



## A psycho-genetic study of associations between the symptoms of binge eating disorder and those of attention deficit (hyperactivity) disorder

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### ABSTRACT

**Objective:** Some recent studies have reported intriguingly strong correlations between ADHD and obesity. This study examined whether ADHD symptoms were more pronounced in adults with symptoms of binge eating disorder (BE) than in their non-binging obese counterparts, and whether the links were stronger with inattentive vs impulsive/hyperactive symptoms. We also assessed the role of the dopamine D3 receptor in ADHD symptoms since the DRD3 gene has been associated with impulsivity and drug addiction – both relevant features of ADHD.

**Methods:** A case (BE:  $n = 60$ ) double-control (normal weight:  $n = 61$  and obese:  $n = 60$ ) design was employed. Assessments of both childhood and adults ADHD symptoms were made, as well as genotyping of seven markers of DRD3 including the functional Ser9Gly polymorphism.

**Results:** Three DRD3 genotypes, including Ser/Ser, had significantly elevated scores on the hyperactive/impulsive symptom scale. In turn, the four ADHD symptom scales were all significantly elevated in the BE and obese groups, who did not differ from each other, compared to those with normal weight.

**Conclusions:** Results indicated a role for the D3 receptor in the manifestation of the hyperactive/impulsive symptoms of ADHD, and that symptoms of ADHD are significantly, but not differentially, elevated in obese adults with and without binge eating. Our findings suggest that ADHD screening in adults seeking treatment for obesity, including those with BE, may be warranted as methods used to treat ADHD may help some to better manage overeating and other factors contributing to weight gain.

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### 1. Introduction

Attention deficit/hyperactivity disorder (ADHD) was initially seen as a childhood disorder that typically remitted with puberty (Mayes and Rafalovich, 2007). Views changed with the evidence that 70–80% of children with ADHD retain some of their symptoms in adolescence, and that in a substantial number of cases, one or more disabling features of the disorder persist into adulthood (Biederman et al., 1996; Mannuzza et al., 1998). However, the quality of the core characteristics tends to change with maturity. For example, the overt and extreme restlessness seen in children is usually channeled into more socially appropriate behaviours (Weiss et al., 1999).

There is a wealth of research demonstrating an association between ADHD and addiction disorders – a co-morbidity that is both

robust and bi-directional (e.g. Fuemmeler et al., 2007; Ohlmeier et al., 2007; Tang et al., 2007). Moreover, the conclusions from a recent familial-risk analysis are that ADHD and drug dependence share a common vulnerability profile rather than present with independent modes of transmission (Biederman et al., 2008). Since both disorders have strong links to the dopamine (DA) system, Biederman and his colleagues propose the conjoint involvement of DA genes that regulate arousal, attention, and the common reward pathway.

#### 1.1. ADHD and obesity

In recent years, we have also become aware of strong links between ADHD and obesity (e.g. Agranat-Meged et al., 2005; Altfas, 2002; Fleming et al., 2005) – an association of particular interest because of their individual connectedness to addictive behaviours. First, there is some evidence that highly palatable food can be an addictive substance, and that compulsive overeating can be modelled as an addictive behaviour (Avena et al., 2008; Davis et al., 2008; Trinko et al., 2007; Volkow and O'Brien, 2007). Second, is

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the compelling that body weight and food intake are regulated – perhaps at least in part – by the same DA brain reward mechanisms as pharmacologic agents like cocaine and nicotine (Hoebel et al., 2007; Kenny, 2007; Campbell and Eisenberg, 2007). Therefore, some cases of obesity may be the consequence of a *food addiction* (see Cassin and von Ranson, 2007) that occurs – like *drug dependence* – with greater prevalence in those with ADHD.

Another unifying thread in these syndromes is the centrality of *impulsivity* – a personality trait characterized by the diminished ability to inhibit behaviour when restraint is the most advantageous and appropriate response in a particular situation. Converging evidence suggests that DA pathways play an important role in the expression of this endophenotype, which varies widely in the general population (e.g. Eisenberg et al., 2007; Limosin et al., 2005; Ondo and Lai, 2008). Impulsivity correlates positively and consistently with drug use and abuse (Verdejo-Garcia et al., 2007), with compulsive overeating (Steiger and Bruce, 2007), and with ADHD, where it serves as one of the diagnostic criteria for this disorder (American Psychiatric Association, 1994; Drechsler et al., 2008).

To date, the research linking obesity and ADHD has focused largely on co-morbidity prevalence data. For example, in a sample of morbidly obese adults recruited from a bariatric clinic, almost half met diagnostic criteria for ADHD (Altfas, 2002). Only a handful of studies has examined mechanisms underlying the ADHD/obesity association. The principal finding is that measures of hedonic eating<sup>1</sup> – including binge eating – may mediate the relationship in adults and adolescents (Cortese et al., 2007; Davis et al., 2006).

### 1.2. Dopamine and DRD3

Because DA has been implicated in the aetiology of ADHD, obesity, and substance abuse, we included a genetic analysis in our study design. The DRD3 gene was targeted for several reasons. For instance, D3 receptors are heavily expressed in the mesolimbic brain areas – in particular the nucleus accumbens – which play a key role in the reward process of addictive behaviours (Black et al., 2002). D3 receptors also mediate dopamine-related prefrontal neurocognition (Lane et al., 2008), and have been associated with impulsive personality traits and addictive behaviours – key features of both ADHD and obesity (Limosin et al., 2005). Various lines of evidence also indicate that D3 activation produces an inhibitory effect on motor response (Muglia et al., 2002).

Previous research has established the functionality of the Ser9Gly polymorphism of the DRD3 gene. The Gly allele appears to have an affinity for endogenous dopamine 4–5 times higher than the Ser allele, and therefore is more responsive to its effects (Jeanneteau et al., 2006; Lundstrom and Turpin, 1996). The Ser/Ser genotype has been associated with substance abuse in schizophrenia (Krebs et al., 1998) and with opiate addiction (Duaux et al., 1998), while heterozygotes displayed higher impulsivity in two recent studies (Limosin et al., 2005; Retz et al., 2003). Ser/Ser has also been associated with eye movement disturbances, which are related to working memory impairments and attention deficits (Rybakowski et al., 2001). By contrast, the Gly/Gly genotype has been correlated with obsessive–compulsive personality traits and disorder (Joyce et al., 2003; Light et al., 2006).

While a few studies have examined associations between polymorphisms in the D3 receptor gene and clinical cases of ADHD (e.g. Barr et al., 2000; Muglia et al., 2002; Payton et al., 2001), the results have all been negative. However, these studies either included

child/adolescent cases of ADHD and/or they did not analyse the data by subtype of the disorder. In other words, associations with D3 were not tested in the inattentive vs the hyperactive/impulsive vs the combined subtype. Examining associations with individual symptoms as dimensional traits expressed in the general population is also likely to produce different results than testing associations with a diagnostic group (ADHD) who are very heterogeneous with respect to their symptoms.

### 1.3. The present study

Since binge eating disorder (BED) is characterized by compulsive overeating and by elevated body weight, it serves as an ideal phenotype for studying links between ADHD symptoms and obesity. There are also claims that obese individuals with BED display greater psychopathology than their non-binging counterparts (see Latner and Clyne, 2008). Using a case-control design (adults with symptoms of BED vs non-binge eating normal weight and non-binge eating obese adults), we tested a model predicting that markers of the DRD3 gene are related to ADHD symptoms, which in turn differentiate our three study groups (see Fig. 1). Our specific aim was to examine whether ADHD symptoms differentiated the two obesity groups, and whether the ADHD–obesity link was moderated by ADHD subtype (viz. inattentive vs hyperactive/impulsive). In particular, we anticipated that those with the Ser/Ser genotype would report higher ADHD symptoms. We also expected that ADHD symptoms would be greater in the binge eating adults compared to obese controls, and that both would be elevated compared to normal weight adults.

## 2. Methods

### 2.1. Participants and procedures

Adults between the ages of 25 and 45 years who met modified criteria for BED ( $n = 60$ : female = 47; male = 13) were recruited from posters placed at universities, local hospitals, and other public institutions, as well as from advertisements in local newspapers. A normal weight ( $n = 61$ : female = 54; male = 7) and a non-binging obese ( $n = 60$ : female = 45; male = 15) control group were recruited in the same manner. The percentage of females in the binge eating, normal weight, and obese control groups was 78.3, 88.5, and 75.0, consecutively. The  $\chi^2$  test of independence for these data was non-significant ( $\chi^2 = 3.859$ ,  $df = 2$ ,  $p = 0.145$ ). Similarly, the percentage of Caucasians in the three groups was 81.4, 82.0, and 72.4, consecutively, and the  $\chi^2$  test was also non-significant ( $\chi^2 = 2.00$ ,  $df = 2$ ,  $p = 0.368$ ).

The group mean ages were 34.5 (6.5) years for binge eaters, 33.3 (7.5) years for normal weight controls, and 37.0 (6.7) years for the obese controls. Analysis of variance (ANOVA) procedures indicated that these values were significantly different ( $F_{2,178} = 4.62$ ,  $p = 0.011$ ). We concluded, however, that a mean age difference across the groups of approximately 4 years would not have a meaningful effect on the relationships among our variables of interest. The three groups also differed significantly ( $F_{2,177} = 89.86$ ,  $p < 0.0001$ ) on BMI (binge eaters: 34.7 [8.6]; normal weight: 22.4 [2.7]; and obese: 39.2 [8]). Least significant difference [LSD] *post hoc* tests indicated that the mean BMI was significantly higher for the obese controls than for the binge eating participants ( $p = 0.001$ ), and both were higher than the normal weight group ( $p < 0.0001$  for each).

Control participants were first screened during a structured telephone interview and excluded if they had any serious medical condition, were not fluent in English, were pregnant (or had recently given birth), and were currently being treated for (or had

<sup>1</sup> This term is typically used to describe eating that is motivated by the desire for, and the palatability of, certain foods in the absence of any energy deficit. In other words, it is motivated by the rewarding properties of food rather than its energy content (see Lowe and Butryn, 2007).

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