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Working memory and reward association learning impairments in obesity

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ABSTRACT

Obesity has been associated with impaired executive functions including working memory. Less explored is the influence of obesity on learning and memory. In the current study we assessed stimulus reward association learning, explicit learning and memory and working memory in healthy weight, overweight and obese individuals. Explicit learning and memory did not differ as a function of group. In contrast, working memory was significantly and similarly impaired in both overweight and obese individuals compared to the healthy weight group. In the first reward association learning task the obese, but not healthy weight or overweight participants consistently formed paradoxical preferences for a pattern associated with a negative outcome (fewer food rewards). To determine if the deficit was specific to food reward a second experiment was conducted using money. Consistent with Experiment 1, obese individuals selected the pattern associated with a negative outcome (fewer monetary rewards) more frequently than healthy weight individuals and thus failed to develop a significant preference for the most rewarded patterns as was observed in the healthy weight group. Finally, on a probabilistic learning task, obese compared to healthy weight individuals showed deficits in negative, but not positive outcome learning. Taken together, our results demonstrate deficits in working memory and stimulus reward learning in obesity and suggest that obese individuals are impaired in learning to avoid negative outcomes.

1. Introduction

The extent to which cognitive functioning is impaired in obesity has been under active investigation for a number of years (e.g., Chelune et al., 1986; Elias et al., 2003; Gunstad et al., 2007; Liang et al., 2014). Obese individuals tend to show deficits on tasks that are associated with executive function, such as cognitive flexibility, working memory, decision-making, planning and problem solving (Fitzpatrick et al., 2013; Van den Berg et al., 2009). For instance, obese, compared to healthy weight individuals show deficits on the one-back visual working memory task (Stingl et al., 2012). Interestingly, a diet high in fat and sugar was found to have no effect on two classical frontal lobe tasks (Trail Making Test and the Wisconsin Card Sort Test) after accounting for BMI (Francis and Stevenson, 2011). This suggests that deficits in executive function might be associated with adiposity, rather than diet.

Less clear is whether there are deficits in learning and memory. In the rodent model, obesity and the so-called "Western diet" (high in saturated fat and simple sugars) have consistently been associated with deficits in learning and memory (see Kanoski and Davidson, 2011 for a review). For example, consumption of a Western diet impairs performance on spatial learning and memory tasks (e.g., Farr et al., 2008; Granholm et al., 2008; Jurdak et al., 2008; Kanoski and Davidson, 2010; Murray et al., 2009; Wu et al., 2003), operant rule learning (e.g., Greenwood and Winocur, 1990, 2001), as well as feature negative discrimination learning, in which rodents fail to reduce appetitive responding to non-reinforced trials (Kanoski et al., 2007, 2010). There is also evidence that diet induced obesity results in decreased dopaminergic signaling, which is in turn associated with a failure to alter responding for food in the presence of a cue signaling impending shock (Johnson and Kenny, 2010).

To our knowledge the influence of diet and adiposity on conditioning or stimulus reward association learning has not been

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examined in humans. However, explicit memory has been examined and produced contradictory findings. In a 2009 review, Van den Berg et al. (2009) reported that only two out of five studies examining explicit memory found evidence of impairment in obese relative to healthy weight individuals. However, the tasks and sample characteristics varied considerably across studies. In one study (Kuo et al., 2006) of men and women between the ages of 65 and 94, BMI had no effect on measures of explicit memory (the Hopkins Verbal Learning Test word lists, the Rey Auditory-Verbal Learning, and the Rivermead Behavioral Memory Test paragraph recall task). In contrast, obese men between the ages of 32–62 displayed deficits in both immediate and delayed recall on a logical memory task (Elias et al., 2003). In another study in which age was entered as a covariate, a negative correlation was observed between BMI and both immediate and delayed recall of a list of words at a 5-year follow-up (Cournot et al., 2006). More recently, Francis and Stevenson (2011) reported clear deficits in explicit learning and memory as a function of a diet high in fat and sugar in a population of young adults. Notably, the effect of diet was not influenced by BMI. Stanek et al. (2013) also failed to observe an effect of BMI on performance of verbal list learning. However, deficits have been reported in immediate recall of stories (logical memory; Benito-León et al., 2013). Miller and colleagues reported explicit memory deficits in one quarter of study participants pre-bariatric surgery, with significant improvement on these measures post-surgery (Miller et al., 2013), but this could be related to either decreased adiposity or fat intake. The effects of BMI on explicit learning and memory thus remain uncertain.

This uncertainty represents an important gap in the literature, not only because it is important to establish the association between obesity and memory, but also because memory plays an important role in food intake, and memory deficits are thought to contribute to overeating (Higgs, 2005, 2008). For example, asking healthy weight individuals to recall items eaten at lunch decreases their food intake later on (Higgs, 2002). This is a robust phenomenon and raises the possibility that reduced memory for food eaten might result in increased intake later in the day (Francis and Stevenson, 2011; Higgs et al., 2008).

The purpose of the current investigation was therefore to examine the effect of adiposity on stimulus reward association learning and explicit learning and memory. Working memory was also assessed in the context of one of the stimulus reward association learning experiments. All tasks employed nonverbal stimuli to facilitate comparisons.

2. Experiment 1

2.1. Method

2.1.1. Participants

Sixty participants were enrolled in this experiment. Participants were members of the New Haven and/or Yale communities. Access to the population was gained by advertising through fliers posted throughout the Yale-New Haven area and by word-of-mouth. All participants were screened over the phone to ensure they met inclusion and exclusion criteria. All participants completed version 1, 2 or 3 (updated versions) of our standard screening form. In version 1 of the form we ask a number of questions related to demographic information (e.g., race, ethnicity, height, weight…), safety questions related to MRI (e.g., implanted devices, brain or cardiac surgery, dental work, metal in body or working with metal), and health questions: ADHD, corrective lenses, visual impairments such as cataracts glaucoma and macular degeneration, head injury, unstable or serious illness, heart attack, stroke, psychiatric disorder, depression, medical hospitalization within the three years, history of drug or alcohol abuse, food allergies, current or recent diet, history of taste and smell impairments, smoker (duration and amount), ear infections in childhood, start date of menstrual cycle, pregnancy. In versions 2 and 3 of our screening form, the questions were similar but slightly more detailed. For instance, participants were also asked to indicate if they have had hypertension, abnormal EKG, Diabetes, HIV/AIDS, kidney failure, chronic pain, seizures, arrhythmia, thyroid problems, hepatitis, liver cirrhosis, abnormal EEG, any heart related conditions, graves diseases, STDs and form of cancer. They are then asked if they have any other past or current medical conditions we have not covered. If the response is yes to any of the above questions the participant is excluded. We additionally ask for the full list of medications people take. Smokers, dieters and heavy drinkers/alcoholics are excluded but not participants with a history of drug abuse, as long as they were not currently taking drugs. If there is evidence of a chronic condition the participant is excluded (e.g. insulin or metformin would suggest diabetes).

Inclusion criteria included age less than 41, being an English speaker and being a non-smoker. Besides the ones mentioned above, exclusion criteria also included being pregnant, a psychiatric or medical diagnosis including diabetes, current dieting, head injury with loss of consciousness, daily medication use or food allergies, or awareness of the probabilistic relationship between the pattern and the reward outcome in the Conditioned Cue Preference Test (CCPT). Eleven participants were excluded. Reasons for exclusion included pregnancy (1), awareness of the probabilistic relationship between the pattern and reward CCPT (3), reported disliking of the treats used in the CCPT (3), performance more than 3 standard deviations from the mean on one of the tasks (2), or missing data on the Abstract Design List (ADL) test or the CCPT (2). Thus data analysis was performed on 49 participants. Participants were recruited to achieve similar distributions of age, gender and education across groups. Demographic information is summarized in Table 1.

2.1.2. Procedure

Participants were asked not to eat for at least two hours prior to the study. Upon arrival the procedures were explained and consent obtained. Next the neuropsychological tests were performed in the order presented below.

2.1.2.1. Abstract design list learning and immediate recall (ADL). The ADL test measures the ability to learn and remember abstract designs (Jones-Gotman, 1986). Participants were told that this is a design-learning test and that they will learn the designs by copying each one on a small piece of paper. The thirteen abstract designs were presented for 10 s each on a computer screen for the participant to copy. Once all 13 designs were copied, a piece of paper was provided to draw, in any order, as many designs as could be remembered. This procedure was repeated four times. Following the learning and immediate recall phase the conditioned cue preference test was performed so that at least 60 min passed before delayed recall and recognition were assessed.

2.1.2.2. Conditioned cue preference test (CCPT). The CCPT (Johnsrude et al., 1999) assesses preference conditioning for initially neutral stimuli. In this task, participants were told that their objective is to locate and remember the number and location of red but not black balls hidden behind boxes. Unbeknownst to participants abstract patterns (not used in the ADL) were revealed at each box selection and were probabilistically associated with finding a red ball. A food reward and pleasant flourish sound was delivered concomitant to uncovering a red ball and an unpleasant buzzer concomitant to uncovering a black ball.