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PERSPECTIVES

Bad food memories? It is just a matter of time

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In order to survive, humans and animals adjust their behaviour to adapt to an ever-changing environment. To this end, the ability to predict the relations between different sensory events (also known as associative learning) is crucial for anticipating future events and adjusting behaviour. Associative learning is particularly important in learning how to avoid sources of threat and danger in the environment. While the effectiveness of an aversive conditioned stimulus to be perceived as a threat often depends on the temporal proximity to the actual aversive event, associative learning can also happen on a larger timescale. For example, in events like food poisoning, humans and animals become averse to a new food even when the negative effect (i.e. malaise) occurs many hours following consumption. This association is crucial for survival: though a new food may be pleasant and highly nutritious it may also be toxic and life-threatening. Thus, it is not surprising that brain circuits have evolved the capability of not only detecting the taste of a novel food but also transforming its chemosensory information into a memory trace (novel-taste memory trace, TMT) (Miranda *et al.* 2003). The neural information contained in the memory trace is essential to bridge the often hours-long time-lag between taste consumption and digestive discomfort and, ultimately, form the taste–visceral malaise association (conditioned taste aversion, CTA). Multiple studies have highlighted the role that many brain regions play as neural substrates in the formation of TMTs. For example, the gustatory cortex (GC) appears to be involved in taste-novelty processing, TMT and CTA (Bermudez-Rattoni, 2014). In addition, the nucleus basalis magnocellularis (NBM), with its cholinergic projection to the GC, has been shown to be involved in novel TMT formation in the GC (Miranda *et al.* 2003). Finally, the basolateral amygdala (BLA), which sends afferents to the GC both directly and indirectly via the NBM, has been implicated in both CTA formation and taste-novelty processing (Nachman & Ashe, 1974).

Yet it remains unclear how these brain regions interact when processing taste novelty, and to what degree the BLA neural dynamics might play a role in the formation of TMT in the GC and in CTA acquisition.

As reported in this issue of *The Journal of Physiology*, Arieli *et al.* (2020) used a CTA behavioural paradigm in combination with neural manipulation and recording to shed further light on the brain dynamics underlying TMT and CTA formation in the GC. Taste-related neural processing in the GC dynamically moves through several temporal epochs of neural activity containing taste identification, palatability, and novelty coding periods (Katz *et al.* 2001; Bahar *et al.* 2004). Thus, the authors reasoned that information crucial to the formation of TMT following novel-taste consumption may be communicated between the BLA and GC through short and specific time windows of neural activity. To test this hypothesis, the authors used optogenetics to perturb BLA neurons in different temporal epochs following the consumption of a novel taste (sucrose), which was then associated with malaise (CTA). In a set of carefully designed experiments, the authors showed that inactivation of BLA neurons during a 3 s interval post-novel taste consumption impairs TMT formation and attenuates CTA. Interestingly, when the temporal windows of BLA perturbations were reduced into shorter epochs, they observed that the BLA neural activity between 0.7 and 3 s (late epoch, LE) was required for CTA acquisition. Critically, the authors found that CTA acquisition was still retained if the BLA was inactivated during an earlier novel-taste encoding epoch (0–0.5 s, early epoch, EE) and that CTA impairment was not the result of BLA-mediated changes in taste perception. To gain further insight on the circuits and neural dynamics underlying TMT and CTA, the authors performed additional experiments. Firstly, by combining c-FOS expression in the GC and optogenetic manipulation of the BLA axonal projections in the NBM, they went on to show that the BLA to NBM pathway is essential for the transmission of the LE-BLA information required to promote CTA. Secondly, using electrophysiology recordings in the GC, Ariel *et al.* investigated the role of LE-BLA activity in shaping palatability coding. Previous studies have shown that GC neural activity during LE correlates with taste hedonics (Katz *et al.* 2001), and the BLA could be the source of both innate (Piette *et al.* 2012) and learned (Grossman *et al.* 2008) taste palatability projections to the GC. Careful analysis of GC spiking activity, both at single neuron and population level, revealed that LE-BLA activity is indeed critical for updating palatability-related coding in the GC following CTA. However, BLA inactivation had no effect on GC palatability representation before CTA.

This latter observation is in contrast to previous reports indicating the BLA as being the central source of innate palatability to the GC. Arieli *et al.* suggest that this discrepancy could be explained by the fact that while the BLA participates in palatability processing, it is likely that other brain areas known to process innate taste-related information and project to the GC may compensate for the temporary lack of palatability-related BLA inputs in the absence of CTA. Nevertheless, the present results highlight the BLA as the central source of palatability coding in the GC following CTA acquisition.

In summary, the new data from Arieli *et al* report novel and important results on the neural circuits that, through temporally specific neural dynamics, promote the creation of a TMT to support the acquisition of taste–malaise association.

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Additional information

Competing interests

None.

Author contributions

M. S.: Conception or design of the work; acquisition or analysis or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work R. V.: Conception or design of the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work.

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