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Anterior Cingulate Taste Activation Predicts Ad Libitum Intake of Sweet and Savory Drinks in Healthy, Normal-Weight Men[1–3]

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Abstract

After food consumption, the motivation to eat (wanting) decreases and associated brain reward responses change. Wanting-related brain responses and how these are affected by consumption of specific foods are ill documented. Moreover, the predictive value of food-induced brain responses for subsequent consumption has not been assessed. We aimed to determine the effects of consumption of sweet and savory foods on taste activation in the brain and to assess how far taste activation can predict subsequent ad libitum intake. Fifteen healthy men (age: 27 ± 2 y, BMI: 22.0 ± 1.5 kg/m^2) participated in a randomized crossover trial. After a >3-h fast, participants were scanned with the use of functional MRI before and after consumption of a sweet or savory preload (0.35 L fruit or tomato juice) on two occasions. After the scans, the preload juice was consumed ad libitum. During scanning, participants tasted the juices and rated their pleasantness. Striatal taste activation decreased after juice consumption, independent of pleasantness. Sweet and savory taste activation were not differentially affected by consumption. Anterior cingulate taste activation predicted subsequent ad libitum intake of sweet ($r = -0.78$; $P < 0.001_{\text{uncorrected}}$) as well as savory juice ($r = -0.70$; $P < 0.001_{\text{uncorrected}}$). In conclusion, we showed how taste activation of brain reward areas changes following food consumption. These changes may be associated with the food's physiological relevance. Further, the results suggest that anterior cingulate taste activation reflects food-specific satiety. This extends our understanding of the representation of food specific-appetite in the brain and shows that neuroimaging may provide objective and more accurate measures of food motivation than self-report measures. J. Nutr. 142: 795–802, 2012.

Introduction

The process of satiation, which ultimately results in meal termination, consists of a complex interaction between neural, hormonal, and gastro-intestinal signals (1,2). Satiation, and thereby intake, is affected by numerous internal (physiological) and external (environmental) factors (3). All these factors are integrated in the brain and ultimately result in a particular pattern of food intake. Ninety percent of the foods that people consume can be categorized as either sweet or savory (4). Sweetness is associated with mono- and disaccharides, which are an important source of energy for the body. Savoriness is associated with umami, fatty and salty tastes (often protein- and fat-containing foods) (5,6), which also signal a source of energy and are essential for maintaining electrolyte balance (7).

It has been suggested that SSS[6], which is defined as the relative decrease in pleasantness of a food (8), is higher for savory than for sweet foods (9). Although SSS, by definition, refers to (changes in) liking, consumption of a food also decreases the motivation to eat, i.e., wanting, and both contribute to a food's reward value (10). Because wanting reflects a need state, it seems likely that changes in wanting are also food specific. Several studies have suggested that liking and wanting have different neural substrates (11–13) but are, however, hard to separate in experimental practice (14–16).

Interestingly, a recent study showed no difference in ad libitum intake between sweet and savory foods matched for palatability, texture, energy density, and macronutrient composition (17). This suggests that differential effects of sweet and savory foods on satiation and possibly on the brain are due to

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[6] Abbreviations used: ACC, anterior cingulate cortex; fMRI, functional MRI; MNI, Montreal Neurological Institute; RMANOVA, repeated measures ANOVA; ROI, region of interest; SSS, sensory-specific satiety; VAS, visual analogue scale.

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differences in these food properties rather than to learned satiety effects associated with sweet and savory taste.

Effects of food consumption on the brain have been examined in several neuroimaging studies, e.g., by comparing taste or odor responses before and after consumption (18–20) and by scanning during satiation (21). Areas affected by consumption include the insula, striatum, ACC, hippocampus, and amygdala (18,19,21). However, the predictive value of food-induced brain responses for subsequent intake has not been established. In particular, taste cues might elicit brain responses indicative of subsequent intake, because tasting provides an assessment of food quality, composition, and palatability.

Therefore, we first aimed to determine which brain areas showed food-specific changes in sweet and savory taste activation following consumption of a preload. We hypothesized that taste responses to an eaten food would decrease in reward-related brain areas like the striatum and amygdala. Second, we aimed to establish the predictive value of taste activation with regard to subsequent food intake for a sweet as well as for a savory food. We expected that brain areas found to be affected by satiety may predict ad libitum intake; the candidate regions were the insula, striatum, ACC, hippocampus, and amygdala (18,19,21).

Materials and Methods

Participants. Healthy, normal-weight, righted-handed men were recruited by flyers posted at the University Medical Center Utrecht. Exclusion criteria were: restrained eating (22) [Dutch Eating Behavior Questionnaire (23) score >2.5], disliking one of the products, smoking, an energy-restricted diet, or changes in body weight >5 kg during the last 2 mo, eating disorder, history of or current alcohol consumption >28 units/wk, or any diseases (including neurological, psychiatric diseases, and taste and smell disorders) and use of medication. In total, 15 normal-weight, right-handed men [age (mean ± SD): 27.3 ± 1.9 y; BMI: 22.0 ± 1.5 kg/m^2] enrolled in the study. All experimental procedures were approved by the Medical Ethical Committee of the University Medical Center Utrecht (NL22266.041.08). Before the experiment, written informed consent was obtained from all participants. The sample size was based on previous fMRI (functional MRI) studies (20,24).

Design. This study had a randomized crossover design with 2 conditions (sweet and savory). Each condition involved 2 scans sessions with at least 1 wk between the 2 study days. The order of the conditions was randomized per participant (**Fig. 1**).

Test foods. Three stimuli were used. The first was a sweet fruit juice, which was a thick peach and orange juice mix (Appelsientje Dubbeldrank Sinaasappel and Perzik, FrieslandCampina; nutritional value of 0.1 L: 13.1 g carbohydrates, of which 12.9 g was sugars; 0 g fat; 0.28 g fiber; 0.001 g sodium; 8 mg vitamin C; and an energy content of 230 kJ). The second was a savory tomato juice (Appelsientje Zontomaatje, FrieslandCampina; nutritional value of 0.1 L: 2.9 g carbohydrates, of which 2.9 g was sugars; 9 g fat; 0.40 g fiber; 0.25 g sodium; 15 mg vitamin C; and an energy content of 69 kJ). The third stimulus was Dutch tap water and this was used as a control stimulus. However, participants did not know that the control stimulus was water; it was presented to them as a control taste. The fruit juice is referred to as the sweet stimulus, tomato juice as the savory stimulus, and water as the control. The taste taken as the preload (independent of which taste) is referred to as the target taste. The other taste, i.e., the one not taken as a preload, is referred to as the nontarget taste.

Experimental procedures. Participants fasted for at least 3 h before the scan sessions. All sessions were scheduled in the afternoon and participants were instructed to eat lunch around noon and to not consume anything afterwards.

When participants arrived, they first completed the appetite questionnaire, in which hunger, fullness, thirst, and desire to eat something sweet and savory were rated on a 100 mm VAS (visual analogue scale). Secondly, they tasted the three stimuli and rated them on pleasantness, intensity, sweetness, and saltiness on a 100 mm VAS (stimulus questionnaire). After the ratings, participants were placed in the scanner for their first scan.

Inside the scanner participants had the tip of 4 bounded tubes in their mouth (internal diameter of 3 mm/tube). The tips were comfortably positioned between the lips so that the tubes delivered the stimuli on the front of the tongue. The 3 stimuli and water (for rinsing) were delivered at room temperature (23°C) by use of 4 programmable syringe pumps. The pumps were programmed to administer 1 mL at 0.028 L/min. The 3 stimuli were pseudo-randomly presented, 7 times each. VAS ratings of pleasantness and intensity during the scan were made by use of a button box. Instructions were displayed on a screen through a computer interface, run by the computer program PRESENTATION. After tasting for 9 s, participants gave either VAS ratings (8 s) (after 4 out of 7 trials) or were directly cued to swallow (4 s). Then participants received a rinse with water (9 s), followed again by a cue to swallow (4 s), and rest (fixation on a crosshair for 4 s).

After the scanner, a 0.35-L preload of either tomato juice (savory taste condition) or fruit juice (sweet taste condition) was consumed. Participants drank the preload through a straw from an unmarked cup. When the preload was finished, the participants again completed the appetite and stimulus questionnaires. Subsequently, participants were scanned again according to the same protocol as the first scan. Finally, participants were given a cup with the preload juice from which they were instructed to drink the juice ad libitum. The participants could not see the amount they drank. After consumption, the appetite and stimulus questionnaires were again completed.

fMRI data acquisition. The scans were performed on a 3-Tesla Philips Achieva at the University Medical Center Utrecht. First, a T_1-weighted anatomical scan was acquired [repetition time/echo time = 61/8.4 ms, flip angle = 30°, field of view = 288 × 175 mm, 175 axial slices, voxel size = 1 × 1 × 1 mm). Second, a fMRI scan was made (3D presto echo planar imaging sequence, repetition time/echo time = 906/15.6 ms, flip angle = 90°, field of view = 224 × 224 × 150 mm, 43 interleaved axial slices, voxel size = 3.5 × 3.5 × 3.5 mm). The total duration of each functional scan was 15 min, during which 990 volumes were obtained. After the functional scan, one additional functional volume was acquired, but with a flip angle of 27° for better anatomical contrast.

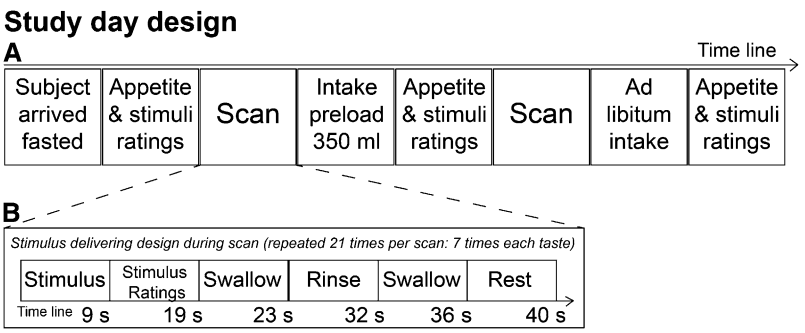

FIGURE 1 Overall design of a study day (*A*) and the scan design (*B*). The savory and sweet condition had the same design. During the 2 fMRI scans, all 3 stimuli were tasted 7 times in randomized order, making a total of 21 taste cycles. fMRI, functional MRI.

fMRI data processing and analysis. fMRI data were preprocessed and analyzed using SPM8 run with MATLAB 7.5 and the WFU Pickatlas-tool (29). First, the functional volumes of every participant were realigned to the first volume of the first run. Second, the anatomical image was co-registered with the additional functional volume with a flip angle of 27°, after which this was co-registered with the mean functional image. Third, the images were normalized (retaining $3.5 \times 3.5 \times 3.5$ mm voxels) to MNI (Montreal Neurological Institute) space (30) and spatially smoothed with a Gaussian kernel of 8 mm full width at half maximum.

A statistical parametric map was generated for every participant by fitting a boxcar function to each time series, convolved with the canonical hemodynamic response function. Data were high-pass filtered with a cutoff of 128 s.

Within-participant analyses. For every scan session, 7 conditions were modeled: tasting the control, sweet stimuli, savory stimuli, swallowing, rinsing, and giving ratings of pleasantness and intensity. The responses to swallowing, rinsing, and rating were neglected in further analyses. Taste activation contrast images were calculated by first subtracting the control stimulus from the other stimuli (sweet and savory stimuli), resulting in 2 contrast images (sweet vs. control and savory vs. control) for each participant per scan.

In total, 8 contrast images for taste activation per participant were calculated ($2 \times 2 \times 2$): sweet before target, sweet after target, savory before target, savory after target, sweet before nontarget, sweet after nontarget, savory before nontarget, and savory after nontarget.

Group analyses. To determine the effect of preload on target and nontarget taste activation, all target and nontarget contrast images were entered into a 2 (before and after preload) ×2 (target and nontarget) RMANOVA with the mean pleasantness ratings per participant as measured during the scan added as a covariate. To determine the effect of preload per taste category all 8 contrast images were entered into a $2 \times 2 \times 2$ (time × target × taste) RMANOVA. The resulting statistical parametric maps were thresholded at $P < 0.001$, $k > 10$; this threshold resembles an overall significance level of $P < 0.05$, corrected for multiple comparisons across the whole brain based on Monte Carlo simulations of random noise distribution using the 3DClustSim module of AFNI (27,28).

A priori ROIs (regions of interest) were the orbitofrontal cortex, striatum, hippocampus, thalamus, amygdala, and insula. These regions have been shown to be involved in effects of consumption and satiation on taste activation in previous neuroimaging studies (20,29,30). ROI masks were made using the WFU Pickatlas tool (25).

To determine the brain regions where taste activation covary with ad libitum intake after the scans, the two target contrast images during the second scan were entered into a repeated-measure ANOVA. The ad libitum intake of the sweet juice was used a covariate for the sweet target contrast image and the savory juice intake was used as a covariate for the savory target contrast image. The liking and desire to eat something sweet and savory ratings were also added as covariates to excluded effect of these factors on the correlations of interest. The same model was used with the nontarget taste activation contrast to check for taste specificity. Correlations ($P < 0.001$, uncorrected for multiple comparisons) between brain activation and ad libitum intake, liking ratings, or desire to eat ratings were tested for in SPM8.

For all significant clusters, mean parameter estimates of taste activation were obtained with the use of MarsBaR.

Statistical analyses. All subjective ratings were analyzed using SPPS 16.0. Data are presented as means ± SD. Mean pleasantness, intensity, desire to eat something sweet or savory, sweetness, saltiness, hunger, and fullness ratings were compared using a $3 \times 2 \times 2$ and a $2 \times 2 \times 2$ RMANOVA with time point [baseline, after preload, and after ad libitum (3) or before and after preload (2)], condition (sweet or savory), and taste (target, nontarget, and control) as factors. Bonferroni-corrected paired t tests were used for post hoc comparison. Pearson correlation coefficients ($P < 0.05$) were calculated to test associations between pleasantness, desire to eat something sweet and savory, hunger, fullness ratings (during and after the second scan), and ad libitum intake.

With the use of the subjective pleasantness ratings, SSS scores were calculated (31). This was done by subtracting the changes in ratings of liking (pleasantness) of the target juice (tomato or fruit) from before the preload to after the preload from the corresponding mean change in ratings of the reference stimuli (control or nontarget juice). Thus, the more negative the SSS scores for a food, the higher the degree of SSS.

Results

Subjective data

Hunger and fullness. There were main effects of time on hunger ($P < 0.001$) and fullness ($P < 0.001$). Hunger ratings decreased after preload and ad libitum intake compared to baseline (both $P < 0.05$). Fullness ratings increased after the preload and ad libitum intake compared with baseline (both $P < 0.05$). Hunger and fullness ratings were not differentially affected by the two conditions (**Table 1**).

Desire to eat something sweet and savory. There was a main effect of time for both desire to eat sweet ($P < 0.05$) and savory ($P < 0.05$). Note that there were missing values at time

TABLE 1 Pleasantness ratings and SSS scores for the fruit (sweet) and tomato (savory) stimuli and desire to eat something sweet/savory, hunger, and fullness ratings during the sweet and savory conditions in healthy, normal-weight, young men[1,2]

	Sweet condition			Savory condition		
	Baseline	After preload	After ad libitum	Baseline	After preload	After ad libitum
Hunger	51 ± 23[a]	37 ± 21[b]	28 ± 23[c]	66 ± 17[a]	44 ± 23[b]	30 ± 21[c]
Fullness	29 ± 17[c]	54 ± 23[b]	69 ± 22[a]	36 ± 18[c]	61 ± 16[b]	74 ± 14[a]
Pleasantness						
Fruit	65 ± 19[a]	54 ± 28[b]	37 ± 24[c]	63 ± 20[a]	62 ± 20[a]	60 ± 23[a]
Tomato	50 ± 26[a]	43 ± 24[a]	38 ± 27[a]	57 ± 21[a]	42 ± 23[b]	30 ± 21[c]
Desire to eat						
Sweet	50 ± 20[a]	41 ± 22[b]	25 ± 16[c]	46 ± 18[a]	52 ± 22[a]	44 ± 22[a]
Savory	59 ± 19[a]	62 ± 18[a]	49 ± 18[b]	54 ± 20[a]	44 ± 17[b]	36 ± 20[b]
SSS scores		−10 ± 23[a]	−16 ± 21[a]		−15 ± 27[a]	−23 ± 25[a]

[1] Values are means ± SD, $n = 15$. Means within a row and condition with superscripts without a common letter differ, $P < 0.05$ (repeated-measure ANOVA, post hoc paired t test). There was no effect of condition and taste stimuli. SSS, sensory-specific satiety; VAS, visual analogue scale.

[2] Rating performed on 100 mm VAS.

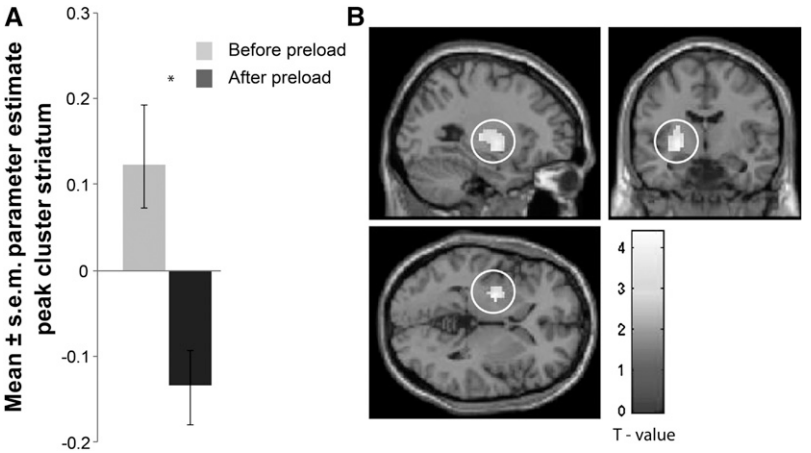

FIGURE 2 Striatum response for the target taste in healthy, normal-weight, young men in both sweet and savory conditions before and after the preload, $n = 15$. In *A*, mean ± SEM parameter estimates of the taste activation are presented in bars. (*B*) A T-map of the taste activation in the striatum (marked with a white circle). Activation is thresholded at $T = 2.8$, which corresponds to $P < 0.005$ uncorrected for multiple comparisons for better visualization. *Activation was significantly greater before the preload (ROI analysis, post-ANOVA *t* test, $P < 0.001$, uncorrected for multiple comparisons).

point 3. Desire to eat something sweet decreased over time in the sweet ($P < 0.05$) but not in the savory condition. Desire to eat something savory decreased after the preload compared to baseline for the savory ($P < 0.05$) but not for the sweet condition.

Pleasantness. There was a main effect of time [2 × 3 RMANOVA ($P < 0.001$), 3 × 3 RMANOVA ($P < 0.005$)] and an interaction between taste and time [outside ($P < 0.001$), inside ($P < 0.005$)]. Pleasantness ratings for the target taste decreased over time ($P < 0.05$ between all time points). For the control and nontarget taste, no changes were observed ($P > 0.05$). Condition did not affect pleasantness ratings (Table 1; **Supplemental Table 1**).

Intensity. There was a main effect of taste ($P < 0.005$). Intensity ratings (outside and inside the scanner) were different among the 3 stimuli ($P < 0.05$). The control stimulus was perceived as less intense ($P < 0.05$) (Table 1). Condition and time did not affect the intensity ratings.

Saltiness and sweetness. There was a main effect of taste [saltiness ($P < 0.001$), sweetness ($P < 0.001$)].The tomato juice was perceived as more salty and the fruit juice as more sweet ($P < 0.05$) (**Supplemental Table 2**). Condition and time did not affect the saltiness ratings.

Correlations. There was no correlation between changes in pleasantness of the fruit juice and the desire to eat something sweet ($r = 0.51$; $P = 0.11$) or between the changes in pleasantness of the tomato juice and the desire to eat something savory ($r = 0.19$; $P = 0.51$).

SSS. SSS occurred during both sessions. SSS scores did not differ between the 2 conditions after preload ($P = 0.29$) (Table 1).

Ad libitum intake. The ad libitum intake of fruit juice was (mean ± SD) 0.28 ± 0.19 L and of tomato juice, 0.26 ± 0.22 L. There was no difference between the fruit and tomato juice ad libitum intake ($P > 0.05$). Ad libitum intake was not correlated with pleasantness ($r = 0.04$; $P = 0.82$), hunger ($r = 0.10$; $P = 0.60$), fullness ($r = -0.19$; $P = 0.32$), and desire to eat the associated taste category ($r = 0.29$; $P = 0.12$) ratings just before the juice was ad libitum ingested.

Neuroimaging data

Consumption. Overall effects of consumption on overall taste activation were observed in the right amygdala, insula, and hippocampus (**Supplemental Table 3**). For the target taste, taste activation in the striatum (pallidum and putamen) and thalamus decreased with consumption of the preload. After consumption, taste activation in the hippocampus increased (**Table 2**; **Figs. 2** and **3**). Nontarget taste activation increased after consumption in the midbrain [MNI (11, −32, −18), Z = 4.39], cingulate gyrus [MNI (7, −49, −18), Z = 4.25], and the right insula [MNI (39, 11, −14), Z = 3.78].

The effect of consumption on target taste activation differed between the 2 tastes. When participants consumed the fruit

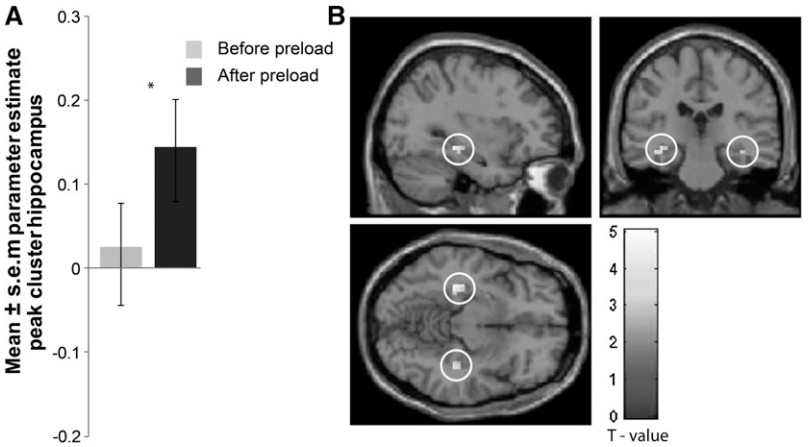

FIGURE 3 Hippocampus response for target taste in healthy, normal-weight, young men in both sweet and savory conditions before and after the preload, $n = 15$. In *A*, mean ± SEM parameter estimates of the taste activation are presented in bars. (*B*) A T-map of the taste activation in the hippocampus (marked with a white circle). Activation is thresholded at $T = 2.8$, which corresponds to $P < 0.005$ uncorrected for multiple comparisons for better visualization. *Activation was significantly greater after the preload (ROI analysis, post-ANOVA *t* test, $P < 0.001$, uncorrected for multiple comparisons)

TABLE 2 Effect of consumption on target taste activation for both sweet and savory conditions in healthy, normal-weight, young men[1]

Regions	Cluster size[2]	Peak voxel coordinates[3] x	y	z	Z-score
Before > after preload					
Striatum *					
Pallidum L*	67	−25	−7	−4	4.20
Putamen L*		−25	−11	14	3.63
Putamen L*		−28	−21	7	3.53
Thalamus L*	51	−25	−28	7	5.02
Before < after preload					
Hippocampus L*	31	−32	−28	−11	4.75
Hippocampus R	22	42	−35	−11	4.00

[1] Values are clusters of mean brain activation, $n = 15$. All are ROI analyses. Clusters are differences in brain activation before and after preload intake. *Also significant at FWE-corrected, $P < 0.05$. . L, left hemisphere; MNI, Montreal Neurological Institute; R, right hemisphere; ROI, region of interest.
[2] Reported clusters were thresholded at $P < 0.001$ uncorrected for multiple comparisons, with a cluster extent threshold k > 10 voxels.
[3] Voxel coordinates are in MNI space (26).

TABLE 3 Effect of consumption on sweet target taste activation in sweet condition and savory target taste activation in savory condition in healthy, normal-weight, young men[1]

Regions	Cluster size[2]	Peak voxel coordinates[3] x	y	z	Z-score
Sweet					
Before > after preload					
Pallidum L	20	−25	−7	−4	4.09
Before < after preload					
Cerebellum	98	28	−56	28	4.16
Amygdala R	13	28	4	−14	3.86
Midbrain	17	−4	−25	−14	3.78
ACC	35	0	4	28	3.43
		0	18	28	3.42
Savory					
Before > after preload					
Striatum ROI					
Putamen L	3	−28	−21	4	3.72
	3	−28	−39	4	3.64
	9	−21	−7	14	3.59
Before < after preload					
Striatum ROI					
Caudate L	7	−14	18	4	3.49
Hippocampus L	9	−35	−32	−11	3.48
Hippocampus R	3	42	−35	−11	3.48

[1] Values are clusters of mean brain activation, $n = 15$. Contrasts were calculated using t tests on the contrast images of before and after preload of the sweet and savory target taste. L, left hemisphere; MNI, Montreal Neurological Institute; R, right hemisphere; ROI, region of interest.
[2] Reported clusters were thresholded at $P < 0.001$, uncorrected for multiple comparisons, which corresponds to a Z-score > 3.0.
[3] Voxel coordinates are in MNI space (26).

preload, the target taste showed a greater response in the amygdala, midbrain, and ACC after the preload. There was a decreased response in the striatum (pallidum) after consumption when the target taste was sweet (**Table 3**).

In the savory condition, the target taste elicited a decreased response in putamen and striatum (caudate) after consumption, whereas activation in the ventral striatum and hippocampus increased (Fig. 3; Table 3).

Activation did not differ between the sweet and the savory target tastes.

Prediction of ad libitum intake. Target taste activation in the ACC during the second scan negatively correlated with subsequent ad libitum intake (**Table 4**). The same was observed when the sweet and savory conditions were analyzed separately (sweet $r = -0.78$ and savory $r = -0.70$, both $P < 0.001$ uncorrected for multiple comparisons in SPM8) (**Fig. 4**; Table 4). Liking ratings were not correlated with any taste activation. The desire to eat a food of the same taste category was correlated with activation in part of the ACC [MNI (0, 49, 7) Z = 3.55; $P < 0.001$ uncorrected for multiple comparisons]. Nontarget taste activation was not correlated with ad libitum intake.

Discussion

We found that after sweet and savory food consumption taste activation decreased in the striatum for the target taste, independent of pleasantness. This was not the case for the nontarget taste. Moreover, ACC taste activation predicted subsequentad libitum intake, which was independent of the type of taste.

Effect of consumption. In previous studies, the effects of consumption related to changes in pleasantness were observed in the orbitofrontal cortex (32,34). The hedonic value that changed during consumption is defined as liking, referring to the palatability of the food, whereas the motivation to eat is associated with wanting; both contribute to food reward (10). In behavioral studies, wanting and liking are assessed by asking participants to rate their desire to eat (wanting) and the pleasantness of a taste on that moment (liking) (34). In our study, the pleasantness and desire to eat something sweet and savory ratings changed during both conditions; however, the relative change of wanting and liking were not correlated. Because SSS occurred for both taste [during both conditions, the pleasantness of the target taste decreased relative to that of the nontarget taste and control following preload consumption (40)], we added pleasantness ratings as a covariate to be able to examine wanting related changed in taste activation. The brain responses that increased or decreased as an effect of consumption were due to the specific wanting-related changes. Preload consumption induced changes in the target taste activation in the striatum, amygdala, anterior cingulate cortex, hippocampus, midbrain, and cerebellum. These areas are known to be involved in reward and memory (21,32,35). In addition, the nontarget taste evoked activation in the midbrain, mid cingulate gyrus, and anterior insula, i.e., known as primary taste cortex areas (6). The effect of consumption occurred in reward-related areas for the consumed taste and in gustatory areas for the nonconsumed taste.

Sweet and savory target taste. When comparing sweet and savory target taste activation, no difference was observed. When only looking at sweet or savory target taste activation after consumption, we found food-specific effects in the amygdala, anterior cingulate cortex, ventral striatum, and hippocampus; even changes in palatability and desire to eat the associated taste did not differ between conditions. There was one notable exception, for the sweet as well as the savory target taste: the

TABLE 4 Brain areas during the second scan that covariate negatively with ad libitum intake in the sweet and savory condition in health, normal weight, young men[1]

Regions	Cluster size[2]	Peakvoxel coordinates[3]			Z-score
		x	y	z	
Overall					
ACC*	28	7	39	4	4.17
Sweet					
ACC	11	4	42	4	3.45
Savory					
ACC	15	7	32	4	3.23

[1] Values are clusters of mean brain activation that correlated with ad libitum intake, n = 15. Contrasts were calculated using t tests on the contrast images of after preload of the sweet and savory target taste. *Also significant at FWE-corrected, $P < 0.05$. ROI analyses. L, left hemisphere; MNI, Montreal Neurological Institute; R, right hemisphere; ROI, region of interest.
[2] Reported clusters were thresholded at $P < 0.001$, uncorrected for multiple comparisons, which corresponds to a Z-score > 3.0, with a cluster extent threshold k > 10.
[3] Voxel coordinates are in MNI space (26).

response in the left ventral striatum decreased after consumption. This is in line with the role of this reward area in food craving (36) and putamen activation has been shown in the prediction of reward (37). Moreover, note that this decreased striatal response was not due to changes in pleasantness, because pleasantness was added as a covariate and because it was not observed for the nontarget taste. This suggests that the decrease in ventral striatal taste activation reflects a diminished motivation to eat a specific food, i.e., a food-specific decline in wanting. According to Cabanac's (38) theory of alliesthesia, taste pleasantness decreases after eating a food, because there is a signal of the absence of any need for the associated food's nutrients (e.g., sweet taste is associated with sugar and salty/savory taste with salt). This theory illustrated how difficult it is to separate liking and wanting (16). Brain response changes, independent of pleasantness, could provide a better understanding of the neural correlation of the desire to eat (wanting) (39).

Activation in the amygdala, anterior cingulate cortex, and midbrain increased only after a sweet preload consumption. It has been shown in previous studies that activation in the anterior cingulate increased with satiation by a sweet food (19,21). The right amygdala response also increased. This area is involved in both positive and negative reward processes (32,35,40). Smeets et al. (20) observed an increased amygdala response for an energy-rich sweet juice after consumption of the same juice, an effect that did not occur when tasting a nonenergy-rich sweet juice. This is in line with our results: the savory juice, which contains very little carbohydrate, did not affect amygdala activation (20).

In the savory condition, taste activation in the ventral striatum and hippocampus was greater after the preload. The ventral striatum receives signals from the hippocampus, a limbic region, which is involved in learning and memory processes but also in the regulation of feeding (41). DelParigi et al. (42) found increased posterior hippocampus activity after satiation in lean participants and some studies suggested that the ventral striatum is involved in satiation (18,43). Jensen et al. (44,45) showed that the ventral striatum is crucial in the reward system and is activated in the anticipation of an aversive stimulus, which is in

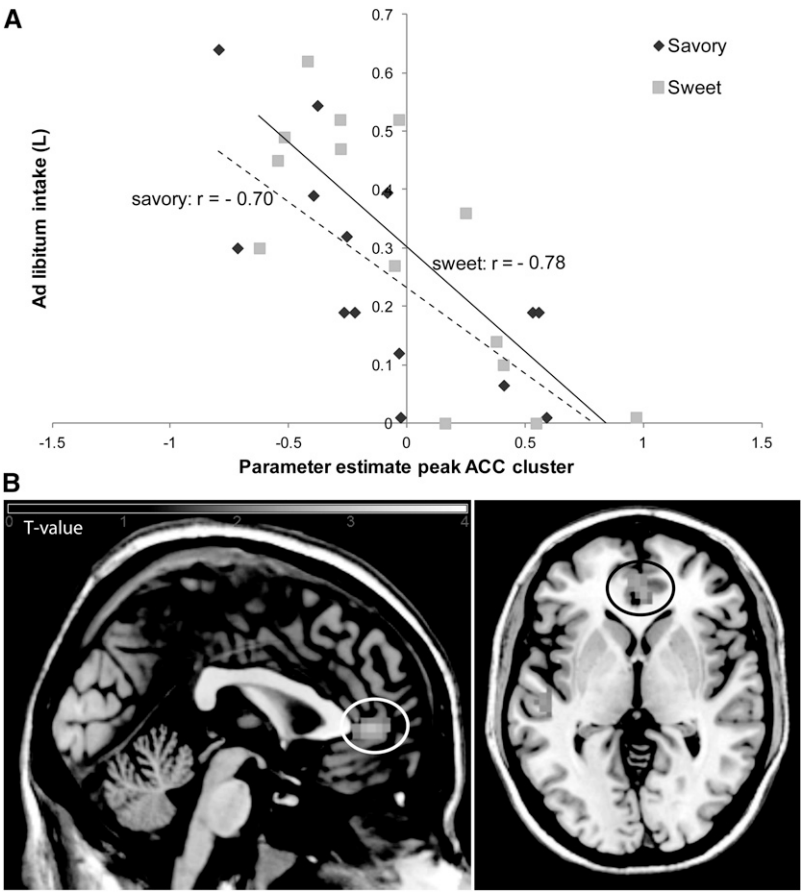

FIGURE 4 Correlation between taste activation in the ACC and ad libitum intake in healthy, normal-weight, young men in both sweet and savory conditions before and after the preload, n = 15. In *A*, a scatter plot represents the parameter estimates of the ACC cluster during the second scan and ad libitum intake of all participants in the sweet and savory condition. The line represents the sweet taste, the dashed line the savory ($P < 0.001$ uncorrected for multiple comparisons). (*B*) A T-map of the taste activation in the ACC (marked with a white and black circle). Activation is thresholded at T = 2.8, which corresponds to $P < 0.005$ uncorrected for multiple comparisons for better visualization.

accordance with the savory findings, were the wanting ratings decreased.

The different changes in brain response for sweet and savory consumption might be explained by the macro-nutrient differences and viscosity, in particular the energy content. Fruit juice contains more energy than tomato juice and drinking the fruit juice may therefore be more rewarding for the body, although when comparing the two, no difference was found.

A study limitation is that our findings cannot be extrapolated to other sweet and savory foods; this remains to be explored in future studies. In general, the use of sweet and savory as categories is challenging, because it is very hard to match food properties like macronutrient composition. To our knowledge, only one study has succeeded in this (17). What would be more feasible is to show general and macro-nutrient–specific effects of consumption on brain response to food stimuli. In addition, it needs to be established whether the same effects occur for more viscous (solid) foods. Such studies are needed to confirm or refine the general and food-specific effects reported here.

Prediction of ad libitum intake. We found that anterior cingulate activation correlated negatively with subsequent ad libitum intake for both sweet and savory juice, i.e., stronger anterior cingulate activation was associated with lower ad libitum intake. To our knowledge, this is the first time that taste activation has been linked to subsequent ad libitum intake. Previous studies implied that the ACC along with the insula, striatum, hippocampus, and amygdala is involved in the process of satiation, which ultimately leads to meal termination (18,19,21,46). In particular, our results extend previous findings of increased anterior cingulate activation in response to satiety and decreasing reward (21). Other studies suggest that this part of the anterior cingulate reflects satisfaction or even aversion (47). Moreover, Small et al. (21) found that the anterior cingulate activation increased during satiation with chocolate, i.e., a sweet high-energy food. In our study, both sweet and savory taste activation in the ACC correlated with ad libitum intake but only when the taste had been consumed as a preload. This suggests that previous findings of sweet taste-associated activation (21) are also indicative for responses to a savory-tasting product. Importantly, nontarget taste activation did not correlate with ad libitum intake, which suggests that anterior cingulate activation represents food-specific satiety. How this is related to specific repletion of nutrients remains to be established. This of importance when understanding people's eating motivation and consumption. Thus, our results strongly suggest that taste activation of the anterior cingulate is indicative of the degree of fullness, i.e., it is inversely related to the degree of specific wanting of that particular taste. Future studies should clarify the importance of the ACC during the process of satiety. The ACC is a extremely active region and is involved in many processes, i.e., desire, addiction, and cognition (48), and its activation was observed in numerous studies where the internal state was altered (19,21).

In conclusion, when a juice was consumed, activation of the striatum, a brain reward area, decreased for the associated taste but not for the other tastes, which indicated a food-specific, wanting-related activation change, independent of pleasantness changes. However, sweet and savory differences in macronutrients and viscosity could evoke the more food-specific wanting-related changes in the amygdala, hippocampus, and anterior cortex. This could reflect associated changes in physiological relevance and may underlie food-specific changes in wanting.

Furthermore, the anterior cingulate response predicted subsequent ad libitum juice intake, irrespective of the type of taste. These findings extended our understanding of the representation of food-specific appetite in the human brain and suggest that neuroimaging may provide an objective and more accurate measure of food motivation than self-report measures.

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