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Review

Conditioned taste aversion, drugs of abuse and palatability

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ABSTRACT

We consider conditioned taste aversion to involve a learned reduction in the palatability of a taste (and hence in amount consumed) based on the association that develops when a taste experience is followed by gastrointestinal malaise. The present article evaluates the well-established finding that drugs of abuse, at doses that are otherwise considered rewarding and self-administered, cause intake suppression. Our recent work using lick pattern analysis shows that drugs of abuse also cause a palatability downshift and, therefore, support conditioned taste aversion learning.

Contents

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1. Introduction

Humans, like other animals, learn to avoid eating poisonous food. Two mechanisms defend against self-poisoning: taste neophobia and conditioned taste aversion (CTA). Taste neophobia limits the ingestion of an unknown, potentially poisonous food. If the novel food proves harmless then the neophobia habituates. However, if aversive postingestive consequences occur then a CTA develops and the taste is avoided on later encounters. In the real world, the food is poisonous, but in the laboratory, to afford greater experimental control, we typically use discrete stimuli for the gustatory (i.e., a taste) and visceral stimulation (i.e., poison); the former is termed the conditioned stimulus (CS), the latter is called the unconditioned stimulus (US). CTA ensures that poisonous foods are consumed neither by accident nor mistake. It is widely agreed that CTA causes a reduction in the hedonic value of the taste CS, a property commonly referred to as palatability. Thus, the reduction in CS intake, the traditional and most commonly employed measure of CTA, can be viewed as a consequence of the conditioned reduction in palatability. However, as the quest to discover the singular nature of the US responsible for CTA acquisition became a major focus of research, the function of CTA was, we believe, somewhat obscured from sight. This was particularly highlighted when drugs of abuse were used as the US. How can an otherwise rewarding drug induce a CTA? Some theorists resolve this issue by claiming that drugs of abuse are possessed of both rewarding and aversive properties whereas others simply deny that drugs cause CTAs. However, recent results from our laboratory indicate that drugs of abuse induce, as defined above, CTAs. Furthermore, this research encourages the speculation that drug-induced CTAs could be false positives. The present article details how we arrived at this analysis and how, in so doing, we find ourselves advocating a view of CTA that is both more comprehensive and more basic than we have previously realized. We begin by describing some relevant characteristics of CTA and the distinction between CTA and taste avoidance learning. Thereafter, two approaches to the assessment of taste palatability, taste reactivity and lick pattern analysis, are introduced along with discussion about how each methodology has been used to benefit our understanding of taste learning.

2. Important features of conditioned taste aversion

> "...I have succeeded in giving him an absolute disgust for all intoxicating liquors, which I hope not even his father or his father's friends will be able to overcome. ...I therefore gave him quite as much [wine] as his father was accustomed to allow him – as much indeed, as he desired to have, but into every glass I surreptitiously introduced a small quantity of tartar-emetic – just enough to produce inevitable nausea and depression without positive sickness. Finding such disagreeable consequences invariably to result from this indulgence, he soon grew weary of it, but the more he shrank from the daily treat the more I pressed it upon him, till his reluctance was strengthened to perfect abhorrence. When he was thoroughly disgusted with every kind of wine, I allowed him, at his own request, to try brandy and water and then gin and water; for the little toper was familiar with them all, and I was determined that all should be equally hateful to him. This I have now effected; and since he declares that the taste, the smell, the sight of any one of them is sufficient to make him sick, I have given up teasing him about them. ...I wish this aversion to be so deeply grounded in his nature that nothing in after life may be able to overcome it." Anne Bronte (1848/1994, pp. 288–289) The Tenant of Wildfell Hall

As the quote above shows, CTA was recognized, if not quite by name most certainly by description, long before Garcia initiated the laboratory study of the phenomenon in the 1950s (e.g., Garcia and Kimeldorf, 1957; Garcia et al., 1955, 1956a,b). In this seminal research, Garcia and colleagues used ionizing radiation as the US. Other categories of events that are effective USs for the induction of CTAs include motion sickness (e.g., Arwas et al., 1989; Braun and McIntosh, 1973; Fox et al., 1990; Green and Rachlin, 1973; Hutchison, 1973) and, of course, poisons or toxins like cyclophosphamide and lithium chloride (LiCl; e.g., Ader et al., 1978; Dragoin, 1971; Garcia et al., 1966, 1967; Garcia and Koelling, 1966; Kalat and Rozin, 1970; Nachman and Ashe, 1973; Wittlin and Brookshire, 1968; for a more comprehensive list see Riley and Tuck, 1985). What these USs share in common is the capacity to produce what has variously been called visceral discomfort or distress, emesis, illness, malaise, nausea, sickness, or toxicosis, and which we will term gastrointestinal malaise (GIM).

Commensurate with a mechanism that evolved to defend animals against the repeated ingestion of naturally occurring food-borne poisons/toxins that threaten survival (e.g., Garcia and Ervin, 1968; Garcia et al., 1974), CTA has a number of special, perhaps unique, features. To begin, CTAs are readily acquired after a single pairing of the taste CS and a GIM-inducing US (e.g., Garcia et al., 1955; Nachman and Ashe, 1973; Revusky and Garcia, 1970; Rozin, 1986). Moreover, CTAs occurs even when many hours separate the CS from the US (e.g., Andrews and Braveman, 1975; Domjan and Bowman, 1974; Etscorn and Stephens, 1973; Garcia et al., 1966; McLaurin and Scarborough, 1963; Nachman, 1970; Nachman and Jones, 1974; Revusky, 1968; Smith and Roll, 1967). The rapidity of learning and the long temporal delays between the component events capture the fundamental value of this mechanism and the fact that the orosensory properties of the food (the CS) and the post-ingestive consequences (the US) are naturally separated in time as the ingested food travels from the mouth and along the gastrointestinal tract; a mechanism possessed of neither of these properties would be of little value in defending the body against ingested poisons. A somewhat underappreciated fact is that CTAs can be obtained even if the animal is deeply anesthetized after consumption of the CS but before administration of the US (e.g., Bermudez-Rattoni et al., 1988; Buresova and Bures, 1977, 1986; Rabin and Rabin, 1984, 1986; Roll and Smith, 1972; Welzl et al., 1990). This finding is important for at least two reasons: first, it indicates that CTAs can be acquired without "conscious" awareness and, second, it demonstrates that the CTA mechanism is blind to the origin of the US. That is, the mechanism merely associates a prior taste with subsequent GIM, irrespective of the origin of the US. From an evolutionary perspective, this makes CTA a highly effective, if blunt, protection mechanism. The downside, however, is that we develop CTAs in situations where we certainly know that the taste did not cause the subsequent GIM, as exemplified by the food aversions induced by "the flu" (Seligman, 1972), a surfeit of alcohol (Dickinson, 2008), or chemotherapy (Bernstein, 1985; Scalera and Bavieri, 2009).

As a defense mechanism, CTA serves to protect the individual after the first taste-GIM pairing has occurred. On first exposure to a new food, taste neophobia restricts intake due to fear of the potentially debilitating and life threatening postingestive consequences (e.g., Barnett, 1956, 1958; Best and Barker, 1977; Brigham and Sibly, 1999; Carroll et al., 1975; Corey, 1978; Domjan, 1977; Garcia et al., 1972a; Green and Parker, 1975; Rzoska, 1953). Thus, an innate mechanism (taste neophobia) works in tandem with a learning mechanism (CTA) to protect against the self-administration of a poisonous food. It should also be noted that learning occurs much more readily when the CS is novel prior to association with the US, a general phenomenon termed latent inhibition (Lubow, 1989, 2009; Lubow and Moore, 1959). With regard to taste stimuli, robust CTAs develop most quickly when the taste is novel (and thus potentially dangerous) than when it is familiar (and known to be safe),

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