various times during this interval. This issue should be taken up in the discussion section. **Reply:** We have included this notion in our limitation section (on page 18) as follows: “The long stimulus presentation time (3000ms) may have contributed to null findings regarding the response latency attention bias index, because several shifts in attention may have taken place, which may have made response latency bias assessment unreliable.”
Reviewer: 3

Comments to the Author
Although the authors examined a study with a sufficient sample of adolescent and adult AN patients with the respective control groups, there are some criticisms that should be considered. Especially since the authors themselves did not include a limitation section.

Major concerns:
1) The description of the survey does not clearly show whether the subjects were all examined at the same time of day. With regard to standardization, it would also have been better to give everyone a standardized breakfast before the examination. Reply: We have included these potential limitations in the Limitation Section. The Limitation Section now reads “Overall, several limitations should be noted: satiety was not experimentally controlled, however, the potential influence of self-reported hunger was accounted for in the analyses. The potential influence of circadian rhythm was not taken into account, as participants were tested at various time points.”
2) It was also not clearly described how long the respective patient group had been in treatment and what it looked like. Reply: We have added information on whether or not participants reported on being treatment “Most (63%) participants with AN were currently in psychological treatment and adolescents with AN did not differ from adults with AN in this regard [X^2(2, N = 73) = .95, p = .62]” (see page 7, ll 6-7), but were not able to provide information on which treatment exactly or treatment duration. To emphasize this shortcoming, we added to the Limitation section that “Participants with AN varied in whether or not they were currently receiving treatment, however, adults with AN did not differ from adolescents with AN with regard to treatment enrolment.”
3) The adolescent AN group is on average more than one BMI point heavier than the adult AN group. This raises not only the question of the duration of the disease as a central moderator of the disease, but also the severity of the disease. This aspect limits the conclusion and could only be partially corrected by a covariance analysis. This point should be clearly described in the Limitation Section. Reply: Results in Table 1 show that there was no statistically significant difference between adolescents with and adults with AN on BMI or symptom severity (based on the EDE-QS), in contrast, however, both groups differed significantly regarding their duration of illness (chronicity). We therefore feel reluctant to discuss whether the non-significant differences may have also impacted results.
4) I recommend to add a table with the relevant correlation coefficients. Reply: We have added a corresponding table, see Table 2 and see reference to Table 2 on page 16, lines 17-18.