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Research report

Ventral pallidal coding of a learned taste aversion

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HIGHLIGHTS

- Pairing nausea with a palatable taste sufficed to induce a learned taste aversion.
- We found that safe hedonic tastes elicited excitatory increases in firing rate of VP neurons.
- Aversion learning reversed the VP response into a conditioned decrease in neuronal firing rate.

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ABSTRACT

The hedonic value of a sweet food reward, or how much a taste is 'liked', has been suggested to be encoded by neuronal firing in the posterior ventral pallidum (VP). Hedonic impact can be altered by psychological manipulations, such as taste aversion conditioning, which can make an initially pleasant sweet taste become perceived as disgusting. Pairing nausea-inducing LiCl injection as a Pavlovian unconditioned stimulus (UCS) with a novel taste that is normally palatable as the predictive conditioned stimulus (CS+) suffices to induce a learned taste aversion that changes orofacial 'liking' responses to that sweet taste (e.g., lateral tongue protrusions) to 'disgust' reactions (e.g., gapes) in rats. We used two different sweet tastes of similar initial palatability (a sucrose solution and a polycose/saccharin solution, CS± assignment was counterbalanced across groups) to produce a discriminative conditioned aversion. Only one of those tastes (arbitrarily assigned and designated as CS+) was associatively paired with LiCl injections as UCS to form a conditioned aversion. The other taste (CS−) was paired with mere vehicle injections to remain relatively palatable as a control sweet taste. We recorded the neural activity in VP in response to each taste, before and after aversion training. We found that the safe and positively hedonic taste always elicited excitatory increases in firing rate of VP neurons. By contrast, aversion learning reversed the VP response to the 'disgusting' CS+ taste from initial excitation into a conditioned decrease in neuronal firing rate after training. Such neuronal coding of hedonic impact by VP circuitry may contribute both to normal pleasure and disgust, and disruptions of VP coding could result in affective disorders, addictions and eating disorders.

1. Introduction

The learning of a taste aversion for a novel food (Pavlovian conditioned stimulus or CS+) that has consequences such as nausea (an unconditioned stimulus or UCS), transforms a palatable taste into a disgusting one, and is an evolved function shared by many species, from humans to rats [43,17]. Many species have been shown to have experimentally-induced taste aversion learning: mammals, birds, fish, and reptiles. Pavlovian taste aversion is an extremely robust form of learning and can occur to a wide range of foods and liquids across all taste categories [17].

In rats, a novel sweet taste paired with visceral illness induced by LiCl becomes not only avoided and no longer ingested, but also if tasted again elicits 'disgust' or aversive affective orofacial reactions, such as gapes, headshakes, and forelimb flails [38,20,21,5]. This conditioned 'disgust' is best measured by the taste reactivity test, in which a flavored solution is infused into the rat's mouth via a previously-implanted oral cannula, to control stimulus exposure while affective reactions are video recorded [20,21]. The taste reactivity test allows full assessment of conditioned 'disgust' reactions because the experimenter can control exposure to the taste,

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whereas conditioned flavor avoidance makes it unlikely that an animal would approach and voluntarily consume a taste that had been paired with illness, making taste reactions difficult to gauge. The taste reactivity test exploits affective orofacial expressions elicited by sweet vs. bitter tastes and shared by many mammals, including human infants, old and new world primates, and rodents [20–22,3].

While affective reactions to taste do not need to be learned, they are at the same time not purely reflexive. Affective reactions to a particular taste are altered by preference learning as well as aversion learning, and by relevant physiological states of caloric hunger or satiety (for sweetness), and specific appetites (for saltiness) [2,4]. Additionally, several brain manipulations of hedonic substrates in forebrain and brainstem are able to manipulate palatability to alter taste reactivity patterns [42,20,21,13,44,3,57,25]. Therefore affective taste reactivity patterns reflect more than mere sensory properties. Rather, the affective reactions reflect the palatability of tastes, i.e., whether the taste is 'liked' or 'disliked'.

The ventral pallidum (VP) is the chief target of the nucleus accumbens and integrates and processes reward information flowing through the mesocorticolimbic system [29,33,46,58,61,66]. VP projections additionally target preoptic regions of the lateral hypothalamus, the mediodorsal nucleus of the thalamus, and in turn connect to larger limbic cortico-striatopallidal-thalamocortical loops, and to additional basal ganglia and brainstem nuclei such as the subthalamic nucleus, substantia nigra, and pedunculopontine nucleus [11,23,32]. Given its extensive connections, the VP has been proposed to be a region that can mediate various aspects of reward [30,33,46,58] and to be involved in translating motivational signals into action [32,34].

In particular, the posterior half of the VP in rats contains an approximately cubic-millimeter 'hedonic hotspot', in which opioid or orexin agonist microinjections can double the number of positive 'liking' orofacial expressions elicited by sucrose taste [24,56]. Further evidence suggests that the VP is necessary for normal levels of 'liking', as excitotoxin lesions that destroy neurons in posterior VP, or temporary inactivations of posterior VP induced by pharmacological microinjections, eliminate positive orofacial expressions to sweet tastes, and replace them with 'disgust reactions' [13,25,53].

The firing rates and population responses of neurons in the posterior VP track the hedonic impact of UCS tastes in electrophysiological recording experiments, as well as the incentive motivation value of learned CS predictors [62–65,57]. For example, a previous study found that VP neurons fired in robust excitatory patterns response to an orally infused sucrose taste that was 'liked', but did not respond to an intensely salty taste (3X seawater concentration) that elicited 'disgust' reactions [64]. However, after animals were pharmacologically put into a physiological state of sodium deficiency, the hedonic value of the intensely salty taste changed from negative 'disgust' to positively 'liked', as assessed by affective orofacial expressions, and the VP neurons now responded to the salty taste with a large firing rate increase that became equal to the sucrose-elicited elevation in firing. In other words, the VP neuronal response represented the hedonic value of the taste. Further, the intensity of VP excitatory firing tracks the degree of 'liking' for a sweet taste, when both are quantitatively enhanced by opioid stimulation in nucleus accumbens [57]. Similarly, human neuroimaging studies have reported that VP activity was correlated with the subject's rating of the inferred pleasantness for appetizing food images, especially in posterior VP, whereas anterior VP activity may correlate more with disgust ratings for images such as rotten foods [8]. In sum, the VP is in an anatomical position to be a principal player for reward functions, and the intensity of excitatory activation patterns of posterior VP neurons appears especially to code the degree of 'liking' for a taste's hedonic impact.

The overall goal of this study was to further investigate how the neuronal activity in ventral pallidum tracks in the hedonic value of a sweet taste from positive 'liked' to negative 'disgust' induced by a learned taste aversion.

Here we discriminatively paired nausea-inducing LiCl injections (Pavlovian UCS) with a particular sweet taste that is normally palatable, while simultaneously recording facial reactions and neural activity in the VP. The discriminative training procedures created a conditioned aversion selectively for just one (CS+) of two tastes. We used two distinctly different sweet, caloric tastes in this experiment (counterbalanced between groups): a sucrose solution vs. a polycose/saccharin combination solution. Both tastes elicited 'liking' taste reactivity patterns prior to conditioned aversion, but are sufficiently different in sensory details that rats can tell them apart. One taste was arbitrarily designated that rat's CS+, to be subsequently paired associatively with several nausea-inducing LiCl injections (the UCS) to induce a conditioned aversion. The other was arbitrarily designated the CS− or safe taste for a particular rat, which was familiarized with that taste by allowing several days of free access to the CS− in the home cage (to induce Pavlovian latent inhibition, making CS− less likely to be included in the subsequently learned aversion).

We used latent inhibition to help preserve the 'safe' status of CS− [5,68], because other studies that did not use pre-exposure reported significant generalization of aversion between one sweet CS+ taste paired with LiCl and other sweet tastes (even though they had not been paired) [6,44,38,36]. CS− pre-exposure may facilitate discriminative recognition of sensory differences between CS− and CS+, as well as inducing Pavlovian latent inhibition specifically for the CS− that protects from aversion generalization between the two sweet tastes. Altogether, this pre-exposure helps make the CS+ aversion more discriminatively specific to that single taste, and allows the CS− to remain relatively palatable after conditioning [5].

We recorded neural activity in the VP, as well as behavioral taste reactivity, in response to each taste at the beginning and end of the experiment. We hypothesized that the shift of the hedonic value of CS+ taste from 'liked' to 'disgusting' would be reflected in a reduction of neural activity in the ventral pallidum. We also hypothesized that the VP activity to the CS− taste would be less altered.

2. Material and methods

2.1. Subjects

Ten adult male Sprague-Dawley rats weighing 300–400 g were used in this experiment. Rats were housed individually in tub cages on a 9:30 AM to 7:30 PM reversed light/dark schedule. Experiments were conducted during late morning to afternoon hours, coinciding with the rats' active (dark) period after acclimating to housing conditions for 1–2 days. Food and water were available ad libitum throughout testing, except when in the recording chamber.

2.2. Apparatus

All training and testing was conducted while rats were placed in a clear plastic test cylinder of diameter 25 cm which was placed inside of a 28 cm × 35 cm × 60 cm clear plastic chamber with a glass floor. The chamber was illuminated with white light from below. The use of white light provided better illumination of the rat's mouth and tongue which was necessary for taste reactivity video scoring (see detailed description of behavioral analysis below). The top of the cylinder and chamber was open, allowing for plastic tubing connections from the oral cannulae to the syringe pump that delivered the tastes and also connections from the electrode to the commutator via a headstage cable.

Delivery of tastes and oral stimuli were controlled by a custom software program, MTASK. Neural activity was recorded during the