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Food quality and motivation: A refined low-fat diet induces obesity and impairs performance on a progressive ratio schedule of instrumental lever pressing in rats

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HIGHLIGHTS

- High fat diets (HFDs) cause obesity and cognitive impairment in rodents.
- HFDs are also highly refined obscuring the causal factors in their effects.
- We fed rats a refined or unrefined low-fat diet (LFD).
- The refined LFD induced significant weight gain and motivational impairment.
- Therefore, diet quality, not fat, is a cause of obesity and cognitive impairment.

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ABSTRACT

Introduction: Purified high-fat diet (HFD) feeding causes deleterious metabolic and cognitive effects when compared with unrefined low-fat diets in rodent models. These effects are often attributed to the diet's high content of fat, while less attention has been paid to other mechanisms associated with the diet's highly refined state. Although the effects of HFD feeding on cognition have been explored, little is known about the impact of refined vs. unrefined food on cognition. We tested the hypothesis that a refined low-fat diet (LFD) increases body weight and adversely affects cognition relative to an unrefined diet.
Materials and methods: Rats were allowed ad libitum access to unrefined rodent chow (CON, Lab Diets 5001) or a purified low-fat diet (REF, Research Diets D12450B) for 6 months, and body weight and performance on an instrumental lever pressing task were recorded.
Results: After six months on their respective diets, group REF gained significantly more weight than group CON. REF rats made significantly fewer lever presses and exhibited dramatically lower breaking points than CON rats for sucrose and water reinforcement, indicating a chronic reduction of motivation for instrumental performance. Switching the rats' diet for 9 days had no effect on these measures.
Conclusions: Diet-induced obesity produces a substantial deficit in motivated behavior in rats, independent of dietary fat content. This holds implications for an association between obesity and motivation. Specifically, behavioral traits comorbid with obesity, such as depression and fatigue [1], may be effects of obesity rather than contributing causes. To the degree that refined foods contribute to obesity, as demonstrated in our study, they may play a significant contributing role to other behavioral and cognitive disorders.

1. Introduction

The consumption of refined, processed foods (REF), a major component of the Western diet, is linked to poor health outcomes in human populations [2–4], including obesity, diabetes, and cardiovascular disease [5,6]. Statistics from the United States Centers for Disease Control currently report that 35.7% of U.S. adults and approximately 17% of children and adolescents are obese, and these trends are not limited to the U.S. [7–9].

Furthermore, the rapid transition to a Western diet of processed foods over the past few decades has resulted in a wholesale shift from one type of food to another. The transition from traditional diets

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including large proportions of locally-grown and harvested plants and animals to industrial diets heavy in mechanically-separated, minced, saturated with artificial flavors and preservatives, salted, and otherwise altered food has been linked to dramatic increases in rates of overweight and obesity among members of traditional ethnic and cultural groups in developing countries [6,10]. In fact, the strength of this connection is so reliable that a percent increase in obesity among these cultural groups can be predicted in accordance with the degree of increase in food-processing [5].

Despite the large body of evidence linking the Western REF diet to elevated cardiometabolic disease risk, less attention has been directed at its relationship to cognition. Most experimental work has investigated the metabolic and cognitive effects of a purified high-fat diet (HFD) in animal models. These effects are often attributed to the diet's high content of fat, while less attention has been paid to other mechanisms associated with the diet's highly refined state. Although the effects of HFD feeding on cognition have been explored [11–15], little is known about the impact of refined vs. unrefined food on cognition, and it remains difficult to disentangle the effects of dietary fat from the effects of HFD-induced obesity. As cognition is a function of brain physiology, any impairment in brain functioning at the mechanistic level may result in cognitive impairments. Brain systems known to be involved in the dysregulation of appetite and consummatory behavior include the hypothalamus [16], hippocampus [17,18], and striatum [19], which also involve the striatal dopamine D_2 receptor [20], the mesolimbic dopamine (DA) pathway [21], and the orbitofrontal cortex (OFC, [22]). As these systems also play a role in cognitive functions, such as motivation, attention, learning and memory, and behavioral control, we may also expect impairments in these cognitive processes.

Many factors differ between refined diets typical of Western industrialized nations, and the unrefined diets that are more characteristic of the non-industrial subsistence cultures as well as health-conscious individuals in industrialized societies. Thus, we chose to compare the effects on cognitive function of an obesogenic REF diet to those of a control diet composed primarily of unrefined ingredients. This approach has strong ecological validity because it approximates the differences between typically refined and unrefined diets consumed by individuals in our society. Characterizing the relationships between a refined diet, obesity, and cognitive function will enable experimental investigations of the causal components of the refined diet that affect health and develop effective interventions that may have practical, real-world significance as treatments.

In the present study, we test the hypothesis that a refined low-fat diet increases body weight and adversely affects cognition relative to an unrefined diet. Rats were allowed ad libitum access to unrefined rodent chow (CON) or a purified low-fat diet (REF) for six months, and body weight and performance on an instrumental lever pressing task were recorded. The lever press task consisted of instrumental lever pressing on progressive-ratio (PR) schedules of reinforcement. In a PR schedule, reinforcement is delivered only after completing a greater number of responses than previously required. The number of lever presses required for reinforcement increases progressively in fixed steps based on the PR ratio. For example, a PR3 schedule requires 3 lever presses for the first reinforcer, then 6, then 9, and so on until the end of the session. PR schedules provide a sensitive assay for motivation [23,24]. The lower the intrinsic motivation of the subject, the sooner should they reach a breaking point and "give up" on making any further instrumental responses. In each experiment, rats received two sessions on a PR3 schedule of reinforcement followed by two sessions on a PR5 schedule of reinforcement.

The REF diet, despite closely matching the macronutrient ratio of the CON diet, differed in the nature of those macronutrients. In particular, the refining process breaks down complex foods into their simple constituents that are more easily absorbed through the intestines and assimilated into the body [4]. This may be one of the major factors for why junk foods are so addictive and obesogenic. Notably, the REF diet consisted largely of simple sugars and refined flour. The CON diet, on the other hand, contained more whey, soy, vegetables, fish meal, and complex carbohydrates. Refining into the simple constituents also can affect the flavor profile, texture, and other features of the food to change its palatability and reward value [25].

We hypothesize that REF diet feeding leads to greater weight gain and greater disruption of motivation processes than CON feeding. Specifically, we should observe less persistence in lever-pressing and earlier breaking points in rats consuming a REF diet. To gauge the generality of motivational impairments, we assessed the effect of diet on PR schedules of lever pressing for either a 20% sucrose solution (Experiments 1 and 3) or water (Experiment 2) on PR3 and PR5 schedules of reinforcement.

2. General methods

2.1. Subjects

Thirty-two experimentally-naïve female Long Evans rats (*Rattus norvegicus*) acquired from Harlan (Indianapolis, IN) served as subjects. Subjects were pair-housed in transparent plastic tubs with a wood-shaving substrate in a vivarium maintained on a 12-h light/dark cycle. Experiments were conducted during the dark portion of the cycle. Prior to the beginning of Experiment 1, a progressive food restriction schedule was imposed so that each cage of pair housed rats received 25 g of their respective diets (REF or CON) daily. Subjects were randomly assigned to either the REF diet or the CON diet ($ns = 16$).

2.2. Diets

The REF (Research Diets 12450B) and CON (Lab Diets 5001) diets were 20% protein vs. 28% protein, 70% vs. 58% carbohydrate, and 10% vs. 13% fat, respectively. The diets, both commercially available rodent chows, differed in the amount of refinement and processing that went into their production (see Appendix for diet sheets provided by the manufacturers). The Lab Diets 5001 was also selected as the CON diet because it is a common diet in other behavioral experiments, including in our laboratory.

2.3. Apparatus

Behavioral training was conducted in a small room containing eight Skinner boxes. Each Skinner box measured 30 × 25 × 20 cm ($L \times W \times H$) and was housed in a separate sound-and-light attenuating environmental isolation chest (ENV-008, Med Associates, Georgia, VT, USA). The front and back walls and ceiling of the chamber were constructed of clear Plexiglas, the side walls were made of aluminum, and the floors were constructed of stainless steel rods measuring 0.5 cm in diameter, spaced 1.5 cm center-to-center. The enclosure was dimly illuminated by a 28-V bulb (ENV-215M, Med Associates) house light located 2 cm from the top of the left-side chamber wall.

Each chamber was equipped with a liquid-dipper (ENV-202M, Med Associates) that could be lowered into a trough of sucrose solution (20% by volume) or water reward and then raised. When in the raised position, a small well (0.05 cm^3) at the end of the dipper arm that contained reward protruded up into the drinking receptacle. Delivery of reward served as the appetitive reinforcer. Each chamber also contained one 3.5-cm wide retractable lever (ENV-112CM, Med Associates), located on the metal wall of the chamber, 8 cm to the left of the drinking receptacle and resting 6.5 cm above the floor grid. During training, the lever protruded into the chamber. Ventilation fans in each enclosure and a white noise generator on a shelf outside of the enclosures provided a constant 62-dB(A) background noise.