

Anorexia Nervosa and the Motivation to Restrict Food Intake: the Effects of Acute Dopamine Precursor Depletion

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INTRODUCTION

Several behaviours associated with anorexia nervosa (AN) are hypothesised to be highly salient and rewarding for these people (e.g., food restriction, weight-loss, and driven exercise). Neurobiological and psychophysiological evidence support a role for altered dopaminergic reward processes in the aetiology of AN and in the valued nature of its symptomatology. More specifically, preliminary data support the hypothesis that, in people with AN, alterations in dopamine (DA) reward circuits result from the attribution of motivational salience to illness-related stimuli (e.g., thinness and exercise). Aberrant reward processing in AN may therefore represent an important developmental and maintaining factor to be targeted by treatments.

Accordingly, in this study, egosyntonic symptoms (e.g., drive for thinness and drive for exercise) were investigated within the framework of a reward-centred model of eating disorders (O'Hara et al., 2015). In this model, a cognitive reluctance to gain weight is proposed to be the initial driver into the pathological state, in that cues compatible with this mode of thinking become rewarding for the individual. This attribution of motivational salience to such cues is hypothesised to promote the development of eating disordered behaviours. As such, this model also suggests that neurological overlaps exist between AN and other aberrant reward-based behaviours (e.g., addiction). Therefore, AN may in part reflect a reward-based learned behaviour in which aberrant cognitions related to eating and shape lead to altered functioning of the central dopaminergic reward system.

OBJECTIVES

The overall aim of this study was to improve understanding of the motivational processes involved in the valued nature of AN symptomatology. This was with the broader intention of improving comprehension of the mechanisms involved in the development and maintenance of this illness.

More specifically, this study aimed to test the hypothesis that DA is involved in maintaining the perceived salience of AN-specific cues (e.g. thinness) and in the willingness to engage in AN-specific behaviours (e.g., exercise).

METHODOLOGY

Women recovered from AN (AN REC, n=17) and healthy controls (HC, n=15) were recruited. The acute phenylalanine/tyrosine depletion (APTD) method was used to transiently decrease DA synthesis and transmission. The effects of APTD on the value attributed to AN-specific cues and behaviours were explored using experimental tasks sensitive to objective motivational states. Specifically, the effects of APTD on drive to exercise and the value attributed to AN-specific cues were explored using a progressive ratio (PR) exercise breakpoint task (O'Hara et al., 2016) and a startle eyeblink modulation task (O'Hara et al., submitted), respectively.

RESULTS

Both groups worked for the opportunity to exercise using the PR exercise breakpoint task, and, at baseline, PR breakpoint scores were higher in AN REC than in HC. Compared to values in the balanced (BAL) amino acid state (i.e., the experimental control session), acute DA depletion (APTD) did not decrease PR breakpoint scores in AN REC, but significantly decreased PR scores (i.e., the willingness to sustain effort for exercise reward) in HC (see Figure 1).

During BAL, AN REC showed an increased appetitive response (i.e., decreased startle potentiation) to illness-compatible cues (i.e., underweight and active female body pictures), whereas HC showed an aversive response (i.e., increased startle potentiation) to these cues. Importantly, these effects, which are consistent with illness and with healthy behaviour respectively, were not present when DA was depleted (i.e., during APTD). Thus, AN REC implicitly appraised underweight and exercise cues as more rewarding than did HC and the process may, in part, be DA-dependent (see Figures 2 and 3).

CONCLUSIONS

This study supports a role for altered dopaminergic reward processes in the facilitation of aberrant reward associations in AN. Specifically, data from the startle eyeblink modulation paradigm suggest that positive motivational salience is automatically attributed to cues of emaciation and physical activity and is, in part, mediated by dopaminergic reward processes. Moreover, data from the PR exercise breakpoint task show that decreasing DA does not reduce the motivation to engage in exercise in people recovered from AN, but in contrast, does so in HC. It is proposed that as illness progresses, overt symptoms associated with AN (e.g., drive to exercise) may develop into behaviours that are largely independent of DA mediated reward processes and become dependent on cortico-striatal neurocircuitry that regulates automated, habit- or compulsive-like behaviours.

Taken together, data indicate that in AN, there does not appear to be a generalised inability to experience reward. In fact, results suggest that several cues associated with AN are perceived as rewarding by these individuals and are consistent with the proposal that, in AN, aberrant reward-based learning contributes to the development of habituation of AN-compatible behaviours. Furthermore, findings suggest that, even after recovery, women with AN attribute increased salience to AN-specific cues. These results support the hypothesis that alterations in DA reward responses may be a neural vulnerability important in eliciting the spiral into, and the inescapability of, the anorexia “habit”.

FIGURES

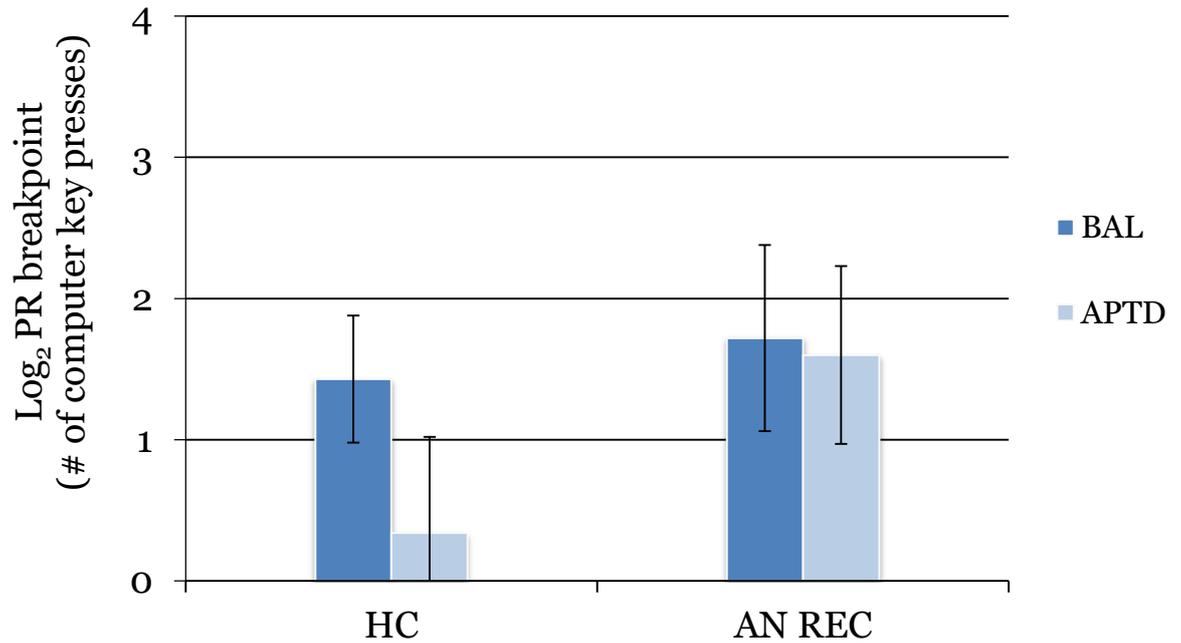


Figure 1. Log transformed exercise breakpoint scores in the balanced (BAL) and DA depleted (APTD) conditions for individuals recovered from anorexia recovered (AN REC, n = 17) and healthy controls (HC, n = 15). A significant Group by Drink interaction indicated that dopamine depletion decreased progressive ratio exercise breakpoint scores (i.e., the willingness to sustain effort for exercise reward) only in the HC ($p < 0.01$, $ES = 0.34$). This suggests that, even in the dopamine depleted state, individuals recovered from AN are just as willing to work for exercise reward.

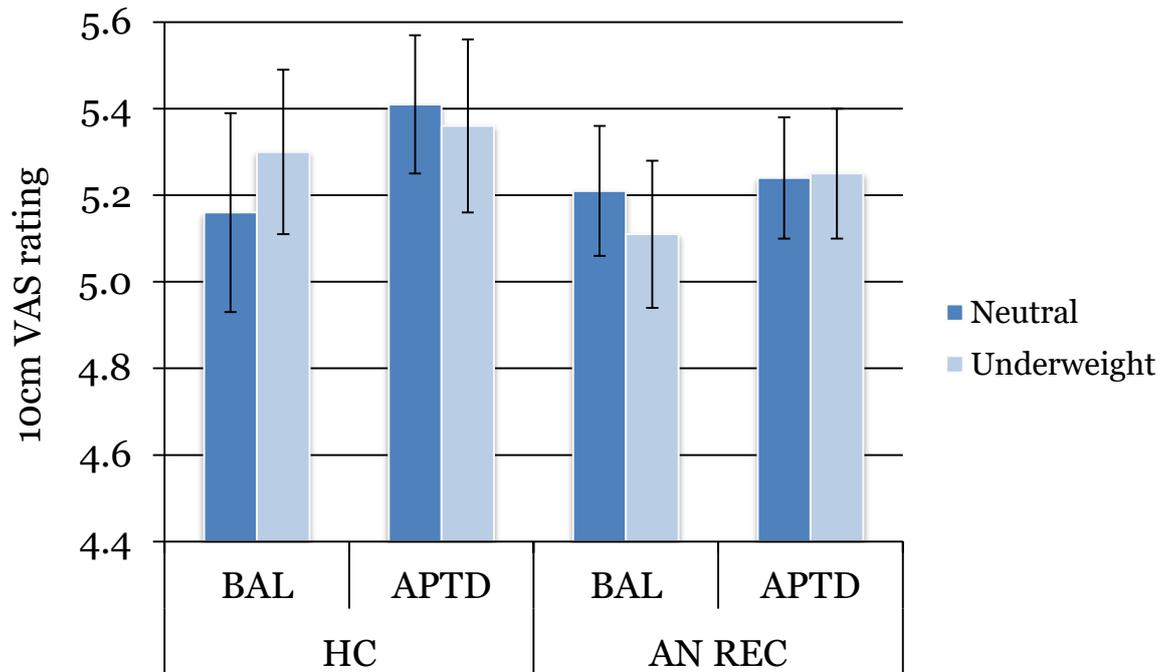


Figure 2. Log transformed startle eyeblink amplitudes in response to underweight and neutral cues in the balanced (BAL) and dopamine depleted (APTD) conditions individuals recovered from AN (AN REC, n = 17) and healthy controls (HC, n = 15). A significant Group by Picture by Drink interaction ($p = 0.01$, $ES = 0.25$) showed that in the balanced amino acid state, HC have increased startle potentiation (i.e., an aversive motivational response) to images of underweight female bodies. This was not the case for the recovered AN group, who showed a decrease in their startle potentiation (i.e., an appetitive response) to underweight cues. In the dopamine depleted condition, however, these effects were not present.

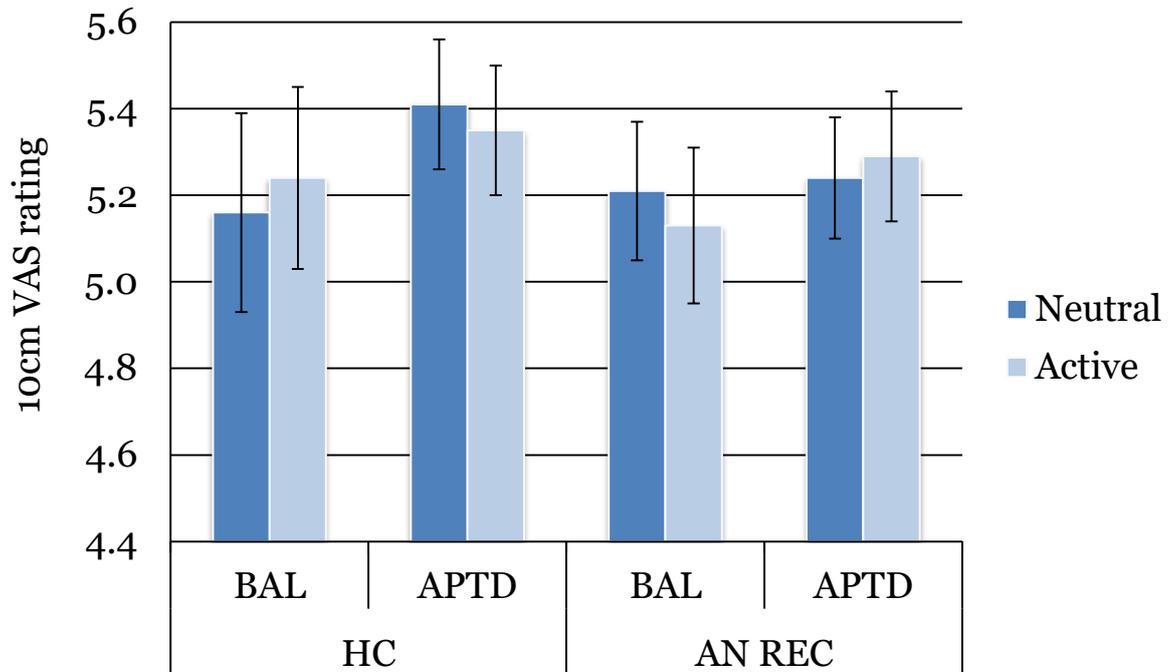


Figure 3. Log transformed startle eyeblink amplitudes in response to active and neutral cues in the balanced (BAL) and dopamine depleted (APTD) conditions for individuals recovered from AN (AN REC, n = 17) and healthy controls (HC, n = 15). A significant Group by Picture by Drink interaction ($p < 0.01$, $ES = 0.28$) showed that in the balanced amino acid state, HC have increased startle potentiation (i.e., an aversive motivational response) to images of active female bodies. This was not the case for the recovered AN group, who showed a decrease in their startle potentiation (i.e., an appetitive response) to active cues cues. In the dopamine depleted condition, however, these effects were not present.

REFERENCES

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3. O'Hara, C. B., Keyes, A., Renwick, B., Giel, K. E., Campbell, I. & Schmidt, U. (submitted). Evidence that illness-compatible cues are rewarding in women recovered from anorexia nervosa: a study of the effects of acute dopamine depletion on eye-blink startle response.

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