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Understanding the reward system functioning in anorexia nervosa: Crucial role of physical activity

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ABSTRACT

Hyperactivity is a potential neurobiological marker and a core psychopathological trait in anorexia nervosa (AN). We investigated the processing of hyperactivity-related information in fifteen AN patients, 15 athletes and 15 non-athletes to examine if they represent disorder-related reward information using eye tracking. We assessed the extent of individually performed physical activity, mood, trait reward sensitivity and serum leptin levels. Results revealed a pronounced bias in overall attentional engagement toward stimuli associated with physical activity in patients and athletes as compared to non-athletes. In patients, relevant correlations were found: trait reward sensitivity and attentional orienting were strongly correlated and amount of physical activity correlated with attentional orienting and engagement. Compared to non-athletes, patients and athletes rated exercise stimuli as more pleasant. Findings suggest that exercise-related stimuli are perceived as rewarding by AN patients. Positive motivational valence of physical activity might contribute to disorder development and maintenance.

1. Introduction

Anorexia nervosa (AN) is a severe and disabling disorder (Arcelus, Mitchell, Wales, & Nielsen, 2011), at the core of which is sufferers' capacity to successfully restrict the generally rewarding experience of food intake. Research on reward system functioning in AN has largely endorsed the view that AN is characterized by a hypo-responsiveness of the reward system (Kaye, Fudge, & Paulus, 2009; Soussignan, Schaal, Rigaud, Royet, & Jiang, 2011; Wagner et al., 2007, 2008; Zink & Weinberger, 2010), which goes some way toward explaining these patients' capacity to successfully restrict the generally rewarding experience of food intake (Herbert et al., 2012). However, Fladung et al. (2010) have recently challenged this notion by demonstrating increased ventral striatal activity in AN patients in response to pictures of underweight females. Such stimuli are closely linked to starvation and seem to have rewarding properties for these patients (Fladung et al., 2010; Zink & Weinberger, 2010). This finding provides preliminary evidence for the positive motivational valence of disorder-specific stimuli possibly underlying the drive for self-starvation (Fladung et al., 2010; Zink & Weinberger, 2010).

Likewise, stimuli related to exercise and physical activity could represent disorder-related reward information. Physical hyperactivity is an ubiquitous symptom of AN (Shroff et al., 2006; Zipfel et al., 2013), with already the earliest descriptions of AN noting this puzzling phenomenon (Gull, 1874; Lasegue, 1873). This ranges from hours of excessive and strenuous exercise beyond the point of injury, through to lengthy walks, through to inability to sit down and relax and needing to be constantly on the go and fidgeting (Hebebrand et al., 2003). Recently, hyperactivity has been proposed as an important neurobiological marker of disorder development and progression (Kas, Kaye, Foulds Mathes, & Bulik, 2009). In view of this Hebebrand & Bulik, (2011), recommend that hyperactivity should be considered part of the core psychopathology of AN.

Nonetheless, there remains a surprising paucity of theoretical and empirical contributions on the nature, development and maintenance of hyperactivity in AN (Meyer, Taranis, Goodwin, & Haycraft, 2011). This is surprising as hyperactivity is a major barrier to recovery as it interferes with weight gain and has been found to predict relapse and chronicity in large long-term follow-up studies (Carter, Blackmore, Sutandar-Pinnock, & Woodside, 2004; Rigaud, Pennacchio, Bizeul, Reveillard, & Verges, 2011). As yet there are few

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treatment approaches available for AN in general (Zipfel et al., in press) and few approaches are available that target hyperactivity (Zunker, Mitchell, & Wonderlich, 2011).

While the interaction of hyperactivity and the psychopathology of AN has been well-documented, physical activity should not solely be understood as a compensatory behavior to influence weight and shape (Meyer et al., 2011). Physical activity has antidepressive and anxiolytic properties (Dishman et al., 2006) and it could be that AN patients engage in such activity to alleviate these symptoms (Davis & Woodside, 2002; Holtkamp, Hebebrand, & Herpertz-Dahlmann, 2004). Evolutionary approaches consider hyperactivity as an increased foraging strategy during food restriction (Fessler, 2002; Scheurink, Boersma, Nergardh, & Sodersten, 2010) – a theory which is underpinned by data from rodent models with animals showing severe hyperactivity during food restriction and unlimited access to a running wheel (Adan et al., 2011). A biophysiological model based on these animal data considers starvation-induced hypoleptinemia crucial for both the development and maintenance of hyperactivity (Hebebrand et al., 2003).

These approaches have in common that rewarding experiences are assumed to underpin or maintain hyperactivity in AN. This is remarkable in light of the current debate on a hypo-responsive reward system in AN. While especially evolutionary models have suggested physical activity as primary reinforcing (Scheurink et al., 2010), most approaches conceptualize it as secondary reinforcing, e.g. by alleviating weight concerns, negative affect and symptoms of exercise withdrawal (Keating, Tilbrook, Rossell, Enticott, & Fitzgerald, 2012; Meyer et al., 2011). Neuroendocrine and neurotransmitter systems, especially the HPA axis and the serotonergic system, possibly communicate these rewarding effects (Hebebrand et al., 2003). However, despite the long-standing debate about the mechanisms of hyperactivity in AN and current promising research on reward system functioning in affected patients, to our knowledge, no study has yet been conducted using neurobiological paradigms to investigate hyperactivity.

The present study is the first to examine attentional processing in response to pictures depicting exercise versus inactivity in patients with AN, healthy endurance athletes and healthy non-athletes using eye-tracking technology. Endurance athletes should show similarly high levels of individually performed physical activity as AN patients, however, their activity is mostly constricted to a specific training and competition context which is clearly separated from every-day life, and they potentially have other motives to engage in physical activity. Eye-tracking has previously been used to investigate gaze behavior when exploring motivationally salient stimuli, e.g. food, alcohol or faces (Chakrabarti & Baron-Cohen, 2011; Giel et al., 2011; Jones et al., 2012). These studies have demonstrated that gaze is generally preferentially allocated to rewarding stimuli and hence, attention allocation can be understood as an appetitive response (Castellanos et al., 2009; Chakrabarti & Baron-Cohen, 2011; Giel et al., 2011; Jones et al., 2012). We therefore hypothesized that patients with AN would show a bias toward activity-related stimuli in both, attentional orienting and attentional engagement. We expected this bias to be more pronounced in patients compared to athletes and to be more pronounced in athletes compared to non-athletes. We expected this bias to be associated with trait reward sensitivity and quantity of physical activity in patients.

2. Materials and methods

2.1. Participants

We recruited fifteen adult patients with AN according to DSM-IV (American Psychiatric Association, 2000) from the inpatient and outpatient service of the Department of Psychosomatic Medicine and Psychotherapy at the University Hospital Tübingen, Germany. We used the expert interview Eating Disorder Examination (EDE; Fairburn & Cooper, 1993; Hilbert & Tuschen-Caffier, 2006) to diagnose the eating disorder and the Structured Clinical Interview for DSM-IV (SCID-I; Wittchen, Wunderlich, Gruschwitz, & Zaudig, 1997) to assess comorbid Axis-I disorders in patients. Both clinical interviews were conducted by trained assessors. Exclusion criteria for patients comprised a body mass index (BMI) < 12 kg/m^2, a psychotic disorder, substance abuse or dependence, a primary obsessive–compulsive or affective disorder and current use of neuroleptics or benzodiazepines.

We recruited two age-matched healthy normal-weight control groups of adult females through local advertisement. One control group consisted of fifteen endurance athletes, the other of fifteen non-athletes. Athletes had to competitively practice endurance sports for at least 5 h per week over at least one year, while non-athletes were only included when performing casual physical exercise. Exclusion criteria for all healthy participants comprised a current or past mental disorder as assessed by the SCID-I.

All participants had normal or corrected to normal vision.

2.2. Ethical consideration

The local medical faculty's ethics committee approved the study (488/2009BO2). After complete description of the study to the subjects, written informed consent was obtained.

2.3. Stimuli

The stimulus material was specifically prepared for the present study. Color pictures were taken from a young female athlete either engaging in a physically active situation (referred to as *active stimulus*) or a physically passive situation (referred to as *inactive stimulus*). The picture set consisted of 52 color photographs, resulting in 26 picture pairs closely matched for color, brightness and visual complexity. Stimulus material was pre-tested for valence, arousal and estimation of physical strain on a five point Likert scale to ensure distinctiveness of stimulus categories. According to results of the physical strain rating, pictures rated 2.1 or less were categorized as *inactive* and pictures rated above 2.1 were categorized as *active*. Pictures of each pair were presented in two opposing corners on a computer screen, with balanced location of the active and inactive stimuli. Pictures were 8 cm high by 11 cm wide and with their nearest corner located 1.5 cm from the center of the computer screen.

2.4. Eye-tracking paradigm

The eye-tracking paradigm comprised free visual exploration of picture pairs presented twice for 3000 ms each in random order. This free-viewing task has previously been used by us and others to investigate reward system functioning as well as psychopathology in eating disorders (Castellanos et al., 2009; Chakrabarti & Baron-Cohen, 2011; Giel et al., 2011). Each picture pair was preceded by a central fixation cross presented for 2000 ms. Participants were asked to fixate this cross whenever presented and to explore the picture pairs as if they were watching television. Gaze behavior of participants during visual exploration was recorded using the remote eye-tracking system iView X Hi-Speed (SensoMotoric Instruments GmbH, Berlin, Germany) which has a sampling rate of 500 Hz and a spatial acuity of .25° to .5°.

2.5. Procedure

At a first separate appointment, research staff gathered demographic data, conducted the clinical interviews SCID-I (Wittchen et al., 1997) and the EDE in patients (Hilbert & Tuschen-Caffier, 2006). All participants completed validated self-report instruments assessing the amount of individually performed physical activity (IPAQ – short form; Craig et al., 2003), eating pathology (EDI-2; Paul & Thiel, 2005), trait reward sensitivity (BIS/BAS; Carver & White, 1994; Strobel, Beauducel, Debener, & Brocke, 2001), depression (PHQ-D; Löwe, Spitzer, Zipfel, & Herzog, 2002; Spitzer, Kroenke, & Williams, 1999) and anxiety (STAI; Laux, Glanzmann, Schaffner, & Spielberger, 1981; Spielberger, Gorsuch, & Lushene, 1970).

We used the short form of the IPAQ questionnaire to assess amount of physical activity. This questionnaire comprises seven questions, assessing amount of vigorous and moderate physical activity, walking and sitting in the last seven days. Participants are asked to report on how many days they e.g. exerted moderate physical activity and to report total daily amount of this activity in hours and/or minutes. In the present study, patients were asked to report physical activity in the seven days before hospital admission as physical activity is usually restricted during inpatient treatment for AN. With respect to criterion validity of the IPAQ, the correlation between self-report data in the short form and accelerometer data yielded $p = 0.3$ in a large validation study (Craig et al., 2003).

We used the BIS/BAS questionnaire to assess trait reward sensitivity. The BIS/BAS is grounded in the neurobiological personality theory by Gray (1970) which comprises two behavioral systems that regulate responses to rewarding stimuli: the behavioral inhibition system (BIS) and the behavioral activation system (BAS). The BAS scales assess persistence in approach behavior to appetitive goals (BAS Drive), tendency to look for rewarding situations and activities (BAS Fun Seeking) and anticipation of and positive affect toward reward (BAS Reward Responsiveness).