

# Selective Alterations Within Executive Functions in Adolescents With Excess Weight

Antonio Verdejo-García<sup>1,2</sup>, Manuel Pérez-Expósito<sup>1</sup>, Jacqueline Schmidt-Río-Valle<sup>3</sup>, Maria J. Fernández-Serrano<sup>1</sup>, Francisco Cruz<sup>1</sup>, Miguel Pérez-García<sup>1,2</sup>, Gemma López-Belmonte<sup>4</sup>, Miguel Martín-Matillas<sup>5</sup>, Jose A. Martín-Lagos<sup>4</sup>, Ascension Marcos<sup>6</sup> and Cristina Campoy<sup>2,4</sup>

Increasing evidence underscores overlapping neurobiological pathways to addiction and obesity. In both conditions, reward processing of preferred stimuli is enhanced, whereas the executive control system that would normally regulate reward-driven responses is altered. This abnormal interaction can be greater in adolescence, a period characterized by relative immaturity of executive control systems coupled with the relative maturity of reward processing systems. The aim of this study is to explore neuropsychological performance of adolescents with excess weight ( $n = 27$ , BMI range 24–51 kg/m<sup>2</sup>) vs. normal-weight adolescents ( $n = 34$ , BMI range 17–24 kg/m<sup>2</sup>) on a comprehensive battery of executive functioning tests, including measures of working memory (letter-number sequencing), reasoning (similarities), planning (zoo map), response inhibition (five-digit test (FDT)–interference and Stroop), flexibility (FDT–switching and trail-making test (TMT)), self-regulation (revised-strategy application test (R-SAT)), and decision-making (Iowa gambling task (IGT)). We also aimed to explore personality traits of impulsivity and sensitivity to reward. Independent sample *t*- and Z Kolmogorov–Smirnov tests showed significant differences between groups on indexes of inhibition, flexibility, and decision-making (excess-weight participants performed poorer than controls), but not on tests of working memory, planning, and reasoning, nor on personality measures. Moreover, regression models showed a significant association between BMI and flexibility performance. These results are indicative of selective alterations of particular components of executive functions in overweight adolescents.

*Obesity* (2010) **18**, 1572–1578. doi:10.1038/oby.2009.475

## INTRODUCTION

Increasing evidence underscores overlapping neurobiological pathways to addiction and obesity (1,2). In both conditions, the motivational valuation of the preferred stimuli (i.e., drugs or high-palatable food) is disproportionately enhanced, whereas the top-down control system that would normally regulate reward-driven responses is altered (1). Positron emission tomography imaging studies have provided support to this notion by demonstrating that individuals with excess weight have reduced availability of dopamine D2 receptors in the striatum, which is correlated with metabolic activity in the dorsolateral prefrontal cortex, medial orbitofrontal cortex, anterior cingulate gyrus, and somatosensory cortices (3); this neural-systems network is also strongly involved in addiction (4,5). Furthermore, positron emission tomography-indexed resting metabolism in the prefrontal cortex and the cingulate gyrus is negatively correlated with BMI in healthy

volunteers (6). The abnormal interaction between homeostatic/motivational signals and top-down executive control mechanisms have also been linked to alterations in decision-making processes, which become characterized by a tendency to select immediate reinforcing choices even at the expense of rising negative consequences (5,7,8). This abnormal interaction can be greater in adolescence, a period characterized by the relative immaturity of prefrontal cortical control systems coupled with the relative maturity of striatal systems responsible for reward processing and motivation (9). On the one hand, functional magnetic resonance imaging studies have shown that adolescents, compared to adults, display enhanced activation of the ventral striatum and the anterior insula during reward anticipation and receipt (10,11). On the other hand, cognitive and functional magnetic resonance imaging developmental studies have shown that different executive control skills and their neural substrates (i.e., the prefrontal cortex) are still improving

<sup>1</sup>Department of Clinical Psychology, Universidad de Granada, Granada, Spain; <sup>2</sup>Institute of Neuroscience F. Olóriz, Universidad de Granada, Granada, Spain;

<sup>3</sup>Department of Nursing, Universidad de Granada, Granada, Spain; <sup>4</sup>Department of Paediatrics, School of Medicine, Universidad de Granada, Granada, Spain;

<sup>5</sup>Department of Physical Education and Sport, School of Physical Activity and Sport Science, University of Granada, Granada, Spain; <sup>6</sup>Immunonutrition Research Group, Department of Metabolism and Nutrition, Institute Frio-ICTAN, CSIC, Madrid, Spain. Correspondence: Antonio Verdejo-García (averdejo@ugr.es)

Received 9 July 2009; accepted 30 November 2009; published online 7 January 2010. doi:10.1038/oby.2009.475

their competence during early and late adolescence: working memory and reasoning can reach adult levels ~12 years old, whereas inhibition and flexibility continue their progression between 13 and 17 years old, and risk-based decision-making skills prolong their maturation until 18–19 years old (12–14). This imbalance makes adolescence a period during which the activity of the reward system prevails over that of the systems governing avoidance or self-control (15). Therefore, there is a need to characterize the neuropsychological functioning of these neural systems in adolescents with excess weight.

One of the few available neuropsychological studies in children and adolescents with weight problems have shown that schoolboys (~12 years old) with excess weight have poorer performance on tests of sustained attention and cognitive flexibility, being flexibility negatively correlated with BMI (16). Similar results have been obtained in adults with excess weight. A study in a large sample of healthy adults demonstrated that increased BMI was associated with poorer performance on tests of response inhibition and flexibility (17), whereas a recent study showed that individuals seeking surgical treatment for obesity (BMI  $\geq 40$ ) had significantly impaired performance on the Rey–Osterrieth complex figure test and the Wisconsin card sorting test (tests indexing planning/memory and flexibility) as compared to normative values (18). Studies on adults with excess weight have also demonstrated an association between BMI and performance on a decision-making test known as the Iowa gambling task (IGT) (19,20), but no studies have examined this process on adolescents with excess weight. The aim of this study is to explore neuropsychological performance of adolescents with excess weight vs. normal-weight adolescents on a comprehensive battery of executive functioning tests, including measures of working memory, analogical reasoning, planning, response inhibition, flexibility, self-regulation, and emotional decision-making. We further aimed to explore personality traits of impulsivity and sensitivity to reward in this sample. According to previous evidence and neurobiological models of obesity and addiction, we hypothesized that excess-weight adolescents would have poorer performance on measures capturing the ability to control and regulate prepotent or reward-driven responses, including inhibition, flexibility, self-regulation, and decision-making; whereas they would perform similar to controls on tests of “cold” executive functions, such as working memory, planning, or reasoning. Furthermore, we hypothesized that those executive functions that have been correlated with progression of addiction and obesity (i.e., flexibility and decision-making) would be significantly associated with BMI in this sample of adolescents.

## METHODS AND PROCEDURES

### Subjects

Twenty-seven adolescents with excess weight (11 F and 16 M; aged 13–16) were selected according to their BMI (weight (kg)/height (m)<sup>2</sup>) and classified as overweight or obese according to the International Obesity Task Force criteria defined by Cole *et al.* (21). At the same time, 34 healthy adolescents (13 F and 21 M; aged 13–16) with normal weight, who had similar sex and IQ distributions, were also enrolled in the study forming the comparison group. Adolescents

with excess weight were recruited as they enrolled in a research-based multidisciplinary therapeutic program aimed to decrease weight and to change eating-related lifestyles (EVASYON study) carried out at the San Cecilio Hospital in Granada, Spain. In all cases, the evaluations reported in this study were conducted before treatment onset. Nineteen participants within the excess-weight group met criteria for obesity according to age- and sex-corrected BMI cutoffs proposed by Cole *et al.* (21); the BMI range in these subjects was 28–51. The remaining eight participants within this group met criteria for overweight according to the same cutoffs; the BMI range in these subjects was 24–28. Individuals with excess weight were evaluated by a physician for exclusion criteria, which included significant medical or psychiatric illness, and current treatment with medication; their characteristics are shown in [Table 1](#). Normal-weight adolescents (BMI range 17–24) were recruited through schools located in the same geographical area, from families with similar sociodemographic background to the ones forming the clinical group.

### Measures

#### *Questionnaire measures of impulsivity and sensitivity to reward/punishment*

*UPPS-P impulsive behavior scale* (22): This scale is a 59-item inventory designed to measure five distinct personality pathways to impulsive behavior: negative urgency, lack of perseverance, lack of premeditation, sensation seeking, and positive urgency. The total scores of each of these five dimensions were obtained for analyses.

*Delay-discounting questionnaire, now or later* (23): This is a monetary-choice questionnaire asking for individual preferences between smaller, immediate rewards and larger, delayed rewards varying on their value and time to be delivered. The dependent measure was the discounting parameter  $k$ , indexing the rate at which the individual depreciate rewards as a function of time, according to the formula:  $V = A/(1 + kD)$ , where  $V$  is the present value of the delayed reward  $A$  at delay  $D$ , and  $k$  is a free parameter that determines the discount rate. As  $k$  increases, the person discounts the future more steeply.

*SPSRQ* (24): The SPSRQ (sensitivity to punishment and reward questionnaire) is a 48 yes–no response item questionnaire aimed to measure two neuropsychological systems driving motivated behavior: the behavioral activation system (SR) and the behavioral inhibition system (SP). The total scores from each scale (SP and SR) were obtained for analyses.

#### *Neuropsychological evaluation*

*IQ–Kaufman brief intelligence test* (25): It consists of two subtests, vocabulary and matrices. The vocabulary subtest provides an estimated verbal IQ, the matrices subtest provides an estimated nonverbal IQ, and the scores from both measures provide a composite IQ, which we used as the main dependent measure from this test.

*Working memory–letter-number sequencing* (26): Participants are read a sequence in which letters and numbers are combined, and are asked to reproduce the sequence heard, first placing the numbers in ascending order and then the letters in alphabetical order. The dependent variable from this test was the number of correct answers.

*Analogical reasoning–similarities* (26): Pairs of words are read that represent common objects or concepts, and participants have to indicate how these objects/concepts are similar or what they have in common. The dependent variable from this test was the number of correct answers.

*Planning–zoo map* (27): It provides information about the ability of the participant to plan a route that allows him to visit 6 of 12 locations in a section of the zoo. The main dependent measure from this test was the total raw score, based on the efficacy of the plan designed minus the number of errors committed.

*Interference/response inhibition–Stroop test* (28): This test consists of three forms, each containing 100 elements. The first form is made up of the words “RED,” “GREEN,” and “BLUE” ordered randomly and printed in black ink. In this condition, participants are asked to read aloud the words written. The second form consists of strings of “XXXX” printed in red, blue, or green ink. In this condition, participants are asked to name

the color. The third form introduces the condition of interference, and it consists of the words from the first sheet printed in the colors of the second. In this condition, participants have to name the color of the ink and ignore the word. The dependent variable used in this test was the interference score.

**Inhibition and shifting–five-digit test (FDT) (29):** This test consists of four parts of increasing complexity. Each of these parts presents a series of 50 boxes that contain 1–5 digits (parts 1, 3, and 4) or stars (part 2), organized in similar patterns to those on domino pieces or playing cards. In part 1 (reading), participants are asked to read as quickly as possible the digit each box contains. In part 2 (counting), participants are asked to count how many stars each box contains. In part 3 (interference), participants are asked to count the number of digits each box contains, producing an effect of interference, as the boxes present groups of digits that do not correspond to their arithmetic value (e.g., in a box with five twos, the correct response would be five and not two). Finally, in part 4 (switching), participants are asked to count, just as in part 3, or read, as in part 1, depending on whether the outline of the box is normal (count, 80% of the stimuli) or of double thickness (read, 20% of the stimuli). Parts 1 and 2 constitute basic measures of attention and processing speed. In contrast, parts 3 and 4 are sensitive to executive processes of inhibition and switching. Therefore, the main dependent variables from this test were the difference between performance time on part 3 and the mean of parts 1 and 2 (FDT interference score), and the difference between performance time on part 4, and the mean of parts 1 and 2 (FDT switching score).

**Set-shifting–trail-making test A and B (TMT):** This test consists of two parts. Part A is a page with 25 numbered circles randomly arranged. Individuals are instructed to draw lines between the circles in increasing sequential order until they reach the circle labeled “End.” Part B is a page with circles containing the letters A–L and 13 numbered circles intermixed and randomly arranged. Individuals are instructed to connect the circles by drawing lines alternating between numbers and letters in sequential order, until they reach the circle labeled “End.” The main dependent measure from this test is the subtraction of time on part B minus time on part A (B–A), which taxes set-shifting abilities after subtraction of visuomotor speed.

**Self-regulation–Revised Strategy Application Test (R-SAT) (30):** This is a multitasking test that consists of three types of activities: figure tracing, sentence copying, and object numbering. The activities are presented on two different stacks (A and B), each containing 120 items. The main goal of the task is to win as many points as possible. However, the items can be of different difficulty: some of them are easy and quick to complete (i.e., they take a couple of seconds and are defined as “brief items”), whereas others are very laborious and time-consuming (i.e., they can take longer than 1 min and are defined as “lengthy items”). Given the limitation of time (10 min), the most efficient strategy (to be discovered) is to complete only the brief items to the exclusion of lengthy items, which the subjects must learn to skip as they are introduced in the latter pages of the test; this way subjects can optimize long-term profit by completing more items during the time limit. The main dependent variable from the R-SAT is the proportion of brief items completed in relation to the total number of items attempted.

**Effective decision-making–IGT (31):** This is a computer task that factors several aspects of decision-making, including uncertainty, risk, and evaluation of reward and punishing events. The IGT involves four decks or cards, decks A', B', C', and D'. Each time a participant selects a card, a specified amount of play money is awarded. However, interspersed among these rewards, there are probabilistic punishments (monetary losses with different amounts). Two of the decks of cards (A' and B') produce high immediate gains; however, in the long run, these two decks will take more money than they give and are therefore considered to be the disadvantageous decks. The other two decks (C' and D') are considered advantageous, as they result in small, immediate gains, but will yield more money than they take in the long run. The main dependent variable from this task was the net score for each block of the task (5 blocks of 20 trials). We calculated net scores by subtracting the number of disadvantageous

choices (decks A and B) from the number of advantageous choices (decks C and D) for each block. We also calculated the global IGT net score applying the same formula to the 100 trials of the task. In addition, we calculated the number of individuals that scored below a cutoff of zero, which represents clinically significant impairment in the task.

## Procedures

Prior to inclusion in the study, all participants and their parents signed an informed consent form. All assessments were conducted in accordance with ethical rules for research in human subjects following the Declaration of Helsinki (Edinburgh, 2000), World Medicine Association (<http://www.wma.net>). Moreover, the ethical approvals were obtained from the Bioethical Committee of the Clinical University Hospital San Cecilio of Granada and the Bioethical Committee of the University of Granada. Subjects were assessed on two different sessions, one for neuropsychological assessment, and one for questionnaire measures in order to avoid potential effects of fatigue. Both sessions were conducted on a comfortable adequately illuminated room at the hospital facilities. Each session had an approximate duration of 1 h. All tests were administered by a research assistant with master's degree in clinical psychology. Neuropsychological test administration was arranged to alternate between verbal and nonverbal tasks, and between more and less demanding tasks; these tests were administered in a fixed order to all participants. Questionnaire measures were counterbalanced for administration across participants.

## Data analyses

Statistical analyses were implemented on SPSS v.17 (SPSS, Chicago, IL). We first explored dependent variables to examine missing data points, normality of distributions (tested by Kolmogorov–Smirnov tests), and presence of outliers (defined by the Explore command of SPSS v.17). Data from questionnaire measures of 10 controls were missed due to nonattendance to the questionnaire measures session (thus,  $n = 24$  for the normal-weight group on these measures). One outlier was detected in the IGT distribution of the excess-weight group, and this subject was removed from further analyses of this task. Preliminary group comparisons for demographic variables showed that, despite having the same age range, the two groups were not significantly matched for age. Age was not significantly associated with any of the dependent variables (with the exception of the Stroop test,  $r = 0.21$ ,  $P < 0.05$ , and the SR subscale from the SPSRQ questionnaire,  $r = 0.40$ ,  $P < 0.01$ ). However, we chose to apply a conservative approach to control for possible effects of this variable on neuropsychological performance. Therefore, we regressed age on the dependent variables using standard regression models, and then we saved the standardized residuals from these models for further analyses. Therefore, group comparisons for neuropsychological and personality measures were conducted on the standardized residual scores, after removing any effect of age. On those variables where residuals followed a normal distribution (UPPS-P subscales—with the exception of lack of perseverance, SR subscale, letter-number sequencing, Stroop interference, FDT interference, FDT switching, TMT B-A, and R-SAT proportion of brief items), we conducted independent sample  $t$ -tests to examine differences between participants with excess weight and participants with normal weight. On those variables where residuals failed to meet normality assumptions ( $k$  delay-discount parameter, UPPS-P lack of perseverance, SP subscale, similarities, zoo map, and IGT net score), we used nonparametric Z Kolmogorov–Smirnov tests. To facilitate reading, in the tables we reported raw descriptive scores from questionnaire and neuropsychological measures (instead of descriptive scores from standardized residuals); on the other hand, we reported  $P$  values obtained from statistical tests performed on the standardized residuals (age-corrected). In addition, to further explore the association between BMI and neuropsychological performance (while controlling for other relevant variables), we performed hierarchical multiple regression analyses. We included two blocks of predictor variables: (i) sex, age, and IQ (in a first block) and



(ii) standardized zBMI scores (in a second block). For each new block of variables entered in the regression model, we estimated the  $R^2$  of the prediction change associated with that block and its statistical significance, with the aim of determining the differential contribution of each of the blocks to the prediction output. The dependent variables were the scores from personality and neuropsychological measures.

## RESULTS

### Demographic variables

The two groups (excess weight vs. normal weight) had similar distributions for sex, height, and IQ; and differed significantly on weight and BMI (Table 1). In addition, as noted above, both groups differed significantly on age.

### Questionnaire measures

There were no significant differences between groups on any of the questionnaire measures of impulsivity (UPPS-P and delay discounting) and sensitivity to reward/punishment (SPSRQ) (Table 2).

### Neuropsychological measures of executive functions

After subtracting potential effects of age through regression models, we found significant differences between groups on the dependent variables of FDT interference and switching scores, TMT B-A flexibility score, and IGT net score. There were also marginally significant differences between groups on the Stroop ( $P = 0.07$ ). In all cases, excess-weight participants performed poorer than normal-weight participants (Table 3). More detailed analyses were conducted for the IGT. To test whether the groups differed on the overall pattern of performance across blocks, we conducted a repeated-measures ANOVA. Results revealed a marginally significant “block  $\times$  group” interaction for performance in the task,  $F(4,54) = 2.15$ ,  $P = 0.07$ . Therefore, we conducted pairwise post hoc analyses comparing both groups on each of the five blocks using non-parametric Z Kolmogorov–Smirnov tests on the standardized residual scores from each block (after controlling for age). These results showed that subjects with excess weight performed significantly poorer than controls on blocks 4 ( $Z = 1.34$ ,  $P = 0.05$ ) and 5 ( $Z = 1.41$ ,  $P = 0.04$ ), and marginally significantly poorer on block 3 ( $Z = 1.23$ ,  $P = 0.09$ ) (Figure 1). In addition, we calculated the proportion of participants within each group who performed within the range of clinically significant deficits as

defined by a net score below zero (meaning overall preference for disadvantageous vs. advantageous decks). A  $\chi^2$  analysis showed that the proportion of participants with relative decision-making deficits was significantly higher on the excess-weight group (Table 3). We found nonsignificant differences between groups on letter-number sequencing, similarities, zoo map, and R-SAT proportion of brief items (Table 3).

Calculation of effect sizes (Cohen's  $d$ ) for significant differences between groups yielded a large effect size for the TMT B-A ( $d = 0.8$ ), and medium effect sizes for the FDT and the Stroop ( $d = 0.6$ ), and the IGT ( $d = 0.5$ ).

### Association between BMI and neuropsychological performance

Results from regression models showed that zBMI scores significantly predicted performance on TMT B-A,  $\beta = 0.49$ ,  $P = 0.000$ , and showed a trend to significant prediction of FDT switching,  $\beta = 0.23$ ,  $P = 0.07$ ; the higher the BMI, the poorer the performance in both tests. In the case of the TMT B-A, the effects of BMI were significantly greater than those of the block of age, sex, and IQ (as shown by significant changes in  $R^2$  values after inclusion of BMI in the models):  $R^2$  for the first block = 0.15 and  $R^2$  after inclusion of zBMI = 0.36 (significance in  $F$  change = 0.000). For the FDT switching, the effects of BMI improved the overall predictive value of the model:  $R^2$  for the first block = 0.11 and  $R^2$  after inclusion of zBMI = 0.16 (significance in  $F$  change = 0.07;  $P$  for the full model = 0.04). Similar results were obtained with the inclusion of BMI percentiles adjusted by sex and age, and based on Spanish norms (32). In addition, IQ significantly predicted performance on the zoo map,  $\beta = 0.39$ ,  $P = 0.005$ , whereas age significantly predicted SR scores,  $\beta = 0.42$ ,  $P = 0.002$ . For the remaining measures, there were no significant effects of the predictor variables.

**Table 2** Descriptive scores and statistics for scores of excess-weight and normal-weight groups on measures of reward sensitivity and impulsivity

	Excess weight ( $n = 27$ ) mean (s.d.)	Normal weight ( $n = 24$ ) mean (s.d.)	$t/Z$
UPPS-P negative urgency	26.3 (5.11)	26.3 (5.94)	$t = 0.07$
UPPS-P premeditation	24.81 (5.28)	23.62 (5.11)	$t = -0.05$
UPPS-P perseverance	21.74 (3.96)	20.5 (3.73)	$Z = 0.56$
UPPS-P sensation seeking	33.93 (7.86)	32.42 (6.06)	$t = 0.80$
UPPS-P positive urgency	25.85 (6.30)	26.04 (7.83)	$t = -0.03$
Sensitivity reward	9.59 (4.82)	11.87 (4.28)	$t = -0.34$
Sensitivity punishment	9.37 (4.52)	11.88 (4.29)	$Z = 0.84$
K (DDT)	0.04 (0.07)	0.01 (0.01)	$Z = 0.84$

K (DDT), K parameter from the delay discounting questionnaire.

**Table 1** Descriptive scores for sociodemographic (age, IQ) and physical characteristics (weight, height, and BMI)

	Excess weight ( $n = 27$ ) mean (s.d.)	Normal weight ( $n = 34$ ) mean (s.d.)	$t$
Age	14.3 (1.2)	15.29 (0.91)	$-3.58^a$
Weight	89.04 (22.09)	57.81 (8.91)	$6.91^a$
Height	161.69 (32.42)	165.15 (9.24)	$-0.59$
BMI	31.58 (7.08)	21.01 (1.97)	$7.53^a$
IQ (K-BIT)	105.07 (10.42)	109.91 (10.21)	$-1.82$

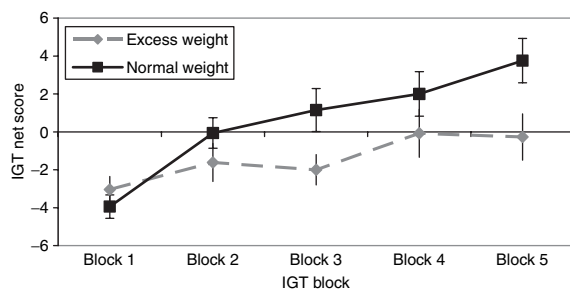
K-BIT, Kaufman brief intelligence test.

<sup>a</sup>Significant differences between groups.

**Table 3** Descriptive scores, statistics, and effect sizes for performance of excess-weight and normal-weight groups on neuropsychological measures

	Excess weight mean (s.d.)	Normal weight mean (s.d.)	<i>t</i> / <i>Z</i> / $\chi$	<i>P</i>	Effect size (Cohen's <i>d</i> )
LNS	19.96 (2.71)	20.41 (2.4)	<i>t</i> = -0.96	0.34	
Similarities	28.7 (4.86)	27.09 (4.9)	<i>Z</i> = 0.87	0.44	
Zoo map	12.44 (3.2)	14 (2.99)	<i>Z</i> = 1.19	0.12	
Stroop interference	0.17 (6.42)	4.96 (7.77)	<i>t</i> = -1.81	0.07	-0.6
FDT interference	9.26 (6.18)	5.38 (6.19)	<i>t</i> = 2.11	0.039	0.6
FDT switching	17.81 (9.4)	12.85 (8.09)	<i>t</i> = 2.12	0.038	0.6
TMT B-A	50.96 (34.47)	26.76 (13.05)	<i>t</i> = 3.24	0.003	0.8
R-SAT% brief items	0.47 (0.09)	0.50 (0.13)	<i>t</i> = -0.94	0.34	
IGT net score	-7 (16.1)	2.85 (19.79)	<i>Z</i> = 1.46	0.03	-0.5
IGT % impaired	77.8%	45.5%	$\chi$ = 6.47	0.017	

FDT, five-digit test; IGT, Iowa gambling task; LNS, letter-number sequencing; R-SAT, revised strategy application test.



**Figure 1** Iowa gambling task (IGT) performance across blocks of the excess-weight and normal-weight groups of adolescents. We obtained significant differences between groups on blocks 4 and 5, plus a trend on block 3.

## DISCUSSION

We show that adolescents with excess weight have poorer neuropsychological performance on tests of response inhibition, flexibility, and decision-making. In addition, regression models showed a significant detrimental effect of BMI on flexibility performance. Inspection of effect sizes indicated that cognitive flexibility (measured by the TMT) was the ability most significantly decreased in adolescents with excess weight. On the other hand, excess-weight adolescents do not differ from normal-weight controls in their performance on tests of working memory, planning, and analogical reasoning, or in self-report measures of impulsivity. These results are indicative of selective alterations within executive functions in adolescents with overweight.

We observed poorer performance of excess-weight adolescents on two independent measures of set shifting (TMT and FDT), which were significantly associated with BMI. In this respect, our results are congruent with previous evidence on children and young adults. A previous study conducted in a group of younger children (~12 years old) demonstrated poorer performance of children with excess weight, compared to normal-weight controls, on perseveration indexes from the Wisconsin card sorting test and on a measure of sustained

attention response accuracy (D2) (16). In this study, poor performance on these indexes was also significantly correlated with BMI. Further resembling our results, performance of excess-weight children did not differ from that of controls on measures of IQ, working memory, and verbal fluency, which were unrelated to BMI. Using a large sample of young and older adults, a recent study also showed that BMI was significantly correlated with neuropsychological measures of flexibility and response inhibition (17). Overall, these findings clearly point to a detrimental effect of increasing BMI on response monitoring and switching. Although these relative deficits could be attributed to generally slower response speed, this is very unlikely because in all cases, performance indexes were time-corrected with respect to control conditions measuring response speed (e.g., the nonincongruent digit condition of the FDT, and the trail A of the TMT).

The notion that these relative deficits in overweight adolescents relate to executive mechanisms is further supported by evidence from functional neuroimaging studies. A recent functional magnetic resonance imaging study of the TMT in healthy individuals showed that the subtraction of part B minus A engages prominent activation of the dorsolateral prefrontal cortex and the anterior cingulate gyrus (33). Similarly, recent findings from a positron emission tomography study demonstrate a significant association between BMI and reduced metabolic activity in the dorsolateral prefrontal and cingulate regions (6), and it has been suggested that these prefrontal cortex regions become dysregulated by altered dopamine D2 receptor signaling from the striatum (3), a basal ganglia nucleus that is structurally altered in obesity (34). Thus, convergent evidence from neuropsychology and neuroimaging point to dysfunctional frontal-executive systems in overweight subjects. Along these lines, it is interesting to note that we document the presence of executive deficits in adolescents that have not yet likely developed a fully functioning executive system (13,35). However, the current data cannot resolve if the association of BMI and executive function is due to the deleterious effects of increased weight on

prefrontal blood flow and executive competence, or to the possibility that children with poor executive skills are more likely to become obese. This question could be addressed by longitudinal designs or by experimental studies manipulating executive function to investigate whether adolescents with higher executive proficiency are more likely to benefit from evidence-based treatments for weight control. In any case, our data have important implications for prevention and treatment interventions, considering that adolescents with relatively weak mental flexibility may be more susceptible to weight gain through several behavioral mechanisms.

Our results also show that adolescents with excess weight performed poorer than normal-weight controls on the IGT. This finding has been previously reported in adults (19,20). Our analysis on the proportion of subjects with clinically decreased performance demonstrates that 78% of the excess-weight adolescents were below the zero cutoff indexing a clear preference for disadvantageous risky decks. Furthermore, inspection of the IGT learning curve indicated that their preference for risky decks was relatively constant throughout the task, suggesting an inability to reverse increasingly disadvantageous choices. These results should be interpreted with caution because decision-making skills are particularly sensitive to age-related neurocognitive changes during adolescence (36–38). Nonetheless, we should note that in our sample, age was not correlated with IGT performance, groups had similar IQ distributions, and age effects were conservatively controlled through regression models. Furthermore, on average, performance scores of our excess-weight subgroup (including adolescents aged 13–16) are substantially poorer than those of the lower limit equivalent age subgroup of adolescents in the Overman *et al.* study (i.e., 13-year-old 9th graders): 46% vs. 65% of advantageous selections. Therefore, the data indicate that decision-making deficits (or maturational delays in this function) are also present in adolescents with excess weight. This is also consistent with recent theoretical models that posit that altered homeostatic/emotional signals may bias decision-making toward short-term reinforcement in different disorders involving motivation and choice, including addiction and obesity (2,5,7,8,39). It has been proposed that parallels between addiction and obesity may have important implications for the treatment of pediatric obesity, which currently lacks a “gold-standard” treatment of choice (1).

This study has worth-noting limitations. First, it is surprising that trait measures of impulsivity and sensitivity to reward failed to discriminate between the groups, especially considering that excess-weight adolescents performed significantly poorer on cognitive measures of response inhibition. There is a long-standing lack of correspondence between questionnaire and neuropsychological measures of impulsivity (40), but in this case, it is possible that social desirability biases are further distorting results. In addition, age was not statistically matched between groups. Although we controlled for age effects through regression models, future studies should attempt to fully match the groups for age distribution. Other relevant limitations of this study are the different sources of recruitment of

the normal-weight and overweight participants, the relatively small sample size, and the high level of missing questionnaire data in the normal-weight group; these limitations should be adequately addressed in the forthcoming studies. Furthermore, our excess-weight group was composed by both adolescents meeting BMI cutoff criteria for obesity and adolescents meeting criteria for overweight (a minority). It could be argued that different results may emerge when studying an exclusive obesity group; however, we conducted post hoc analyses (data not shown) and found that obese and overweight adolescents did not differ significantly on cognitive performance, and that comparison of the subgroup of obese adolescents with controls did not alter results at all. These results further strengthen the need to perform early interventions in children/adolescents at risk for overweight and obesity.

#### ACKNOWLEDGMENTS

This study has been funded by grants from the Spanish Ministry of Health (Fondo de Investigaciones Sanitarias, grant 05/2369), and the Andalusian Service of Health (Servicio Andaluz de Salud, grant PI-0416/2008).

#### DISCLOSURE

The authors declared no conflict of interest.

© 2010 The Obesity Society

#### REFERENCES

- Acosta MC, Manubay J, Levin FR. Pediatric obesity: parallels with addiction and treatment recommendations. *Harv Rev Psychiatry* 2008;16:80–96.
- Volkow ND, Wang GJ, Fowler JS, Telang F. Overlapping neuronal circuits in addiction and obesity: evidence of systems pathology. *Philos Trans R Soc Lond, B, Biol Sci* 2008;363:3191–3200.
- Volkow ND, Wang GJ, Telang F *et al.* Low dopamine striatal D2 receptors are associated with prefrontal metabolism in obese subjects: possible contributing factors. *Neuroimage* 2008;42:1537–1543.
- Goldstein RZ, Volkow ND. Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. *Am J Psychiatry* 2002;159:1642–1652.
- Verdejo-García A, Bechara A. A somatic marker theory of addiction. *Neuropharmacology* 2009;56(Suppl 1):48–62.
- Volkow ND, Wang GJ, Telang F *et al.* Inverse association between BMI and prefrontal metabolic activity in healthy adults. *Obesity (Silver Spring)* 2009;17:60–65.
- Berthoud HR. Interactions between the “cognitive” and “metabolic” brain in the control of food intake. *Physiol Behav* 2007;91:486–498.
- Paulus MP. Decision-making dysfunctions in psychiatry—altered homeostatic processing? *Science* 2007;318:602–606.
- Chambers RA, Taylor JR, Potenza MN. Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. *Am J Psychiatry* 2003;160:1041–1052.
- Van Leijenhorst L, Zanolie K, Van Meel CS *et al.* What motivates the adolescent? Brain regions mediating reward sensitivity across adolescence. *Cereb Cortex* 2009; e-pub ahead of print 30 April 2009.
- Ernst M, Nelson EE, Jazbec S *et al.* Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *Neuroimage* 2005;25:1279–1291.
- Bunge SA, Wright SB. Neurodevelopmental changes in working memory and cognitive control. *Curr Opin Neurobiol* 2007;17:243–250.
- Waber DP, De Moor C, Forbes PW *et al.*; Brain Development Cooperative Group. The NIH MRI study of normal brain development: performance of a population based sample of healthy children aged 6 to 18 years on a neuropsychological battery. *J Int Neuropsychol Soc* 2007;13:729–746.
- Crone EA, Bullsens L, van der Plas EA, Kijkuit EJ, Zelazo PD. Developmental changes and individual differences in risk and perspective taking in adolescence. *Dev Psychopathol* 2008;20:1213–1229.
- Ernst M, Pine DS, Hardin M. Triadic model of the neurobiology of motivated behavior in adolescence. *Psychol Med* 2006;36:299–312.

16. Cserjési R, Molnár D, Luminet O, Lénárd L. Is there any relationship between obesity and mental flexibility in children? *Appetite* 2007;49:675–678.
17. Gunstad J, Paul RH, Cohen RA *et al*. Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Compr Psychiatry* 2007;48:57–61.
18. Boeka AG, Lokken KL. Neuropsychological performance of a clinical sample of extremely obese individuals. *Arch Clin Neuropsychol* 2008;23:467–474.
19. Pignatti R, Bertella L, Albani G *et al*. Decision-making in obesity: a study using the Gambling Task. *Eat Weight Disord* 2006;11:126–132.
20. Davis C, Levitan RD, Muglia P, Bewell C, Kennedy JL. Decision-making deficits and overeating: a risk model for obesity. *Obes Res* 2004;12:929–935.
21. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000;320:1240–1243.
22. Whiteside SP, Lynam DR. Understanding the role of impulsivity and externalizing psychopathology in alcohol abuse: application of the UPPS impulsive behavior scale. *Exp Clin Psychopharmacol* 2003;11:210–217.
23. Kirby KN, Petry NM, Bickel WK. Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *J Exp Psychol Gen* 1999;128:78–87.
24. Torrubia R, Avila C, Molto J, Caseras X. The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. *Pers Individ Dif* 2001;31:837–862.
25. Kaufman AS, Kaufman NL. Kaufman Brief Intelligence Test. Tea Editions: Madrid, 2000.
26. Wechsler D. Wechsler Intelligence Scale for Children, 4th edn. Tea Editions: Madrid, 2005.
27. Alderman N, Burgess PW, Emslie H, Evans J, Wilson B. *Behavioral Assessment of the Dysexecutive Syndrome (BADS)*. Thames Valley Test Company Eds: London, 1996.
28. Golden CJ. Stroop: Test of Colors and Words. Tea Editions: Madrid, 1994.
29. Sedó M. Five Digits Test. Tea Editions: Madrid, 2008.
30. Levine B, Dawson D, Boutet I, Schwartz ML, Stuss DT. Assessment of strategic self-regulation in traumatic brain injury: its relationship to injury severity and psychosocial outcome. *Neuropsychology* 2000;14:491–500.
31. Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* 1994;50:7–15.
32. Carrascosa Lezcano A, Fernández García JM, Fernández Ramos C *et al*.; Grupo Colaborador Español. [Spanish cross-sectional growth study 2008. Part II. Height, weight and body mass index values from birth to adulthood]. *An Pediatr (Barc)* 2008;68:552–569.
33. Zakzanis KK, Mraz R, Graham SJ. An fMRI study of the Trail Making Test. *Neuropsychologia* 2005;43:1878–1886.
34. Pannacciulli N, Del Parigi A, Chen K *et al*. Brain abnormalities in human obesity: a voxel-based morphometric study. *Neuroimage* 2006;31:1419–1425.
35. Lenroot RK, Giedd JN. Brain development in children and adolescents: insights from anatomical magnetic resonance imaging. *Neurosci Biobehav Rev* 2006;30:718–729.
36. Hooper CJ, Luciana M, Conklin HM, Yarger RS. Adolescents' performance on the Iowa Gambling Task: implications for the development of decision making and ventromedial prefrontal cortex. *Dev Psychol* 2004;40:1148–1158.
37. Overman WH, Frassrand K, Ansel S *et al*. Performance on the IOWA card task by adolescents and adults. *Neuropsychologia* 2004;42:1838–1851.
38. Crone EA, van der Molen MW. Development of decision making in school-aged children and adolescents: evidence from heart rate and skin conductance analysis. *Child Dev* 2007;78:1288–1301.
39. Finlayson G, King N, Blundell JE. Liking vs. wanting food: importance for human appetite control and weight regulation. *Neurosci Biobehav Rev* 2007;31:987–1002.
40. Verdejo-García A, Lawrence AJ, Clark L. Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. *Neurosci Biobehav Rev* 2008;32:777–810.