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Decision-making in obesity without eating disorders: A systematic review and meta-analysis of Iowa Gambling Task performances

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Running title: Impaired decision-making in obesity

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Abstract

Background: There is evidence that obesity is associated with impairments in executive functions, such as deficits in decision-making, planning or problem solving, which might interfere with weight loss in obese individuals. We performed a systematic review and meta-analysis of decision-making abilities, as measured with the Iowa Gambling Task (IGT), in obesity without eating disorders.

Methods: A systematic search was conducted to identify studies comparing IGT performances between groups of obese patients without eating disorders and groups of healthy control groups. The standardized mean differences (SMDs) were calculated for the total IGT scores and for the course of IGT scores. Meta-regression analyses were performed to explore the influence of clinical variables on SMDs.

Results: Total IGT scores were significantly lower in obese patients compared to normal-weight healthy controls. IGT performances did not differ between groups for the first trials of the task. Significant effect sizes for the last trials of the task were subjected to a high degree of heterogeneity.

Conclusion: Risky decision-making is impaired in obesity. The clinical importance of non-food-related decision-making impairments remains to be assessed especially in terms of consequences in daily life or the achievement of weight-loss.

This meta-analysis has been registered in the Prospero database (CRD42016037533).

Introduction

The prevalence of obesity, which represents a major public health concern, has substantially increased worldwide over the last decades (1). Obesity enhances the risk of other chronic diseases such as type 2 diabetes, cardiovascular diseases, obstructive sleep apnea, and several cancers (2-5). Regarding obesity management, maintaining weight loss is often difficult or unsuccessful (6). To improve the current therapeutic strategies, it appears crucial to identify the factors hampering the achievement of weight loss and weight maintenance in obese individuals.

Many studies have reported impairments in executive functions associated with obesity both in children and adults (7). For example, Fergenbaum et al. (8) and Gunstad et al. (9) reported lower performances in executive functioning tasks in obese patients compared to normal-weight healthy controls in 207 and 408 participants, respectively. Although some inconsistencies appear across studies, a recent qualitative review highlighted strong deficits in decision-making, planning or problem solving in obese patients (7). Impairments in executive functioning have been proposed as a barrier to the achievement of weight loss (10), suggesting the importance to target specific cognitive impairments related to obesity in therapeutic strategies. Consistent with the NIMH RDoC approach (11) aiming to understand the basic dimensions of functioning underlying human behaviors, there is an urgent need to better identify the cognitive deficits in obesity to analyze how they impact weight loss and weight maintenance and subsequently to identify possible cognitive biomarkers of weight maintenance.

According to the food addiction model, drawing a parallel between cognitive and behavioral characteristics of addictive disorders and obesity (12), it appears relevant to study decision-making abilities in obesity according to their clinical importance in the maintenance of addictive behaviors. The Iowa Gambling Task (IGT) is the gold standard procedure for assessing decision-making abilities (13), which include many cognitive and emotional processes allowing to make a choice from several alternative options based on objective and/or subjective values. IGT is based on non-food stimuli, rewards, or penalties. During IGT, participants receive no specific instructions and have to repetitively choose 100 cards from four different decks without knowledge of the contingency of the options. Each choice results in a gain or in a loss of money. The task consists in five blocks of 20 cards. Card decks characterized by high immediate rewards or penalties are long-term disadvantageous, whereas card decks characterized by low immediate rewards or penalties are long-term advantageous. Subjects without decision-making impairments, learn to avoid long-term disadvantageous options in favor of long-term advantageous options. Interestingly, the course of IGT performances allows discriminating decisions under ambiguity and decisions under risk, which have different cognitive and neural correlates (14). The very first trials correspond to decisions under ambiguity characterized by unknown contingencies, whereas the following trials correspond to decisions under risk characterized by known probability distribution of possible outcomes. Very little is known about the course of IGT performances in obesity.

Possible impairments in decision-making associated with obesity have to be elucidated. For this purpose, two main issues are considered. First, many decision-making or gambling tasks, with or without food stimuli, have been used through different studies. However, those different tasks may involve different cognitive processes, such as ambiguous or risky decisions that can be disentangled with the standardized versions of IGT. For this reason, we

focused on IGT decision-making. Second, obesity is often associated with eating disorders, especially binge eating disorders (15), which are associated with impaired decision-making (16). Therefore, it is of major interest to describe decision-making specifically related to obesity without eating disorders. To provide a quantitative overview of decision-making abilities in obesity, we have conducted a systematic review and meta-analysis of studies comparing IGT performances between obese patients without eating disorders and healthy subjects.

Materials and methods

Data sources and study selection process

This meta-analysis has been registered in the Prospero database (CRD42016037533). We searched the MEDLINE and PsycINFO databases through January 2016, without limits on year of publication, using the keywords "obesity" and any of the following terms: "decision-making", "Iowa gambling task" or "gambling task". The reference lists of identified articles were screened to obtain additional papers. Studies were considered for inclusion if (i) they were published in English in a peer-reviewed journal, (ii) they reported IGT performances (means and SD), (iii) they compared a group of obese patients (body mass index, BMI ≥ 30 kg/m²), explicitly without binge eating disorders, and a group of normal-weight healthy controls. Studies that included patients with binge eating disorders or any other eating disorder were excluded.

Data extraction

For each identified study and for each included group, mean and SD were extracted for IGT net score (advantageous choices minus disadvantageous choices). The same data were also extracted for each of the five blocks to assess the time course of IGT performances allowing to disentangle decision-making under ambiguity and decision-making under risk. When data were not reported in the text, they were extracted from figures with an open source software, Plot Digitizer, as described previously (17). **Demographic and clinical** data were also extracted, particularly age (mean and SD), gender (% female) and BMI (mean and SD).

Data analyses

Data analyses were performed using RevMan version 5.3.5 (The Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). Effect sizes were determined by standardized mean differences (SMDs) between the obesity group and the control group. SMDs were calculated as the differences between group means divided by the pooled SD. Individual SMDs from each study were then combined to estimate the overall SMD. All analyses were conducted with the random-effect model that considered both between-study and within-study variabilities (18). SMDs were considered significant when the 95% confidence interval (95% CI) excluded 0 and when the p value was strictly below 0.05.

When SMDs were found significant, study heterogeneity was assessed by the Q statistic. The I^2 index, an estimate of the total variation across included studies that was due to heterogeneity rather than chance, was then calculated as follows: $I^2 = [(Q - df) / Q] * 100\%$ (19). I^2 values of 25, 50, and 75 were used as indicators of mild, moderate, and high heterogeneity between trials, respectively. Leave-one-out sensitivity analyses were performed by repeating the analyses with the consecutive exclusion of each study to ensure that significant SMD or heterogeneity was not driven by one single study. The possibility of

publication bias was analyzed using funnel plots, which plot the standard error of each SMD against the SMD. Funnel plots symmetry was assessed to identify putative publication or location biases (20). Regression analyses based on linear regression models were conducted with age, gender, and BMI as independent variables, with the aim to assess whether clinical variables could contribute to explain significant SMDs or heterogeneity.

Results

Out of 1,594 potentially relevant studies, the study selection process led to the identification of seven studies fulfilling the inclusion criteria (Figure 1; 21-27). Table 1 summarizes the main characteristics of included studies. Included studies involved a total of 250 obese patients and 362 healthy controls. The mean age ranged from 14.3 to 52.2 years. The percentage of females varied from 40% to 100%. The mean BMI ranged from 30.8 to 42.2 kg/m² in obese groups.

IGT net scores were decreased in the obesity group in comparison to healthy controls (Figure 2A; SMD = -0.83, 95% CI = -1.34 to -0.33, $p < 0.0001$); however, heterogeneity tests were significant ($\chi^2 = 28.03$, $p < 0.0001$, $I^2 = 82\%$). The study by Davis *et al.* (23) could not be included in this analysis because of missing data. Leave-one-out analyses showed that heterogeneity was driven by one single study. Indeed, the exclusion of the study by Brogan *et al.* (22) affected the heterogeneity tests ($\chi^2 = 2.06$, $p = 0.73$, $I^2 = 0\%$) but not the significance of SMD (SMD = -0.48, 95% CI = -0.68 to -0.27, $p < 0.0001$). This study differed from other studies by a very high IGT net score in the healthy group (32.9 vs. 2.8 – 17.3). All other leave-one-out analyses did not markedly change SMDs or heterogeneity, particularly the exclusion of studies, which included obese patients but also overweight adolescents (24) or

patients who underwent bariatric surgery (22). Funnel plots revealed no publication bias. Using regression models, no significant relationship was found between SMDs and any of the clinical variables: age, gender, and BMI (all p values > 0.05).

To assess the course of performance throughout the task, SMDs were calculated for each of the five blocks (20 trials per block) between the obesity group and the healthy group (Figure 2B). These data could be extracted from four studies (21, 22, 24, 27). For block #1, no difference was observed between groups (block 1: SMD = 0.07, 95% CI = -0.38 to 0.51, $p = 0.77$). For the four next blocks, obese patients chose significantly more disadvantageous options than healthy controls (block 2: SMD = -0.43, 95% CI = -0.79 to -0.06, $p < 0.05$; block 3: SMD = -1.15, 95% CI = -2.19 to -0.11, $p < 0.05$; block 4: SMD = -1.35, 95% CI = -2.33 to -0.38, $p < 0.01$; block 5: SMD = -1.11, 95% CI = -2.04 to -0.18, $p < 0.05$). Heterogeneity tests demonstrated no significant heterogeneity for block #2, giving confidence in the observed difference. In contrast, they showed a very high level of heterogeneity across studies for blocks #3 to #5, making the differences more difficult to interpret for these blocks (block 2: $\chi^2 = 6.12$, $p = 0.11$, $I^2 = 51\%$; block 3: $\chi^2 = 40.83$, $p < 0.0001$, $I^2 = 93\%$; block 4: $\chi^2 = 34.83$, $p < 0.0001$, $I^2 = 91\%$; block 5: $\chi^2 = 33.14$, $p < 0.0001$, $I^2 = 91\%$). Leave-one-out analyses did not markedly alter the results; in particular, the high level of heterogeneity for blocks #3 to #5 was not driven by one single study. Funnel plots revealed no publication bias. Regression models demonstrated no relationship between SMDs and any of the clinical variables: age, gender, and BMI (all p values > 0.05).

Discussion

The present systematic review and meta-analysis showed that obesity was associated with impairments in decision-making. More specifically, decisions under ambiguity (i.e. without knowledge of the contingencies of the different options) did not differ between the obesity group and the control group, whereas decisions under risk (i.e. with knowledge of such contingencies) were affected in the obesity group in comparison to the control group. However, there was a great heterogeneity across studies and **no relationship between obesity-related impairments in decision-making and age, gender, or BMI was found.**

The present results are in line with studies having assessed decision-making performances with other non-food-related tasks, such as delayed discounting task. A recent review of delay discounting performance suggested that obese patients without eating disorder demonstrated increased rates of delay discounting in comparison with healthy controls (28). Increased rates of delay discounting reflects a preference for smaller and sooner reward rather than larger and later reward, a hallmark of choice impulsivity. Accordingly, impaired risky decision-making in IGT suggest that obese patients may be more prone to prefer high-risk and long-term disadvantageous options rather than low-risk and long-term advantageous options. Taken together, these findings claim for an association between obesity and cognitive impulsivity, as a manifestation of disrupted self-regulatory control (29, 30). Impulsivity is thought to be an endophenotype facilitating the development of habit or compulsive behaviors, as involved in obsessive-compulsive, pathological gambling, addictions, etc (30). Concurrently, impulsivity has been associated with overeating and obesity (31, 32). Decision-making impairments might thus be interpreted as the expression of an impulsivity endophenotype predisposing individuals to obesity. However, risky decision-making is a multidimensional construct, involving many cognitive or affective processes, such as processing internal states for instance.

According to the somatic marker hypothesis, which claimed that emotional and internal states may affect decision-making, obese patients might give priority to positive somatic markers related to the possible high immediate reward rather than to negative somatic markers warning the negative consequences of the decision (33). As described in the field of addiction, obese patients may thus have a "myopia for the future" (i.e. less sensitive to the long-term consequences of their decisions) or a hypersensitivity to reward leading to engage in behaviors directed to highest rewards (33, 34) or both. This view is in accordance with the food addiction model supporting that some eating behaviors in obesity may have characteristics and neural correlates similar to addictive behaviors (12). Furthermore, neuroimaging studies demonstrated the involvement of brain circuits in IGT, such as the orbitofrontal cortex and the insula, which are critical to select "now vs. later actions" based on interoceptive information (35). Therefore, impairments in risky decision-making might contribute to explain, at least in part, the difficulty to manage eating behaviors leading to seek and consume highly palatable food items despite known long-term negative consequences of such behavior (12, 36, 38).

A high level of heterogeneity across studies, unexplained by the clinical variables analyzed, was found for decision-making under risk. This heterogeneity could not be explained by methodological differences as all included studies used the very same version of the IGT. It could thus be assumed that this heterogeneity could be supported by interindividual differences in IGT. Indeed, whereas some obese patients may have a normal pattern of decisions, others may have a strong preference toward risky options and others may have an intermediate profile. **Some demographic or clinical characteristics, which could not be taken into account in the present meta-analysis, such as socio-economic status, sleep disorders or**

psychiatric comorbidities, may interfere with decision-making processes and therefore might represent the missing link for explaining heterogeneity across studies. Future large scale studies assessing decision-making in obesity should therefore provide a full characterization of the participants and explore possible mediations between these characteristics and decision-making performances. Finally, it remains to be determined whether these different patterns of decision-making might be clinically relevant, especially in relation to weight loss, and might be used as cognitive biomarkers of patient profiles. For example, it has been shown that individuals with high sensitivity to reward may be at risk of attrition in weight management (37), but it remains unknown whether decision-making deficits may annihilate weight loss achievements and whether therapeutic strategies directed against these executive deficits may help in losing weight. Future studies are thus required to address these issues that may have some considerable clinical implications. For example, one may hypothesize that cognitive remediation targeting decision-making impairments may contribute to weight loss, especially by improving self-regulatory control. With the assumption that decision-making alterations might represent a cognitive endophenotype, it would be of interest to test whether it may predict outcomes or complications of bariatric surgery for instance.

The present meta-analysis has some limitations. There was a limited number of included studies. Seven studies were included for the analyses of the IGT net scores and four for the analyses of the course of IGT performances. Furthermore, sample size was small in some studies, for example, three studies included ≤ 20 obese individuals (21, 22, 26), and in some studies included samples were unmatched for age (22, 27) or education (23). This disparity might also contribute to the heterogeneity of effect sizes across studies. This small number of studies should also be considered regarding a possible lack of statistical power in regression models to detect any putative relationship between SMDs and demographic and clinical

variables. However, all included studies used the same IGT task, which represents an important strength of the present work. Indeed, this allowed assessing the course of performances and it provided high precision and specificity regarding the assessed cognitive functions. In addition, the risk of heterogeneity due to different methodological procedures was limited.

In conclusion, the results of this study suggest that obesity might be associated with impairments in decision-making under risk. The clinical impact of such decision-making deficits remains to be further investigated, especially regarding its influence on how obese individuals perform in daily life and regarding weight loss outcomes.

Figure legends

Figure 1: Article identification process of studies assessing decision-making with the Iowa Gambling Task in obesity in comparison to healthy controls.

Figure 2: Individual and overall SMDs for IGT net scores (**A**, **n=6 studies**) and the course of SMDs throughout IGT trials (**B**, **n=4 studies**). Positive SMDs were in favor of the obesity groups and negative SMDs were for the control groups.

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Table 1. Included IGT studies

Study	Number of IGT trials	Obesity groups					Control groups					SMD (95% CI)	Main outcomes and comments
		N	Mean age	% female	Mean BMI	Mean education years	N	Mean age	% female	Mean BMI	Mean education years		
Pignatti et al., 2006 (21)	100	20	43.4	70	42.2	10.2	20	46.7	50	22.2	11.7	-15.7 (-29.5 to -2.0)	Net scores and IGT performances of blocks 2, 3, 4 and 5 were impaired in obesity
Davis et al., 2010 (23)	100	73	35.2	100	38.6	42.5%#	71	31.8	100	21.7	75.7%#	NA	Net scores and the course of IGT performances (# blocks were not available) were impaired in obesity
Verdejo-Garcia et al., 2010 (24)	100	27	14.3	40.7	31.6	NA	34	15.3	38.2	21.0	NA	-9.8 (-18.8 to -0.8)	Net scores and IGT performances of blocks 4 and 5 were impaired in obesity
Brogan et al., 2010 (22)	100	18	52.1	100	36.2	14.0	20	27.8	100	21.6	12.2	-34.0 (-41.2 to -26.9)	Net scores and IGT performances of blocks 3, 4 and 5 were impaired in obesity. 55% obese participants had undergone bariatric surgery
Brogan et al., 2011 (25)	100	42	52.2	71.4	41.5	14.0	50	47.3	66.0	24.4	13.9	-15.9 (-26.6 to -5.1)	Net scores and IGT performances of blocks 3, 4 and 5 were impaired in obesity

Danner et al., 2012 (26)	100	18	44.6	100	30.8	7.0*	30	36.1	100	22.3	6.9*	-12.1 (-24.8 to 0.5)	Net scores and the course of IGT performances (# blocks were not available) were impaired in obesity
Fagundo et al., 2012 (27)	100	52	40.5	100	39.8	14.3	13 7	24.8	100	21.5	15.5	-8.8 (-18.3 to 0.7)	Net scores and IGT performances of blocks 2 and 3 were impaired in obesity

IGT: Iowa Gambling Task; BMI: Body Mass Index; **SMD: Standardized Mean Difference; 95% CI: 95% Confidence Interval**; NA: Not Available

*The reported values consisted in mean education level (and not in mean education years)

#The reported values consisted in the percentage of subjects with an undergraduate or graduate degree

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Supplementary Figures

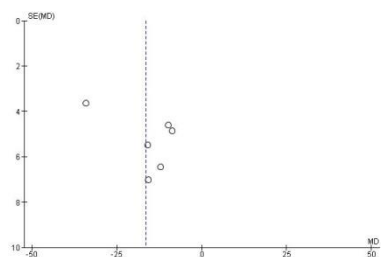


Figure S1. Funnel plots for IGT net scores.

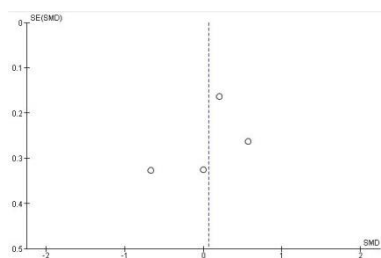


Figure S2. Funnel plots for IGT block-1 scores.

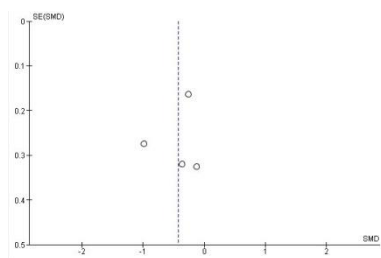


Figure S3. Funnel plots for IGT block-2 scores.

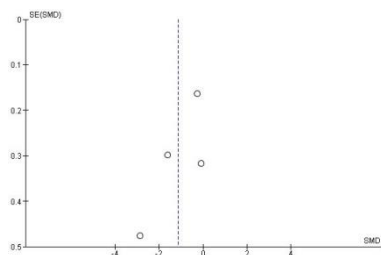


Figure S4. Funnel plots for IGT block-3 scores.

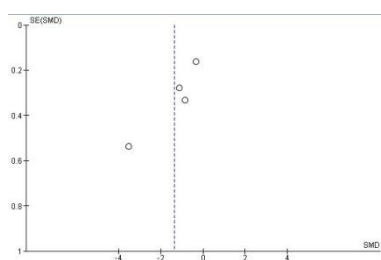


Figure S5. Funnel plots for IGT block-4 scores.

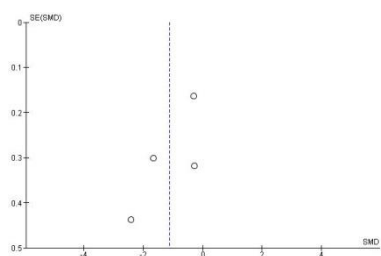


Figure S6. Funnel plots for IGT block-5 scores.