PAIN® 155 (2014) 712–722

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Decreased food pleasure and disrupted satiety signals in chronic low back pain

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 6 September 2013
Received in revised form 10 December 2013
Accepted 20 December 2013

Keywords:
Chronic back pain
Obesity
Pleasure
Satiety

ABSTRACT

Chronic low back pain (CLBP) and obesity are interrelated, but the physiological mechanisms linking the 2 conditions remain to be determined. Functional brain imaging data from CLBP patients show functional and structural alterations in areas mediating the attribution of hedonic value to food. Accordingly, we hypothesized that CLBP patients would exhibit alteration in the hedonic perception of highly palatable, calorie-containing foods. CLBP patients and matched healthy controls initially rated their perception of highly palatable puddings of varying fat content and sugary drinks of varying sucrose content without ingesting significant amounts of either stimulus. In a subsequent intake test, hungry participants ingested their preferred pudding ad libitum. Compared to healthy controls, CLBP patients exhibited significantly lower ratings of food pleasure when sampling the fat puddings but not when sampling the sugary drinks. In contrast, the patients' sensory evaluation of these stimuli was not different from those of healthy controls. In addition, whereas in healthy controls caloric intake from pudding closely matched hedonic ratings and decreased hunger after ad libitum pudding intake, such effect was totally abolished in CLBP patients. Our data thus reveal a decoupling between hedonic perception and fat calorie intake in CLBP patents, suggesting altered hedonic perception of fat as a potential mechanism linking CLBP to overeating and obesity.

1. Introduction

Chronic pain and obesity both constitute a huge burden to affected individuals and to society [28,43,66], and prevalence of both is increasing [32,77]. Evidence suggests that these conditions are interrelated. For example, the prevalence of obesity is higher in those with chronic pain [53,74,98,107], and the prevalence of chronic pain is higher in those who are obese [43,83,88]. This interaction is believed to negatively affect treatment response in chronic pain [87] and success rates of weight loss programs [104]. Despite its clinical relevance, little is known about the neurobiological mechanisms underlying the epidemiological association between chronic pain and obesity [50].

Mounting evidence indicates that the alarming increase in the prevalence of obesity results from an interaction between the abundance of palatable energy-dense foods that act to stimulate brain reward systems and individual variations in the responsivity of these systems [54,103]. Among the brain reward systems, the ventral striatum (VS) and medial prefrontal cortex (mPFC) have been consistently implicated as critical to the expression of appetitive and consummatory feeding behaviors [4,48,49,68,80,93]. Consistent with an association between obesity and chronic pain, chronic low back pain (CLBP) patients exhibit disrupted reward-related behaviors concomitantly to altered activity in VS and mPFC [2,6,9–11]. Moreover, in CLBP patients, back pain intensity ratings correlate with activity levels in VS and mPFC [6] and with VS–mPFC functional connectivity [9]. In particular, mPFC shows increased activity in CLBP patients compared to healthy subjects [5,8], an effect reversed by successful CLBP treatment [10,46,47]. More importantly, the strength of functional connectivity between VS and mPFC predicts the likelihood that a subacute back pain patient with backache for 6 to 12 weeks will seek care for back pain 1 year later [11]. Finally, VS volume shrinks only in subacute back pain patients whose pain persists after 1 year but not in those who recover [11]. Collectively, these results strongly support a role for VS–mPFC circuits in chronic pain.

VS–mPFC circuits are also well known to mediate the attribution of hedonic value such as disliking and liking to negative and positive reinforcers, respectively [36,39,81,85], including palatable food [4,15,25,40,49,57–60,75,90,91,96]. Animal and human studies also show that in VS, both hedonic responses to food and pain relief

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0304-3959/$36.00 Published by Elsevier B.V. on behalf of International Association for the Study of Pain.
http://dx.doi.org/10.1016/j.pain.2013.12.027

are mediated by μ-opioid receptor signaling [4,86,93,97,110,111], which is in turn altered in different chronic pain conditions [29,45,64]. Interestingly, μ-opioid receptor inverse agonist administration in humans decreases hedonic perception and caloric intake of palatable fat– or carbohydrate-rich foods but not of foods low in sugar and fat [72]. These findings support a critical role for VS and mPFC opioid signaling in the hedonic perception of food. Given the strong evidence for overlapping neural circuits for chronic pain and hedonic perception of palatable food, we set out to test whether patients with CLBP have altered hedonic perception of highly palatable foods.

2. Methods

2.1. Subjects

All subjects provided written informed consent to participate in the study, which was approved by the Yale University institutional review board. Nineteen healthy subjects (4 men) and 18 CLBP patients (4 men) participated in this study. Subjects were recruited through flyers in the New Haven area and advertisements posted on the Internet. We received approximately 50 responses to our ads from patients with back pain. Thirty-three CLBP patients were screened in detail, 18 of whom participated in the study. Subjects were briefly screened at first to check (1) the location of pain, (2) whether they were otherwise healthy, (3) whether they were nonsmokers, and (4) whether they had pain duration of more than 2 years. If they passed this initial brief screening, a more detailed screening was conducted where we assessed demographics; location, possible cause, duration, and radiation of the pain; nonopiate analgesic medication use; medical assessments of the back pain; substance misuse; recent or past history of opioid medication use; complete medical and psychiatric history; recent or past fluctuations in body weight; history of olfactory or taste impairments; or nasal sinuses surgery. Healthy control subjects were likewise screened. In addition, the presence of any current back pain and any history of back pain of more than 6 weeks' duration were exclusion criteria.

Because we have a large database of healthy subjects, we used it to target recruitment of healthy participants whose gender, age, and body mass index (BMI) would be within the range of recruited CLBP patients. Participants had no history of psychiatric disorders, other medical conditions, and loss of consciousness, chemosensory impairment, or food allergies. To be included in the study, CLBP patients had to (1) fulfill the International Association for the Study of Pain criteria of chronic back pain [70], (2) not be currently, or during the month before the study, receiving any opioid analgesics, and (3) have a pain duration of at least 2 years. We chose to include patients with at least 2 years of back pain to make sure that they were in the time window when VS and mPFC alterations would have set in [11]. CLBP diagnosis was confirmed on the basis of history collected by experienced clinician (PG). Briefly, all patients had pain more days than not for more than 2 years, primarily localized to the lumbosacral region, including buttocks and thighs, with and without radiation. All participants were financially compensated $60 for taking part in both sessions of the study.

2.2. Stimuli

A set of 4 pudding samples were prepared with 0%, 1.6%, 3.1%, and 6.9% fat weight by weight (w/w) [69]. The samples were prepared by mixing instant pudding (Jell-O, Kraft Foods) in milk (Guida's Dairy) with varying fat content. The sugar content was held constant between the 4 stimuli at 4.6% (w/w). In order to maximize liking ratings, subjects were asked to pick a preferred flavor out of a choice of vanilla and chocolate during the prestudy screening interview. A set of 4 Kool-Aid-based orange-flavored juices with 0, 0.018, 0.1, and 0.56 M sucrose concentration were also prepared.

2.3. Procedures

Subjects were asked to participate in 2 sessions on 2 different days. During session 1, they sampled and rated food stimuli as described below. During session 2 they were offered a pudding to consume ad libitum. The maximum interval between the 2 sessions was 7 days.

Session 1. Subjects presented to the laboratory between 9 AM and 3 PM. They were asked to arrive neither hungry nor full and to rate their hunger level upon arrival using a visual analog scale (VAS; 0 = "I am not hungry at all" and 100 = "I have never been more hungry"). Testing continued only if hunger ratings were less than 30. If they rated hunger at greater than 30, they were given a small snack and were asked to wait 30 min, after which the hunger ratings were repeated. We thought it was important to test subjects in the absence of hunger or satiety in order to minimize homeostatic effects on food liking. Before testing, each subject was trained to use the General Labeled Magnitude Scale (gLMS) to rate overall intensity and sweetness [41], the Labeled Hedonic Scale (LHS) to rate liking or disliking [62], and the VAS to rate hunger, fullness, thirst, oiliness, fattiness, creaminess, and wanting of the stimuli. The gLMS is a computerized psychophysical tool that requires subjects to rate the perceived intensity of a stimulus along a vertical axis lined with adjectives that are spaced semilogarithmically on the basis of experimentally determined intervals to yield ratio-quality data. The LHS was derived using similar methods as the gLMS but asks subjects to rate hedonic liking or disliking [62]. Subjects were then asked if they preferred the chocolate or vanilla pudding. The preferred pudding was used to conduct the remainder of the experiment.

The different pudding or juice stimuli were presented in 3 blocks with the order of presentation randomized. Subjects sampled 5 mL of the juice and expectorated without swallowing; for the pudding, they sampled approximately 3 to 5 mL at the tip of a spoon without swallowing. After tasting each sample, subjects used the scales to rate their perceptions. They rinsed in between samples and paused for 30 s before taking the next sample. Subjects who chose chocolate pudding were asked to wear a blindfold during testing because we could not equate the color of the different concentrations. At the end of the session, another set of hunger, fullness, and thirst ratings was obtained.

Session 2. Subjects presented hungry around lunchtime between noon and 2 pm. They were asked to eat breakfast and then refrain from eating anything until the time of testing. Subjects were tested only if their hunger level at arrival was rated >30 on the VAS. Otherwise they were rescheduled for a different day. First, percentage body fat was assessed using air displacement plethysmography (Bod-Pod; Cosmed). Because the percentage of body fat that is considered healthy differs in men and women (21%–25% range in men and 30%–35% range in women) [27,94], we divided the absolute output values from plethysmography by 31% and 21% for women and men, respectively. Two CLBP patients refused to undergo body fat mass assessment. Immediately after, subjects rated hunger, fullness, and thirst; they were then offered pudding and instructed to eat as much as they liked. For each subject, the pudding given a maximum liking rating during session 1 was used. Hunger, fullness, and thirst were rated after ad libitum pudding consumption. Subjects also provided ratings for intensity, liking, fullness, thirst, oiliness, fattiness, creaminess, and wanting after consumption.

Questionnaires. Subjects were also asked to fill out feeding behavior questionnaires, and CLBP patients also completed pain-related questionnaires. CLBP was assessed using the following pain questionnaires and scales: VAS for pain intensity, the short form of