A biphasic reduction in a measure of palatability following sucrose consumption in mice

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ABSTRACT

Consumption of foods results in a transient reduction in hedonic value that influences the extent and nature of feeding behavior. The time course of this effect, however, is poorly specified. In an initial experiment, using an analysis of the microstructure of licking in mice we found that consumption of sucrose led to a rapid reduction in lick cluster size, a measure of palatability, which recovered after 10 min, but reemerged 60 min after initial consumption. We then replicated the finding that lick cluster size is reduced after 60 min, but not 10 min, under conditions in which a number of potential behavioural confounds were removed. In Experiment 2 the effect was replicated using a between-subjects design that ruled out the possibility that the effect was a specific consequence of the within-subjects procedures used in the first experiment, in which mice may have come to expect sucrose at different time points within the feeding session. While Experiments 1 and 2 confounded the time between periods of access to sucrose with time since the start of the feeding session, this confound was removed in Experiment 3, and, similar to the previous experiments, it was found that a second reduction in palatability occurred after 60 min. Therefore, the effect was dependent only on the time since the previous exposure to sucrose, demonstrating that sucrose consumption initiates a biphasic reduction in palatability. The reduction in lick cluster size after 60 min was not typically accompanied by a reduction in consumption suggesting that the more slowly developing reduction in the palatability measure was not simply a consequence of post-ingestive satiety. The cause of the biphasic change is not yet clear, and may reflect independent processes or the consequence of a single process that initiates multiple changes in palatability over time.

1. Introduction

Identifying the factors involved in the short-term reduction of feeding is important for understanding the potential causes of overeating. Thus, it has been proposed that overeating, and ultimately obesity, may occur due to a failure to habituate to properties of foods during a meal [10,15]. While the rate of consumption during continuous access to food (e.g., within a meal) decreases, the palatability of food also rapidly decreases [6,13,17]. This suggests that initial reductions in consumption may reflect reduced palatability, while subsequent reductions in consumption, that ultimately lead to the cessation of eating, may reflect post-ingestive satiety. The short-term reductions in palatability that occur as a consequence of recent consumption likely reflect sensory adaptation or habituation due to the influence of short-term memory [16]. Although the reductions in palatability that occur as a consequence of consumption of food rapidly recover, the time course of this recovery is unknown.

Examining rapid changes in palatability in humans is difficult due to the requirement for repeated self-reporting of hedonic responses. It is possible, however, to measure rapid changes in palatability in rodents by analysis of the microstructure of licking. Rodents drink by making by a series of licks in quick succession (a lick cluster) with each cluster separated by pauses typically > 0.5 s [8]. The number of licks in a cluster (lick cluster size) provides a measure of palatability that is dissociable from levels of consumption, as measured by the overall total number of licks. Thus, lick cluster sizes increase monotonically as a function of sucrose concentration, whereas the total number of licks follows an inverted U-shaped function with licking being maximal for intermediate sucrose concentrations and being lower for both high and low concentrations [5,8,18]. Therefore, while rodents will drink more of intermediate concentrations of sucrose than low concentrations, potentially due to the differences in palatability of the concentrations, they drink less of high concentrations than intermediate concentrations. Although this may indicate that they find high concentrations of sucrose less palatable than low concentrations, the reduction in consumption may also reflect the increased satiety caused by high

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concentrations. The fact that lick cluster sizes increase monotonically as a function of sucrose concentration indicates that the reduction in consumption of high sucrose concentrations does likely reflect increased satiety, and that lick cluster size provides a purer measure of palatability. Indeed, manipulations that affect lick cluster size typically also affect tests of taste reactivity (orofacial responses) in a similar manner, suggesting that these behavioural measures in rodents can be used to gauge the hedonic value of a substance (see [9], for a detailed discussion). Importantly, lick cluster sizes in mice are sensitive to a variety of memory manipulations [3,5] suggesting that they provide a measure of experience-dependent changes in palatability.

We have previously investigated changes in lick cluster size in mice during a 10-min period of exposure to 16% sucrose and found that lick cluster sizes rapidly reduced during that period, with a significant reduction in the mean lick cluster size between the first and second minutes of exposure [19]. Furthermore, massing access to sucrose (e.g., one 5-min access) leads to lower lick cluster sizes than spacing of access (e.g., five 1-min periods of access each separated by four minutes) despite not affecting the overall levels of consumption [19]. Similar effects have been seen in brief access tests in mice in which consecutive 1-min periods of access to sucrose were separated by a 5-min interval [11]. These results suggest that palatability changes over exposure as a function of the time since the last period of consumption. The purpose of the present study was to examine the time course of the effect of recent consumption of sucrose on palatability and consumption. While it may be expected that recent consumption of sucrose will lead to a short-term reduction in palatability that recovers given a sufficient period of time, we instead found that, surprisingly, there was a biphasic reduction in palatability (Experiment 1).

In Experiment 1 mice received sessions in which they were allowed two 1-min periods of access to 16% sucrose. The interval between the exposures varied across sessions and could be 5 s, 10 min or 60 min. These intervals were chosen because our unpublished observations suggested that the reductions in lick cluster size are rapid, and, therefore, will be present after 5 s, but will have likely recovered after 10 min, and any effect should be minimal after 60 min. As expected, sucrose consumption led to a rapid decline in palatability when measured after 5 s, but there was no effect of recent consumption when the periods of feeding were separated by 10 min. Surprisingly, however, there was a reduction in palatability after a 60-min interval.

The finding that sucrose consumption led to a reduction in palatability after 5 s and 60 min, but not 10 min, was not anticipated. Therefore, the purpose of the subsequent experiments reported here was to test the reliability of the effect under conditions that rule out particular accounts. Experiment 2 replicated the effect of reduced palatability after 60 min but not 10 min using a between-subjects design that ruled out the possibility that reduced palatability after 60 min was a frustrative nonreward effect caused by extinction of the temporal expectation of sucrose. Experiment 3 replicated the finding of reduced palatability after 5 s and 60 min, but not 10 min, using a procedure that matched the time since the start of the feeding session, ruling out the possibility that the reduction in palatability after 60 min was due to the length of exposure to experimental test conditions.

2. Methods

2.1. Subjects

In Experiment 1, 12 experimentally naive C57BL/6 mice (six male, six female) bred in the Life Sciences Support Unit at Durham University were used. The mice were between five and seven months old at the start of testing and weighed between 15.8 g and 26.4 g. In Experiment 2, 24 experimentally naive female C57BL/6 mice from Charles River UK were used. They were approximately ten weeks old at the start of testing, weighing between 17.1 g and 20.8 g. In Experiment 3, 48 female C57BL/6 mice bred in the Life Sciences Support Unit at Durham

University were used. The mice had previously received unrelated feeding procedures and were experienced at consuming sucrose solutions in the testing apparatus. They were between three and eight -months old at the start of testing and weighed between 16.8 g and 26.3 g. Mice were caged in groups in a temperature controlled housing room with a 12 h light-dark cycle. Testing was conducted during the light period. During testing mice were motivated to consume the sucrose solution by being maintained at 85% of their free-feeding body weights. Using this method, we have previously shown that palatability, as measured by lick cluster size, can be manipulated by sucrose concentration, negative contrast, and habituation effects [3–5]. Mice had ad libitum access to water in their home cages. All procedures were in accordance with the United Kingdom Animals (Scientific Procedures) Act 1986 and were approved by the UK Home Office under project license number PPL 70/7785.

2.2. Apparatus

A set of eight identical operant chambers (interior dimensions: 21.6 × 17.8 × 12.7 cm; ENV-307 W, Med Associates, Inc., Fairfax, VT, USA), enclosed in sound-attenuating cubicles (ENV-022V, Med Associates) were used. The operant chambers were controlled by Med-PC IV software (Med Associates). The side walls were made from aluminium, and the front and back walls and the ceiling were made from clear Perspex. The chamber floors each comprised a grid of 24 stainless steel rods (0.32 cm diameter), spaced 0.79 cm apart and running perpendicular to the front of the chamber (ENV-307W-GFW, Med Associates). Retractable sippers (ENV-352AW, Med Associates) and a small hole in one wall of each chamber allowed graduated pipettes to be extended into, and retracted from, the chambers. The graduated pipettes (10:0.1 ml) allowed measurement of consumption by comparing the volumes before and after testing. Contact lickometer controllers (ENV-250, Med Associates) allowed contacts between the mice and the graduated pipettes to be recorded at a resolution of 0.01 s. A fan (ENV-025F, Med Associates) was located within each of the sound-attenuating cubicles and was turned on during sessions. Sucrose solutions were made weight/volume with commercially available sucrose in distilled water.

2.3. Procedure

2.3.1. Experiment 1

Mice received two 1-min periods of access to 16% sucrose solution (0.47 mol/l) per session. This was achieved by inserting the sipper tube into the chamber and then withdrawing it at the end of each 1-min period. The first period occurred 5 min after the start of the session. After the first period of access the second occurred after one of three possible intervals: 5 s, 10 min or 60 min. The session ended immediately after the second period of access to sucrose. Mice received fifteen sessions, one per day, with five of each interval (5 s, 10 min, and 60 min). The order of intervals across sessions was randomised with the constraint that on any given session one third of the mice received each interval and over each block of three sessions each animal received one session with each interval.

2.3.2. Experiment 2

Mice received six sessions in which they were allowed two 1-min periods of access to 16% sucrose (0.47 mol/l). For one group of mice (N = 12) the two periods were separated by a 10-min interval, and for another group (N = 12) the interval was 60 min. All other details were the same as Experiment 1.

2.3.3. Experiment 3

Mice received three sessions in which they were allowed ten 1-min periods of access to 16% sucrose (0.47 mol/l). After the first period of access the subsequent periods occurred after intervals of 5 s, 10 min or