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Extinction and renewal of cue-elicited reward-seeking

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ABSTRACT

Reward cues can contribute to overconsumption of food and drugs and can relapse. The failure of exposure therapies to reduce overconsumption and relapse is generally attributed to the context-specificity of extinction. However, no previous study has examined whether cue-elicited reward-seeking (as opposed to cue-reactivity) is sensitive to context renewal. We tested this possibility in 160 healthy volunteers using a Pavlovian-instrumental transfer (PIT) design involving voluntary responding for a high value natural reward (chocolate). One reward cue underwent Pavlovian extinction in the same (Group AAA) or different context (Group ABA) to all other phases. This cue was compared with a second non-extinguished reward cue and an unpaired control cue. There was a significant overall PIT effect with both reward cues eliciting reward-seeking on test relative to the unpaired cue. Pavlovian extinction substantially reduced this effect, with the extinguished reward cue eliciting less reward-seeking than the non-extinguished reward cue. Most interestingly, extinction of cue-elicited reward-seeking was sensitive to renewal, with extinction less effective for reducing PIT when conducted in a different context. These findings have important implications for extinction-based interventions for reducing maladaptive reward-seeking in practice.

1. Extinction and renewal of cue-elicited reward-seeking

Reward cues can influence behaviour aimed at obtaining both natural (e.g. food) and artificial rewards (e.g. drugs). This can lead to maladaptive reward-seeking such as overeating and drug abuse, where reward cues may pose a significant threat to self-regulatory behaviour and lead to relapse in those attempting to abstain or moderate their intake (Niaura et al., 1988). Understanding how to reduce the impact of reward cues on reward-seeking is therefore critical to reducing maladaptive reward-seeking.

The majority of reward-related cues are learned. For example, a child may learn that particular music signals the arrival of an ice cream truck. Once learned, such reward cues can have a variety of effects on the individual. For instance, reward cues can induce significant physiological responses, such as changes in heart rate, sweat gland activity, and skin temperature – particularly in individuals addicted to drugs of abuse (see Carter & Tiffany, 1999 for a review). Such ‘cue reactivity’ may produce a withdrawal-like source of motivation whereby the reward is sought to provide relief from the aversive affective state induced by the cue (e.g. opponent process models of addiction: Solomon & Corbit, 1974). However, there is also evidence that reward cues can directly influence motivation to obtain rewards. This process is known as Pavlovian-to-instrumental transfer (PIT). PIT is an associative learning process that occurs when a Pavlovian cue that predicts a reward elicits instrumental responses (actions) to obtain that and other rewards, despite the Pavlovian and instrumental relationships being acquired separately (Estes, 1943).

PIT has been documented in a range of animal (see Holmes, Marchand, & Coutureau, 2010 for a review) and human studies (Allman, DeLeon, Cataldo, Holland, & Johnson, 2010; Bray, Rangel, Shimojo, Balleine, & O'Doherty, 2008; Hogarth, Dickinson, Wright, Kouvaraki, & Duka, 2007). As shown in Fig. 1, the standard procedure for testing PIT involves three phases: Pavlovian acquisition, instrumental acquisition, and a transfer test (Colwill & Rescorla, 1988; Estes, 1943; Holland, 2004). In Pavlovian acquisition, a cue (e.g. a tone) is paired with the delivery of a reward (e.g. food). In a separate instrumental acquisition phase, the same reward can be obtained by making an instrumental response (e.g. pressing a lever). In the transfer test, instrumental responding is measured in the presence of the reward cue and an unpaired cue. PIT occurs when the reward cue elicits increased responding

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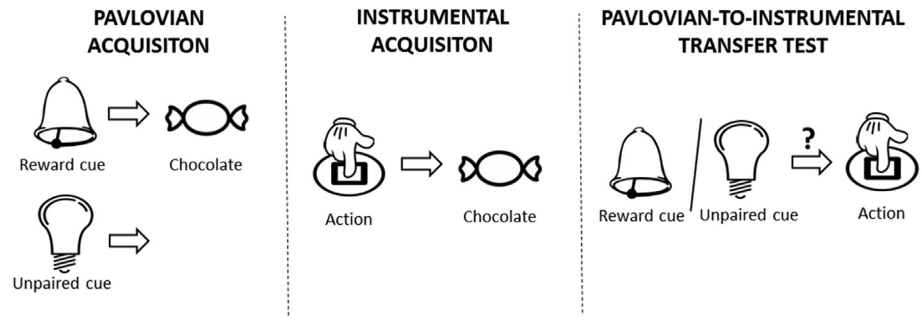

Fig. 1. Typical PIT design involving three phases: Pavlovian acquisition, instrumental acquisition, and transfer test. PIT occurs when the reward cue triggers instrumental responding aimed at obtaining the reward in the transfer test, despite the reward cue and the instrumental response being trained separately.

relative to the unpaired cue.

One of the most concerning features about PIT is its apparent insensitivity to devaluation manipulations. In rodents, for example, numerous studies indicate that reward cues can continue to facilitate reward-seeking via PIT even when the animal has had a taste aversion conditioned to the relevant reward (Corbit, Janak, & Balleine, 2007; Holland, 2004; Rescorla, 1994). This insensitivity to devaluation extends to humans, with a number of studies demonstrating that PIT is insensitive to devaluation manipulations for symbolic rewards such as money (Allman et al., 2010), drug-related symbols (Hogarth & Chase, 2011; Hogarth, 2012) and natural food rewards (Colagiuri & Lovibond, 2015; Eder & Dignath, 2016; Watson, Wiers, Hommel, & de Wit, 2014). The insensitivity of PIT to devaluation is concerning in terms of maladaptive reward-seeking, because it suggests a way in which biological feedback systems intended to regulate reward-seeking, e.g. satiety, can be overridden by reward cues. Further, insensitivity to devaluation may suggest that PIT is beyond cognitive control, which would render cognitive strategies, e.g. self-regulation, futile for reducing maladaptive reward-seeking. As such, reducing the ability of reward cues to directly facilitate reward-seeking via PIT appears critical for the treatment and reduction of potentially harmful reward-seeking behaviours.

Extinction is one of the most obvious methods of attempting to reduce PIT. Extinction refers to presenting a cue in the absence of its prior reinforcer, with this procedure typically reducing conditioned responding (Bouton, 2002; Pavlov, Petrovich, & Anrep, 1927). Only a handful of studies have tested the extent to which extinction can reduce PIT. One study using rats (Delamater, 1996) found that extinction was ineffective for reducing PIT. Two human studies have also found evidence that extinction is ineffective for reducing PIT (Hogarth et al., 2014; Rosas, Paredes-Olay, Garcia-Gutierrez, Espinosa, & Abad, 2010), both of which used symbolic rewards (e.g. points). In contrast, we recently found that extinction successfully reduced PIT in humans when they were responding for a natural high value reward, i.e. chocolate (Lovibond, Satkunarajah, & Colagiuri, 2015).

Apart from the qualitative differences in rewards across the human studies testing for extinction of PIT, i.e. symbolic versus natural, one potentially critical difference between the human studies demonstrating effects of extinction and our own study demonstrating that extinction attenuated PIT, is that the former involved strong experimental incentives to respond during the transfer test (e.g. forced choice responding) whereas in the latter, participants were entirely free to respond or not respond. For example, in Hogarth et al. (2014) participants were forced to choose between two response options when the reward cues were presented during the transfer test. In contrast, in our previous study (Lovibond et al., 2015), during the transfer test participants were explicitly told that they could respond as much or as little as they liked. One could imagine that in situations in which an individual is forced to select a response, a cue with even the slightest association with a reward could bias responding towards a response also associated with that reward. On the other hand, when participants are free to respond or not respond, there is likely some absolute (rather than relative) criterion for the strength of association between the cue and the reward needed to induce the relevant instrumental response. Therefore, if extinction does reduce the strength of the association between a reward cue and the relevant reward (either directly or via competing inhibitory learning) but does not fully eradicate the association, then designs with forced choice or high incentives to respond may substantially underestimate the ability of extinction to reduce PIT. Further, as we have argued previously (Colagiuri & Lovibond, 2015; Lovibond & Colagiuri, 2013; Lovibond et al., 2015), models of PIT that involve voluntary responding, i.e. including the option not to respond, are likely to better reflect real world settings in which individuals have the option not to engage in any action. Therefore, the evidence that extinction can attenuate PIT when responding is voluntary may generalise better to non-laboratory settings.

However, one *a priori* limitation to the possibility of using extinction to reduce cue-induced reward-seeking is renewal. Renewal refers to the recovery of conditioned responding following extinction when the extinguished cue is encountered in a context different to the one in which extinction was conducted (Bouton, 2002). Renewal and related effects (e.g. spontaneous recovery, reinstatement) have led most researchers to adopt the view that extinction involves new inhibitory learning (cue → no outcome), which co-exists with the prior excitatory learning (cue → reward), rather than extinction actually erasing the excitatory learning (Bouton & Bolles, 1979; Bouton, 2002; Konorski, 1967). Renewal effects suggest that extinction may only be effective for reducing reward-seeking in the specific context in which extinction is conducted. If, for example, a therapist extinguishes drug cues with an addicted patient in her clinic, the drug cues will likely still elicit responses (i.e. renew) when they are encountered outside of the clinic. Renewal is often proposed as the main reason that cue-exposure therapy fails to reduce actual relapse rates despite reducing cue-reactivity in the clinic (Conklin & Tiffany, 2002; Rachman, 1989).

Renewal has been demonstrated in terms of reactivity to fear cues (Bouton & Bolles, 1979), drug reward cues (Collins & Brandon, 2002), and food reward cues (Van Gucht, Vansteenwegen, Beckers, & Van den Bergh, 2008). For example, in a study by Van Gucht et al. (2008), human participants had the opportunity to learn the association between the colour of a tray (cue) and chocolate (reward) before undergoing extinction in either the same or a different context to training. Participants' expectancies and cravings were