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Research report

# Insula tuning towards external eating versus interoceptive input in adolescents with overweight and obesity \*

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#### ABSTRACT

This study was aimed to examine if adolescent obesity is associated with alterations of insula function as indexed by differential correlations between insula activation and perception of interoceptive feedback versus external food cues. We hypothesized that, in healthy weight adolescents, insula activation will positively correlate with interoceptive sensitivity, whereas in excess weight adolescents, insula activation will positively correlate with sensitivity towards external cues. Fifty-four adolescents (age range 12–18), classified in two groups as a function of BMI, excess weight (n = 22) and healthy weight (n = 32), performed the Risky-Gains task (sensitive to insula function) inside an fMRI scanner, and completed the heartbeat perception task (measuring interoceptive sensitivity) and the Dutch Eating Behaviour Questionnaire (measuring external eating as well as emotional eating and restraint) outside the scanner. We found that insula activation during the Risky-Gains task positively correlated with interoceptive sensitivity and negatively correlated with external eating in healthy weight adolescents. Conversely, in excess weight adolescents, insula activation positively correlated with external eating and negatively correlated with interoceptive sensitivity, arguably reflecting obesity related neurocognitive adaptations. In excess weight adolescents, external eating was also positively associated with caudate nucleus activation, and restrained eating was negatively associated with insula activation. Our findings suggest that adolescent obesity is associated with disrupted tuning of the insula system towards interoceptive input.

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#### Introduction

The current food environment is full of cues that keep thoughts of palatable, energy-dense food almost constantly in mind (Swinburn et al., 2011). Therefore, individual differences in the relative value given to external food cues versus current homeostatic needs (e.g. hunger, satiety) may contribute to understanding the increasing prevalence of obesity (Carnell, Benson, Pryor, & Driggin, 2013). In this context, obesity is viewed as a condition characterized by difficulties in resisting the urge to respond to external food cues, which may override homeostatic control of food intake (Blundell & Finlayson, 2004). The insula is the brain hub that integrates homeostatic feedback with

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external information and expected outcomes (Craig, 2009), and therefore it is key to understanding the neural balance between interoceptive and external information. Recent research suggests that during adolescence insula function is sensitized towards external reward cues and comparatively less sensitive to risk (Smith, Steinberg, & Chein, 2014). It is however yet unclear whether this pattern translates into greater insula weighing of external versus interoceptive information in adolescents with overweight and obesity. This question is relevant as in that case insula related adaptations may contribute to the establishment and maintenance of a highly palatable yet unhealthy (hence risky) diet.

Risky decision-making involves cognitive evaluation of potential rewards and outcomes, but it is also critically modulated by homeostatic signals that project to the insula cortex (Paulus, 2007). The insula receives the major sources of interoceptive input (i.e., gut, hormonal) and gives rise to awareness of homeostatic states, which guide behaviour in the direction of satisfying body needs (Craig, 2009). The insula is centrally involved in basic functions related to perception of physiological needs such as thirst and hunger as evidenced by animal (Hollis, McKinley, D'Souza, Kampe, & Oldfield,







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2008; Saker et al., 2014) and human studies (Craig, 2009; Frank, Kullmann, & Veit, 2013). In relation to food intake, the insula cortex receives gut motility and hormonal signals of appetite and satiety, processes sensory and gustatory aspects of food and guides food related decisions (Frank et al., 2013; Volkow, Wang, & Baler, 2011). Moreover, the insula is typically engaged when subjects make risky decisions involving gains and potential losses (Preuschoff, Quartz, & Bossaerts, 2008) and specifically involved in signalling the probability of aversive outcomes (Bossaerts, 2010; Venkatraman, Payne, Bettman, Luce, & Huettel, 2009). Therefore, it is reasonable to assume that the insula plays a relevant role on food decisions involving reward, but potentially associated with health related costs.

Adolescents with excess weight have decreased activation of the insula during anticipation of higher rewards in the Risky-Gains task, which opposes a less rewarding safe choice with more rewarding risky choices (Delgado-Rico, Soriano-Mas, Verdejo-Roman, Rio-Valle, & Verdejo-Garcia, 2013). The insula also plays a crucial role in interoceptive sensitivity, which is decreased in individuals with excess weight (Herbert & Pollatos, 2014). Importantly, individual differences in interoceptive sensitivity modulate decision-making processes regarding food intake. Higher interoceptive sensitivity has been shown to predict adaptive eating behaviours (guided by awareness of internal cues of hunger or satiety), which indeed is negatively associated with BMI levels (Herbert, Blechert, Hautzinger, Matthias, & Herbert, 2013). Conversely, poor interoceptive sensitivity in the face of the current obesogenic environment may predispose obese individuals to rely on external cues rather than on internal feedback on physiological states (e.g., hunger and satiety) (Schachter, 1968).

In this study, we used functional magnetic resonance imaging to examine whether insula activation during risk-based decisionmaking is associated with sensitivity towards external food cues versus perception of interoceptive feedback in adolescents with excess weight. Decision-making was challenged using the Risky-Gains task (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003), which reliably induces recruitment of insula activation (Delgado-Rico et al., 2013). The perception of interoceptive feedback was measured by a heartbeat perception task (Schandry, 1981). It has been demonstrated that cardiac interoception is strongly correlated with gastric interoception, which indicates that this is a general index of interoceptive sensitivity (Herbert, Muth, Pollatos, & Herbert, 2012). Sensitivity towards external food cues was measured by the external eating subscale of the Dutch Eating Behaviour Questionnaire (Van Strien, Frijters, Bergers, & Defares, 1986). We hypothesized that in excess weight adolescents insula activation would positively correlate with external eating, at difference with positive correlations with interoceptive sensitivity in healthy weight controls.

#### Methods

#### Participants

Fifty-four adolescents (age range 12–18) participated in this study. They were classified in two groups (excess weight [n = 22] or healthy weight [n = 32]) according to their age- and sex-adjusted BMI percentile, following the criteria of the International Obesity Task Force (IOTF) defined by Cole and Lobstein (2012). The demographic data, BMI, percentage of fat and the biochemical parameters are summarized in Table 1. The two groups did not differ significantly in age, sex or any biochemical parameter. Participants were recruited from the pediatrics and endocrinology services of the Hospital "Virgen de las Nieves" in Granada, Spain, and from schools located in the same geographical area. The inclusion criteria were as follows: (i) aged between 12 and 18 years old, (ii) BMI values falling within the intervals categorized as excess weight or healthy weight according to the IOTF, (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parents interviews and the Eating Disorder Inventory (Garner, 1994, (iv) absence of significant abnormalities on MRI (Magnetic Resonance Imaging) or any contraindications to MRI scanning (including claustrophobia and implanted ferromagnetic objects) and (v) absence of history of brain injury involving loss of consciousness (LOC) for longer than 5 minutes. All of them had normal or corrected-tonormal vision. The study was approved by the Ethics Committee of the University of Granada. All participants and their parents were briefed about study aims and detailed procedures, and both signed an informed consent form certifying their voluntary participation.

#### fMRI task

We used the Risky-Gains task described by Paulus et al. (2003). In each trial, participants are presented with the numbers 20, 40 and 80 in a fixed order. The task requires the participant to acquire as many points as possible by choosing between safe (20 points) and risky (40, 80 points) options. Each number (20, 40 or 80) is presented on the screen for 1 s, and the participant is instructed to press a button while the selected number is on the screen in order to win the corresponding amount of points. If participants fail to press the button within the required time, a 'too late' message is displayed on the screen and they miss the points for that trial.

The first number in the sequence (20) is always a safe choice. Participants are told that if they choose to press the bottom while the 20 is on the screen they would always receive 20 points. Moreover, participants are told that they have the option to wait and select one of the two subsequent choices (40 and 80); in that case they

Table 1

Socio-demographic characteristics, BMI, percentage of fat and biochemical parameters for each group.

	Excess weight (n = 22) Mean (SD <sup>b</sup> )	Healthy weight (n = 32) Mean (SD)	p-value
Demographic variables			
Age	15.14 (2.03)	15.53 (1.70)	0.443
Sex (male/female)	11/21	10/12	0.412
BMI <sup>a</sup>	29.40 (3.00)	21.17 (2.24)	< 0.001
Fat (%)	33.14 (8.85)	19.01 (6.73)	< 0.001
Biochemical parameters			
Insulin	45.58 (59.90)	39.13 (38.69)	0.635
Basal glucose	92.34 (3.91)	92.17 (7.19)	0.91
Triglycerides	71.70 (31.80)	65.15 (29.05)	0.437
HDL <sup>c</sup>	55.15 (13.13)	56.88 (10.81)	0.6
Total cholesterol	154.64 (27.77)	146.00 (18.34)	0.174

<sup>a</sup> Body Mass Index.

<sup>b</sup> Standard deviation.

<sup>c</sup> High-density lipoprotein.

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