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Oral sucrose stimulation increases accumbens dopamine in the rat

Andras Hajnal,[1] Gerard P. Smith,[2] and Ralph Norgren[1]

[1]*Department of Neural and Behavioral Sciences, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033; and* [2]*Bourne Behavioral Research Laboratory, Weill Medical College of Cornell University, New York-Presbyterian Hospital, White Plains, New York 10605*

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Hajnal, Andras, Gerard P. Smith, and Ralph Norgren. Oral sucrose stimulation increases accumbens dopamine in the rat. *Am J Physiol Regul Integr Comp Physiol* 286: R31–R37, 2004. First published August 21, 2003; 10.1152/ajpregu.00282.2003.—Although taste can influence meal size and body weight, the neural substrate for these effects remains obscure. Dopamine, particularly in the nucleus accumbens, has been implicated in both natural and nonnatural rewards. To isolate the orosensory effects of taste from possible postingestive consequences, we investigated the quantitative relationship between sham feeding of sucrose and extracellular dopamine in the nucleus accumbens with microdialysis in rats. Sucrose intake linearly increased as a function of concentration (0.03 M, 18.07 ± 2.41 ml; 0.1 M, 30.92 ± 2.60 ml; 0.3 M, 43.28 ± 2.88 ml). Sham feeding also stimulated accumbens dopamine overflow as a function of sucrose solution concentration (0.03 M, 120.76 ± 2.6%; 0.1 M, 140.28 ± 7.8%; 0.3 M, 146.27 ± 5.05%). A second experiment used the same protocol but clamped the amount of sucrose ingested and revealed a similar, concentration-dependent dopamine activation in the nucleus accumbens. This is the first demonstration of a quantitative relationship between the concentration-dependent rewarding effect of orosensory stimulation by sucrose during eating and the overflow of dopamine in the nucleus accumbens. This finding provides new and strong support for accumbens dopamine in the rewarding effect of sucrose.

orosensory positive feedback; control of food intake; motivation

ALTHOUGH SUBSTANTIAL PROGRESS has been made in understanding the neural code for the sensory properties of gustatory stimuli, much less is known about the neural basis for the hedonic qualities elicited by the same chemicals. For taste and behavioral studies, sucrose is commonly used as an exemplar of a palatable tastant because it is innately preferred by both humans and rodents (28, 33, 44, 59). In brief exposure tests, preference increases as a monotonic function of concentration (19, 67). Sham-feeding studies in rats demonstrate that the orosensory stimulating effect of sucrose is sufficient to initiate and maintain ingestion also in a concentration-dependent manner (25, 44, 63, 74). Human nutrition studies also reveal a strong effect of sweet tastants on regulation of hunger and satiety (15, 18, 26, 37, 42, 43).

Considerable evidence implicates the mesencephalic dopamine (DA) system in motivational and reward processes (9, 21, 35, 40, 53, 75). Although its exact role remains controversial (10, 21, 35, 40), in the rat both natural and nonnatural (i.e., drug of abuse) rewards activate DA neurons in the ventral tegmental area (VTA; A10) that project to the ventral striatum, predominantly to the medial shell of the nucleus accumbens (NAcc) (11, 70). The evidence for the involvement of DA systems in sucrose reward derives from studies that demonstrate a suppression of both real and sham feeding by systemically applied DA antagonists (22, 25, 34, 56, 57, 66). Conversely, manipulations that increase DA levels also enhance preference for and real intake of sucrose (12, 29, 62, 69). Sham-feeding studies also have investigated the potency of sugar solutions to alter forebrain DA systems (65, 73), but none has directly assessed extracellular DA in the NAcc.

Microdialysis experiments demonstrated that intraorally applied saccharin causes an increase in extracellular levels of NAcc DA in naive rats (Ref. 41; A. Hajnal, unpublished data). In a previous experiment (29), we used chronic microdialysis to demonstrate that a single sucrose concentration (0.3 M) increased NAcc DA in experienced real-feeding rats. These results eliminated the problems associated with in vitro neurochemistry but left open the specific contribution of pre- and postabsorptive components of the ingested sucrose. Therefore, in the present experiments, a gastric fistula preparation was used to assess the role of orosensory factors alone in NAcc DA activation. In the first experiment, ad libitum-fed rats were given unrestricted access to different concentrations of sucrose solutions during daily 20-min sham feeding and microdialysis sessions. After the main effect was proven, we repeated the study in an additional group of rats with a similar protocol but clamped the intake of sucrose to control for the differential ingestion normally driven as a function of concentration.

Results from subsets of these data have appeared as abstracts (31, 32).

METHODS

Subjects and surgeries. Nineteen adult male Sprague-Dawley rats (275–325 g, Charles River, Wilmington, MA) were housed individually on a 12:12-h light-dark schedule (lights on 7 AM) and kept on a standard laboratory diet [Rodent Diet (W)8604; Harlan Teklad, Madison, WI]. For implantation of microdialysis cannulas, the subjects were anesthetized with pentobarbital sodium (50 mg/kg ip) after a pretreatment with atropine sulfate (0.15 mg/kg ip). The rats were implanted stereotaxically with bilateral, 21-gauge stainless steel guide cannulas positioned above the posterior medial NAcc (A 1.0 mm, L 1.0 mm from the bregma, and V 4.0 from the surface of the skull; Ref. 48).

After 1-wk recovery, the rats were deprived of food for 18 h and anesthetized as before to implant stainless steel gastric cannulas. Cannula design and implantation surgery are described in detail elsewhere (64). The rats recovered for at least 14 days before the start of sham-feeding training.

All the procedures used in this experiment were approved by the Institutional Animal Care and Use Committee of the Pennsylvania State University College of Medicine and comply with the American Physiological Society's "Guiding Principles for Research Involving Animals and Human Beings."

Address for reprint requests and other correspondence: A. Hajnal, Dept. of Neural and Behavioral Sciences H181, Coll. of Medicine, Pennsylvania State Univ., Hershey, PA 17033 (E-mail: ahajnal@psu.edu).

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Training and tests for sham feeding with sucrose. The rats were maintained on regular lab chow ad libitum, except for 1 h before and 1 h after the training and test sessions. A mild overnight water deprivation (8 PM–10 AM) served to initiate licking during training and, later on, to maintain the behavior when 0.03 M sucrose was presented. Experience with real feeding reduces intake for three to five tests during subsequent sham feeding (20, 74). Therefore, the rats in the present experiments were naive to the postingestive effects of sucrose; they never ingested sucrose with a closed gastric fistula.

Because of the limits of the microdialysis probes, each rat had only three test days. Thus, to collect data for each concentration from each rat, only three concentrations of sucrose were used (0.03, 0.1, and 0.3 M). These concentrations represent the dynamic range in the behavioral concentration-response function for sucrose in sham-feeding rats (20). For the same reason (i.e., the failure of the microdialysis probes after 3 days) and because a previous study failed to show DA responses to water (29), water as a stimulus was omitted from this study.

Throughout training, the different concentrations of sucrose were presented randomly to minimize contrast effects (24, 27) or other expectancies (58). The rats were trained to sham feed each sucrose solution at least three times before the microdialysis tests were initiated. Training continued until the rats initiated sham feeding reliably and 20-min intakes were stable across test days. Thus training lasted for 9–12 days before the tests in the microdialysis chambers.

Experiment 2 was designed to vary concentration while fixing the volume of intake to control for the difference in the amount of movement required to ingest volumes that ranged from ~18 ml (0.03 M) to ~43 ml (0.3 M). The same training protocol was used in *experiment 2* with the following modifications. *1*) Before random presentation of the three sucrose concentrations, the rats ($n = 5$) sham fed the lowest concentration of sucrose (0.03 M) for 3 days to establish a baseline intake for clamping volume. *2*) From *day 4* on through the remaining training and the microdialysis tests, the rats received the same volume of the two concentrations of sucrose. This volume was 75% of the average intake of 0.03 M sucrose by each rat on the last 2 days of the baseline period. This criterion was used because pilot studies in a separate set of rats ($n = 5$) revealed that, at the concentrations to be used at testing, rats would not necessarily consume 100% of the 0.03 M sucrose volume but they did ingest 75% consistently.

Microdialysis and HPLC. Microdialysis probes were constructed with silica glass tubing (37-μm ID; Polymicro Technologies, Miami Lakes, FL) inside a 26-gauge stainless steel tube with a tip of cellulose tubing (20-kDa cutoff, 0.2-mm OD × 2-mm length; Spectrum, Ranch Dominguez, CA). They were perfused through a microdialysis swivel (375/D/22QE; Instech Laboratories, Plymouth Meeting, PA) with artificial cerebrospinal fluid [aCSF; in mM: 145 NaCl, 2.7 KCl, 1.2 $CaCl_2$, 1.0 $MgCl_2$, and 2.0 Na_2HPO_4 in HPLC-grade water (Fisher Scientific International, Pittsburgh, PA) adjusted to pH 7.4] at a rate of 1.0 μl/min with microsyringe pumps (model A99; Razel Scientific Instruments, Stamford, CT). The outlet branch of the probe led to a 400-μl vial clipped to a flexible cable 15 cm above the head of the rat. To reduce the oxidation of DA, the vials were prefilled with 5 μl of aCSF solution containing 0.1 M HCl and 100 μM EDTA. Microdialysis was conducted in three sessions on each animal, one session per day. At least 12 h before the first test day, the bilateral microdialysis probes were inserted. They extended 4.0 mm beyond the guide shafts to reach the target area and were left implanted for all three test days.

DA and the monoamine metabolite 3,4-dihydroxyphenylacetic acid (DOPAC) were analyzed by reverse-phase HPLC with coulometric detection. Samples (15 μl) were injected with an autosampler (ESA 540, Chelmsford, MA) to a 15-cm column with 3-mm bore and 3-μm C-18 packing (ESA MD-150). The mobile phase contained 60 mM sodium phosphate, 100 μM EDTA, 1.24 mM heptanesulfonic acid (Sigma), and 6% (vol/vol) methanol at pH 3.6. Once separated, the compounds were measured with a Coulochem II system (ESA; analytic cell: model 5014B, *electrode 1* −175 mV, *electrode 2* +175 mV; guard cell: model 5020, +300 mV). For our system, the detection limit for DA is ~2.0 fmol/15 μl standard sample. In brain microdialysates, DOPAC levels typically are >100-fold higher than DA, so detection limits are not an issue.

Histology. Histology was performed to verify placement of the microdialysis probes. The rats received an overdose of pentobarbital sodium (150 mg/kg ip) and, once deeply anesthetized, were perfused transcardially with 0.9% saline solution followed by 10% formalin. Blocks of the brains that included the NAcc were frozen and serially sectioned at 50 μm. The sections were mounted on microscope slides, stained with cresyl violet, and examined with a light microscope. Of the 38 probes implanted in *experiments 1* and *2*, six failed to impinge on the target, the posterior shell of NAcc as defined in the Paxinos and Watson atlas (48). Data from these six cases were discarded.

Statistical analyses. Although both hemispheres were sampled, as it happened, data were analyzed from only one probe in each rat. The selection was made on the basis of the probe placement, the stability of the baseline samples, and the number of days (up to 3) that the probe remained functional. On this basis, the final statistical analyses included data for samples from 10 right and 9 left probes. DA data obtained from the left and right hemispheres did not differ statistically [*sample 4*: $F(1,55) = 0.829$, $P < 0.37$; $n = 19$].

Basal recovery of DA and DOPAC varied considerably between subjects. For this reason, peak overflow of both molecules [area under the peaks analyzed on a personal computer with a Chromatographic Data System (ESA501)] was converted to a percentage of the mean values of three 20-min baseline samples taken during the hour before the sham-feeding tests with the sucrose solutions. These percentage data for DA and DOPAC were analyzed by separate two-way ANOVAs (sample × concentration) with repeated measures on the time factor, i.e., 20-min samples, followed by post hoc Newman-Keuls tests when justified (i.e., between samples across concentrations and their respective baseline). In addition, Wilks' lambda test was used to test for the effects of a combination of dependent variables. Covariance and linear regression analyses were used for assessment of dose-response curves and interactions. The 20-min fluid intakes were analyzed with one-way ANOVAs for the concentration effect and two-way ANOVAs for interactions between concentration × day of presentation. Statistical analysis was carried out with Statistica 6.0 software (Tulsa, OK), and differences were considered significant when $P < 0.05$.

RESULTS

Sham-fed intake of sucrose. During the first set of microdialysis tests, there was a significant effect of sucrose concentration on sham feeding [0.03 M, 18.07 ± 2.41 ml; 0.1 M, 30.92 ± 2.60; 0.3 M, 43.28 ± 2.88 ml; $F(2,39) = 22.88$, $P < 0.0001$; Fig. 1] but no effect from the order of presentation [concentration × day of presentation: Wilks' lambda = 0.91, $F(8,76) = 0.46$, $P = 0.87$]. With one exception, the individual concentration-response functions were positive, near linear, and highly correlated [$r = 0.69$, $F(1,43) = 38.96$, $P < 0.0001$; Fig. 2].

In *experiment 2*, all rats established stable sham-fed intake of 0.03 M sucrose (19.80 ± 1.98 ml) with 3 days of training. To fix the volume ingested while varying the concentration, during microdialysis each rat was given 75% of its training volume when it was tested with 0.03 M and 0.3 M sucrose. All rats consumed all of this volume of both concentrations within 20 min.

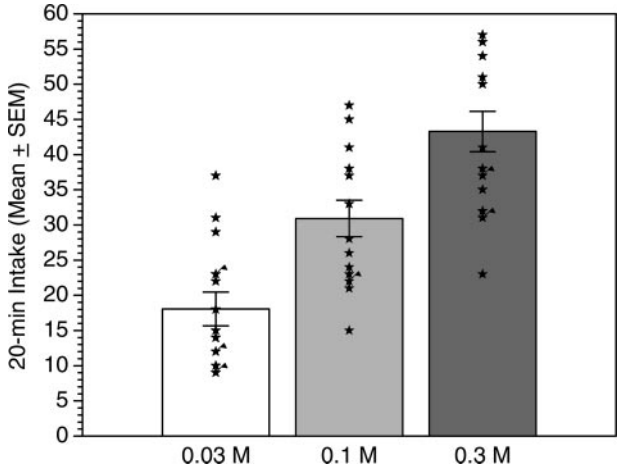

Fig. 1. Intake of sham-fed sucrose in daily 20-min sessions at different concentrations. Values are means (±SE) and include data from the microdialysis sessions. Asterisks depict intake of individual rats (in ml; $n = 14$). Flags indicate overlapping data points. Intake in the microdialysis cages and in the training cages did not differ statistically. For more details and statistics, see RESULTS.

DA and DOPAC changes in response to sham-fed sucrose. The basal amount of DA and DOPAC (mean ± SE) in the dialysate was 34.8 ± 12.4 fmol/15 μl and 0.41 ± 0.1 pmol/15 μl, respectively.

In *experiment 1*, extracellular DA in the NAcc increased in response to sham-fed sucrose across all concentrations (0.03 M, 120.76 ± 2.6%; 0.1 M, 140.28 ± 7.8%; 0.3 M, 146.27 ± 5.05%; *sample 4* in Fig. 3, *top*). The concentration effect was statistically significant [*sample 4*: $F(2,39) = 6.5725$, $P < 0.01$], as was its positive linear correlation [$r = 0.407$, $F(1,55) = 10.901$, $P < 0.002$]. Post hoc tests revealed that whereas the effect of the lowest concentration (0.03 M) on DA overflow was significantly different from that of the higher concentrations (0.1 and 0.3 M; $P = 0.008$ and $P = 0.003$, respectively), there was no statistical difference between the effect of 0.1 M and 0.3 M ($P = 0.432$).

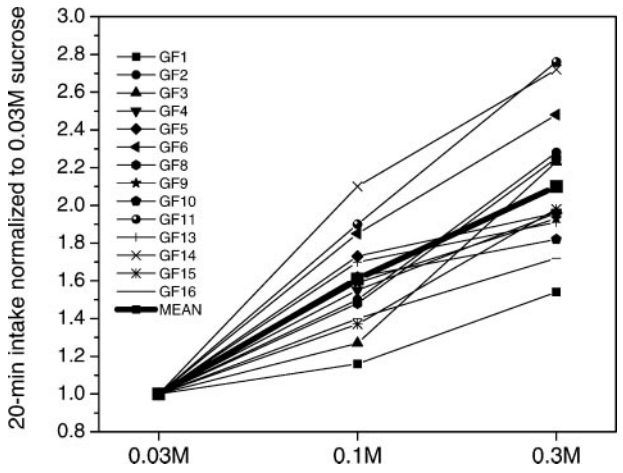

Fig. 2. Individual dose-response curves in sham-feeding sessions with different concentrations of sucrose. The volumes ingested in the 20-min sham-feeding sessions during microdialysis were normalized to the intake of the lowest concentration. Thin lines represent intakes from individual rats identified by log names (GF1–16). [Data from 2 rats (GF7, 12) were excluded from the analysis and from this article because of either misplacement or malfunction of the probes.] Thick line represents the mean ($n = 14$).

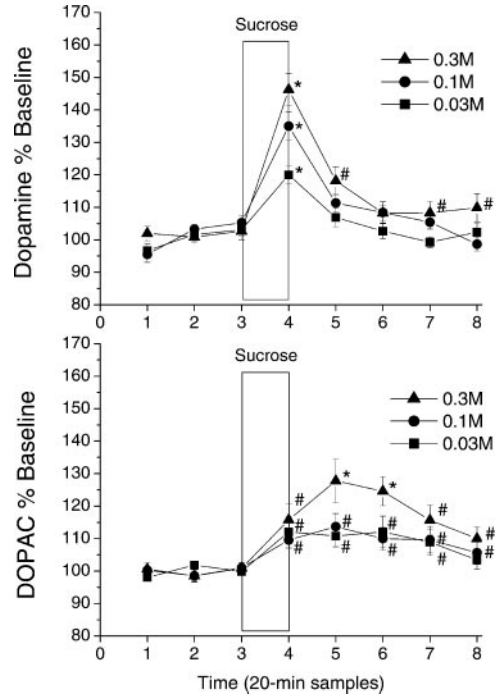

Fig. 3. Extracellular levels of dopamine (DA; *top*) and 3,4-dihydroxyphenylacetic acid (DOPAC; *bottom*) in the nucleus accumbens (NAcc) in response to sham licking of sucrose in *experiment 1*. Values are expressed as % of mean baseline (±SE; $n = 14$) before, during, and after 20 min of unrestricted sucrose access (sucrose). Different concentrations were presented on consecutive days in the same ad libitum-fed rats, in a counterbalanced fashion. Statistical symbols indicate results of post hoc tests with significant differences from the baseline (*sample 3*: $*P < 0.01$, $\#P < 0.05$). For further analyses see RESULTS.

Sham feeding all three concentrations of sucrose also increased DOPAC (Fig. 3, *bottom*). The increase began during sucrose ingestion and lasted for at least 80 min when sampling ceased. There was a dose effect [$F(2,280) = 6.6160$, $P < 0.02$; Fig. 3, *bottom*], which was a result of the strongest sucrose concentration differing from the lower concentrations that were statistically identical (post hoc tests: *samples 5* and *6*, $P < 0.02$ and $P < 0.04$, respectively).

In *experiment 2*, sham feeding of equal volumes of weak and strong sucrose increased extracellular DA significantly over baseline and the increase was greater for 0.3 M than for 0.03 M [$F(1,71) = 28.66$, $P < 0.02$; *sample 4*: 156.05 ± 11.78% vs. 126.47 ± 2.83%; post hoc test, $P < 0.03$; Fig. 4, *top*]. The correlation between sucrose concentration and the DA response was statistically significant [$r = 0.639$, $F(1,8) = 5.546$, $P < 0.05$; Fig. 5]. Comparison for DOPAC also yielded a statistically significant concentration effect [$F(1,71) = 13.79$, $P < 0.05$; Fig. 4, *bottom*] carried by differences at 20 min after the sham-feeding session (post hoc test: *sample 5*, $P < 0.02$).

Histology. The tips of all probes that provided data were located in the caudomedial NAcc (A 10.0–10.6 according to Ref. 48) medial to the anterior commissure (L 0.8–1.8). The area from which samples were collected was reconstructed from individual probe placements and is depicted in Fig. 6. The actual tracks of probe tips were often curved because of the flexibility of the membrane and gliosis in the surrounding brain tissue. This feature and the extensive overlap of the probe sites

made a more precise analysis of individual sampling sites impractical. Overall, the sampled brain region corresponded to the midposterior aspect of the medial shell and medial core of the NAcc.

DISCUSSION

Our present data reinforce previous findings showing that rats sham feed sugar solutions in a concentration-dependent manner (25, 44, 74). This observation underscores the role of orosensory factors in the preference of sucrose ("sweet reward") without the confounding metabolic effects of ingested food. The fundamental finding of our study was to demonstrate a concentration-dependent increase in extracellular DA levels in the NAcc. Moreover, the second experiment in which the intake volume was fixed substantially controlled for motor activity. Although this finding (i.e., dose-response function of accumbens DA to a rewarding stimulus) is unique, several prior studies do support the observation. Previous behavioral data showed a differential reinforcing effect of concentration when small volumes of sucrose were consumed during operant conditioning and other tasks (1, 72). Conversely, the reinforcing efficacy of sucrose concentration on progressive ratio performance was dose-dependently suppressed by the DA D2/D3 receptor antagonist raclopride (16). In contrast to our experiment, however, the small volumes used in these studies minimized but did not eliminate postingestive feedback of sucrose. Further support comes from pharmacological data in sham-feeding studies that revealed a dose-dependent inhibition

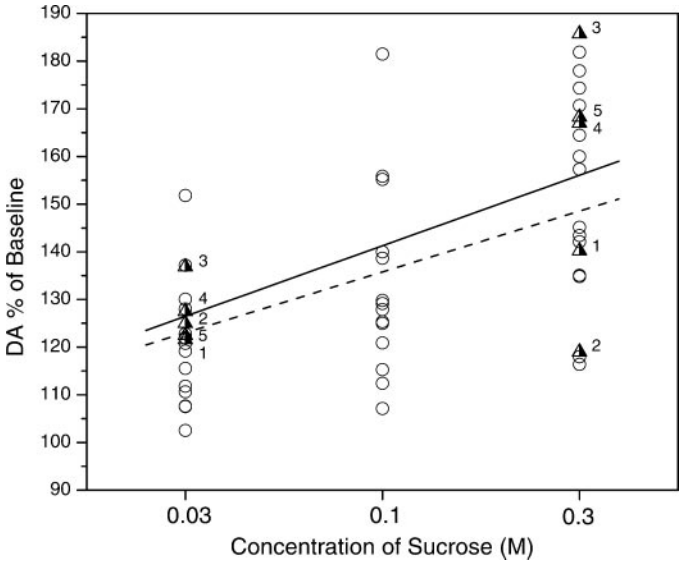

Fig. 5. Correlation between DA release in the NAcc and concentration of sucrose in *experiments 1* and *2*. Symbols depict individual data of peak DA release expressed as % of the baseline (identical to *sample 4* in Figs. *3*, *top*, and 4) across different concentrations of oral sucrose (0.03, 0.1, and 0.3 M in *experiment 1* and 0.03 and 0.3 M in *experiment 2*). Open circles: data from *experiment 1*, in which rats with open gastric fistula had unlimited access to sucrose. Half-filled triangles: data from *experiment 2*, in which rats sham fed a restricted amount of sucrose. Dashed line: regression line for *experiment 1*. Solid line: regression line for *experiment 2*. Numbers are the log numbers of individual rats in *experiment 2*. For further explanation and statistics, see RESULTS.

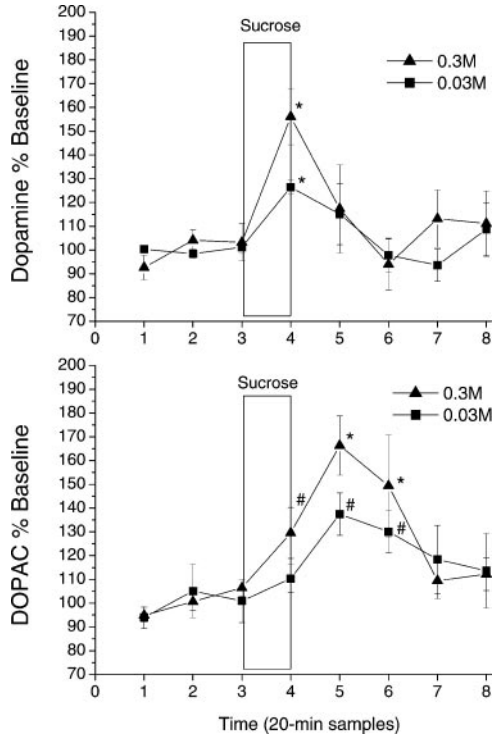

Fig. 4. Extracellular levels of DA (*top*) and DOPAC (*bottom*) in the NAcc in response to sham licking of sucrose in *experiment 2*. Values are expressed as % of mean baseline (±SE; $n = 5$) before, during, and after 20-min sham feeding of the same volume of 0.03 M or 0.3 M sucrose. Statistical symbols indicate results of post hoc tests with significant differences from the baseline (*sample 3*: $*P < 0.01$, $\#P < 0.05$). For further analyses see RESULTS.

of sucrose intake by D1 and D2 DA receptor antagonists (34, 57, 76).

The effects of the systemic antagonists and the reward produced by sucrose are consistent with a dose-dependent release of DA rather than with its tonic effect. Our prior study (29) using intra-accumbens reverse microdialysis of DA receptor antagonists revealed no tonic effect by D1 receptors on real sucrose intake. When basal DA levels and sucrose intake were increased with nomifensine, however, the same blockade did dampen ingestion (29). Strong support for the importance of phasic DA release comes from a recent in vivo voltametry study demonstrating the specificity of DA transients in the accumbens during cocaine administration (50).

Nonetheless, tonic DA levels remain relevant because they regulate the phasic release of DA. Indeed, parallel experiments in our laboratory (7, 8) revealed that experience with restricted sucrose access may result in presynaptic neuroadaptation in the NAcc, including upregulation of the DA membrane transporter and downregulation of the D2/D3 autoreceptors, both factors that determine DA tone as well as the effectiveness of phasic DA release. A further experiment illustrated the effects by showing that experience with scheduled sucrose feeding resulted in augmented extracellular metabolite levels in response to a subsequent chow (30). Because the rats in the present experiment also had experience with the sucrose protocol before the microdialysis sessions, the sustained high DOPAC levels after the tests may also reflect altered tonic regulation. Follow-up studies that control for contextual variables and feeding conditions are needed to clarify the specificity and relevance of this finding.

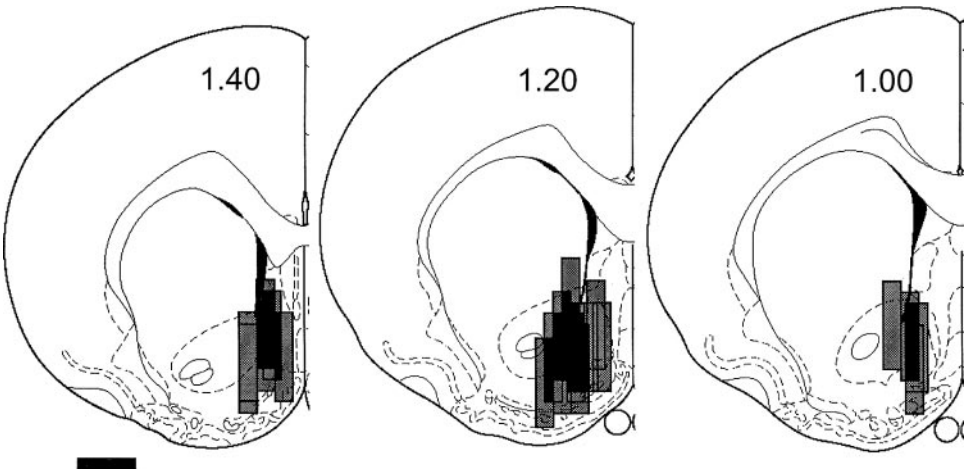

Fig. 6. Schematic frontal sections of the rat brain's left hemisphere showing microdialysis sites in the NAcc. Gray bars depict reconstructed extent of the active membrane of the microdialysis probes (0.2 mm × 2 mm) as identified in the histological analysis. Black fields represent the areas of overlap and, in turn, indicate the most often sampled brain area. The number on each section is the distance in millimeters anterior from the bregma according to Paxinos and Watson (48). Scale bar, 1 mm.

How does oral sucrose affect accumbens DA? In fact, the mesoaccumbens DA system has many potential connections with the gustatory system. Palatable foods, including sucrose, activate VTA neurons (47). Conversely, VTA lesions selectively reduce consumption of preferred sucrose solution (61). The nucleus of the solitary tract (NST), the first central relay of the gustatory system (45), possesses neural connections with the VTA (36, 39). The NAcc also receives afferent projections from the caudal NST (77) and communicates back to the NST (13, 68) via a circuit that includes the parabrachial nucleus (PBN) (71). The PBN, the second central gustatory relay, projects to the gustatory cortex via the gustatory thalamus and also projects heavily to limbic structures including the central nucleus of the amygdala, the lateral hypothalamus, and the bed nucleus of the stria terminalis (45), all of which send axons to the NAcc shell (38) and are connected also to the VTA (46, 51). The cortical gustatory area can also reach NAcc via substantial connections to the central nucleus of the amygdala, the lateral hypothalamus, and the prefrontal cortex (45, 60). In summary, the anatomy suggests many avenues through which gustatory neural activity in both the hindbrain and forebrain could influence DA release in the terminal fields. Thus some of these neural substrates are very likely to be involved in behavioral activation by sucrose sham feeding.

Increases in NAcc DA, however, also occur in conjunction with motor activity, reward learning, and the relative salience of the stimulus driven by the deprivation state (3, 10, 14, 17, 40, 49, 53–55). To control for these factors, we first used rats that received water instead of sucrose. In contrast to the present experiment, overnight water deprivation failed to induce intake comparable to that of the weakest concentration of sucrose. For this reason, and also because of the limited number of microdialysis sessions possible in a given rat, water was omitted as a control from the present study. Nonetheless, in prior experiments using deprived rats with extensive training in 20-min licking sessions, real water intake (i.e., nongastric fistula) failed to influence NAcc DA release (29, 30). This observation suggests a dissociation of mechanisms that are responsible for incentive salience induced by need state and those that are driven by the orosensory rewarding effects of sucrose (9).

As mentioned above, in a prior experiment that did include water training in addition to sucrose, the control fluid produced no detectable DA responses (29). In the present experiment, we specifically presented the three different concentrations of sucrose randomly during training to mitigate the chances of habituation or Pavlovian conditioning confounding the test results (2–6, 21). Finally, the fact that the DA responses were concentration dependent further reduces the probability that a conditioned response could account for a large proportion of the phenomenon. Another observation was made contrary to previous studies, in which a single preexposure to a complex food stimulus reduced the DA response from the NAcc shell during the second trial (3, 4, 6). Because of the extensive training given to our rats, if any habituation took place, it presumably was complete before our test trials. Thus the responses that we measured after the training trials probably reflected the direct sensory events. Another possible explanation for the lack of habituation is anatomic. Although DA responses assayed in the NAcc shell show evidence of habituation, under similar circumstances those produced in the NAcc core do not (2). Our probe placements were such that, on balance, we probably measured some DA release from both subdivisions.

Interestingly, the magnitude of the DA peaks in response to sham licking the most preferred 0.3 M sucrose solution in the present experiment was significantly lower (i.e., 50–65%) than that of the DA responses to real feeding of the same concentration of sucrose in our previous experiments (29, 30). This difference may reflect a contribution of postabsorptive factors. Specifically, insulin has been proposed to influence DA function in the mesoaccumbens system (23, 52). Even in the sham-feeding rat, an effect of preabsorptive insulin release on the NAcc DA cannot be excluded.

In conclusion, the results demonstrate a significant, monotonic relationship between the intensity of orosensory stimulation provided by different concentrations of sucrose and the overflow of DA from the nucleus accumbens. This relationship was caused by the oral concentration of sucrose because postingestive effects were excluded by the use of sham feeding. This relationship was not caused by the amount of ingestive movements because it occurred when the volume ingested was fixed. This is the first demonstration of such a quantitative relationship with a natural food reward. It provides strong and

additional support for the importance of mesolimbic DA mechanisms in the motivating and rewarding effects of sweet taste.

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