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Verbal descriptors influence hypothalamic response to low-calorie drinks

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ABSTRACT

Messages describing foods constitute a pervasive form of reward cueing. Different descriptions may produce particular appeal depending upon the individual. To examine the extent to which verbal descriptors and individual differences interact to influence food preferences, we used functional magnetic resonance imaging to measure brain responses to the same low-calorie drinks preceded by the spoken verbal descriptor “treat” or “healthy” in 27 subjects varying in BMI, eating style and reward sensitivity. Subjects also sampled a prototypical milkshake treat. Despite the fact that the verbal descriptor had no influence on pleasantness ratings, preferential responses to the low-calorie drinks labeled “treat” vs. “healthy” were observed in the midbrain and hypothalamus. These same regions were also preferentially responsive to the prototypical treat. These results reveal a previously undocumented influence of verbal descriptors on brain circuits regulating energy homeostasis.

Keywords Neuroimaging; Feeding; Hypothalamus; Value; Midbrain; Top-down modulation

1. INTRODUCTION

In modern societies, marketing and food labels constitute a pervasive form of reward cueing. For example, providing information about brand [1], edibility [2], price [3], affective value [4], and caloric content [5] strongly influences perceptual and neural responses to the sight, taste, and smell of foods. Product descriptions might also be used to promote healthy food choices. Simply asking subjects to focus attention on the healthiness of food items displayed in pictures increases the frequency with which healthy but less “tasty” food items are selected for consumption [6]. When these healthy choices are made dorsolateral prefrontal cortex produces stronger modulation of value signals generated in ventromedial prefrontal cortex. This suggests that directing attention to healthful qualities of foods enables brain circuits that orchestrate self-control to increase the value of health.

Incidental verbal descriptions highlighting the health (e.g. “high in calories” or “low in fat content”) vs. the taste (“sweet and juicy”) qualities of food images can also bias hedonic perception and choice [7]. However, in the absence of explicit instructions to attend to healthy vs. tasty attributes amygdala response appears sensitive to the descriptions and predictive of choice, irrespective of whether its response reflects ratings of pleasantness. Unknown is how descriptive labels about health vs. taste influence neural and perceptual responses to actual food consumption. This is an important issue because it is well known that the outcomes of decisions serve to update and optimize an individual's decision-making strategies.

Another important consideration is that different descriptions may produce particular appeal depending upon the individual. In fact, it has been shown that individuals who consistently exhibit self-control in making food choices are better able to incorporate information about health in the computation of ventral medial prefrontal cortex value signals [8]. Accordingly it is well established that dietary restraint and disinhibition strongly influence eating behavior [9–16]. Less understood is the extent to which other individual factors interact with the nature of food descriptions to influence preferences. Further, the identity of brain circuits that could mediate such interaction has not been established. This issue is important because variation in sensitivity to reward (STR),[1] eating style (ES) and body mass index (BMI) may constitute a vulnerability factor for overeating and may interact differently with different food messages.

In the current study we used functional magnetic resonance imaging (fMRI) to examine whether verbal descriptors about the healthfulness and tastiness of a low-calorie beverage could alter neural and hedonic response. We also examined the influence of individual differences in STR, ES, or BMI. Perceptual and neural responses to moderately pleasant flavored drinks presented concomitantly to one of two auditory descriptors (“healthy” or “treat”) were assessed. Unbeknownst to subjects, the same flavor was associated with both descriptors at different trials. We predicted that when the low-calorie drink was described as a treat, hedonic and neural responses would be more similar to a prototypical treat (milkshake) than when it was described as healthy. We also sought to determine the influence of individual

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[1]Abbreviations used: ES, eating style; BMI, body mass index; STR, sensitivity to reward; fMRI, functional magnetic resonance imaging (fMRI); gLMS, generalized labeled magnitude scale; BAS, behavioral approach scale; BIS behavioral inhibition scale; TFEQ, three factor eating questionnaire; PAG, periaqueductal gray; SN, substantia nigra.

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differences in STR, ES, and/or BMI in the ability of the verbal descriptors to affect the hedonic and brain responses to the low-calorie drinks.

2. SUBJECTS AND METHODS

The experiment consisted of one behavioral session, a training session in the mock fMRI scanner, and one fMRI scanning session.

2.1. Subjects

Twenty-seven right-handed subjects participated (9 males, 28 ± 7.4 years) with informed consent and the Yale Human Investigation Committee approved the study. BMI ranged from 19.4 to 43.6 kg/m^2 (lean to obese). Subjects were excluded if they had a known taste, smell, neurological, psychiatric, or other pathological disorder (e.g., cancer, diabetes). Four subjects were excluded from all analyses due to excessive movement during fMRI scanning (exceeding 1 mm of movement in any direction in more than one out of four runs). Thus all analyses are based on data from 23 subjects (5 males, 27 ± 6.7 years) with a mean Edinburgh Handedness Inventory score of 80.3 ± 14.4 [17], and an average BMI of 26.9 ± 6.0 kg/m^2 with a range of 19.4–43.6. The subject with a BMI of 43.6 kg/m^2 was an outlier in BMI (*z*-score of 2.98), and we note that this subject was left out of any regression analyses with BMI as an independent variable. We also note that exclusion of this subject from any of the other fMRI analyses did not appreciably change the observed results.

2.2. Stimuli

Stimuli included flavored Sobe Lifewater and Ben & Jerry's milkshake beverages. The three Lifewater flavors used in the first behavioral sessions were pomegranate cherry, strawberry kiwi and orange tangerine ("fruity flavors" from here on), containing 40 kcal per 237 ml each. Milkshake flavors were chocolate fudge brownie, cherry Garcia and chunky monkey ("milkshake flavors" from here on), containing 340, 320 and 330 kcal per 237 ml respectively. Artificial saliva was used as a tasteless/odorless control stimulus. This solution has been shown to provide a superior baseline condition compared to water [18] because water activates gustatory cortex as effectively as taste [19] and has a taste [20]. Subjects were presented with four versions of the tasteless solution (2.5 mM sodium bicarbonate and 25 mM potassium chloride, plus three dilutions at 25%, 50%, and 75% of the original concentration) and asked to select the one that tasted most like nothing. Eighteen subjects chose the 25%, two subjects chose the 50% dilution, and the 75% and 100% dilutions were each chosen by one subject. Only subjects who rated two milkshakes and two fruity flavors as pleasant were asked to participate in the fMRI session.

2.3. Stimulus delivery

During the behavioral session, 0.5 ml aliquots of the stimuli were presented to the subjects by the experimenter via a handheld pipette. During mock and actual scanning, the liquid stimuli were delivered using our custom-built gustometer and gustatory manifold [21]. The gustometer device operates via infusion pumps (BrainTree Scientific) that released a 0.5 ml aliquot of the appropriate stimulus at a rate of 7.5 ml/min in each trial. Pumps were controlled by custom made software (Matlab, MathWorks, Inc) whose operation was linked to scanner pulses. Each pump held a 60 ml syringe connected to a 25-foot length of Tygon beverage tubing that terminated into a custom designed Teflon, fMRI-compatible gustatory manifold that was anchored to the MRI headcoil. The manifold was mounted by rigid tubing onto an anchoring block that clamped onto the bars of the headcoil. Tastant lines were arrayed around a tasteless line in a circular pattern and all tastants and rinses are delivered through a 1 mm channel that passes through the entire manifold. These 1 mm channels converged at a central point at the bottom end of the manifold. To prevent the subject's tongue from coming in contact with the 1 mm holes, a 7 mm sphere was positioned directly under the end of the 1 mm channels and rested directly above the subject's tongue. All subjects were instructed to allow the liquid to roll off of the sphere onto the tip of the tongue, but to refrain from swallowing until instructed. In prior studies we have measured swallowing using a respiratory bellows placed around the neck. However, we have found that subjects complain that the bellows is uncomfortable and that swallowing rarely occurs outside the instructed time [22,23]. Therefore we did not measure swallowing in the current study. The sphere ensured maintenance of constant tactile stimulation across events.

2.4. Experimental design

2.4.1. Behavioral session

Subjects sampled and provided ratings of the Sobe Lifewaters and the Ben & Jerry's milkshakes. Using a pipette, 0.5 mL Lifewater and milkshake samples were administered in random order. Subjects rated pleasantness ("How pleasant is this taste?": "Most unpleasant sensation ever" $= -100$ mm, "Neutral" $= 0$, "Most pleasant sensation ever" $= +100$ mm), familiarity ("How familiar is this taste?": "Not familiar at all" $= -100$ mm, "Neutral" $= 0$, "Very familiar" $= +100$ mm) and wanting ("How much do you want to eat more of this?", "I would never want to eat this" $= -100$ mm, "Neutral" $= 0$, "I would want to eat this more than anything" $= +100$ mm) for each stimulus on a visual analog scale, and flavor intensity using the generalized Labeled Magnitude Scale (gLMS) [24,25]. This is a vertical line-scale of 100 mm with the label "no sensation" at the lower anchor, and the label "strongest imaginable sensation" at the upper anchor. In between these labels the following words were approximately logarithmically spaced: "barely detectable" (1.5 mm), "weak" (6 mm), "moderate" (17 mm), "strong" (35 mm), and "very strong" (53 mm). Before tasting the Lifewaters subjects were told "You will be sampling a variety of flavored drinks". Thus subjects were not explicitly informed about the caloric content of the original formulation. After receiving and rating the Lifewaters, but before receiving and rating the milkshakes, subjects were told they just sampled the "original formulation" of a drink which has been reformulated by the manufacturer in two ways. One formulation was designed to be healthy and contained compounds known to produce health benefits, whereas the other formulation was designed to be highly palatable and contained highly palatable ingredients. They were further told that these two alternative formulations were to be presented during the fMRI scanning session, to take place on a second day. They were also informed that, during fMRI scanning, at the beginning of each trial, the identity of the formulation would be revealed to them via auditory cues (a human voice enunciating the words "treat" or "healthy") concomitant to the intra-oral delivery of the flavored beverage. Unbeknownst to subjects, however, was the fact that the two auditory descriptors were to be associated with the delivery of the same fruity flavored beverage (the "original" formulation of the fruity flavors) at different selected trials. We chose to convey information about the drink content as a spoken word rather than a written label so that the sight of the drinks would be identical to the original formulation. Next, participants were given the milkshake solutions and were asked to rate their pleasantness, familiarity, flavor intensity and wanting (as above). The two fruity flavored solutions and the two milkshakes that

