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Relapse of generalized bait shyness in rats after constant and graded extinction procedures

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ABSTRACT

Oral ingestion of a toxic lithium chloride (LiCl) solution yields a conditioned aversion to a safe sodium chloride (NaCl) solution in rats, presumably because of the common quality of saltiness. By using this generalized bait-shyness paradigm, we examined the relapse of acquired and subsequently extinguished salty taste aversion. After conditioning by oral ingestion of a 0.15 M LiCl solution, extinction was induced by two different experimental procedures. In the constant extinction group, rats were repeatedly exposed to 0.15 M NaCl solution. For rats in the graded extinction group, the concentration of NaCl was gradually increased from a low level to 0.15 M and an additional interfering sweet taste was gradually faded out. Rats in the graded extinction group were more prone to relapse than animals that underwent the constant extinction treatment. This difference was manifested in the following three response reoccurrence phenomena: renewal upon return to the acquisition context (Experiments 1A–C), spontaneous recovery after a 23-day interval (Experiment 2), and reacquisition caused by the second LiCl intake (Experiment 3). Theoretical and clinical implications of these results are discussed.

Conditioned responses that have been established and then extinguished reappear when animals are removed from the extinction context, when a delay occurs between the extinction and test phases, and when subsequent reconditioning takes place. These phenomena, respectively, named renewal, spontaneous recovery, and reacquisition, have been considered as animal models of relapse after exposure therapies for maladaptive behavior such as phobia (Bouton, 2000, 2002, 2004; Bouton & Nelson, 1998; Bouton & Swartzentruber, 1991; Bouton, Woods, Moody, Sunsay, & García-Gutiérrez, 2006b; Laborda, McConnell, & Miller, 2011; Urcelay, 2012). Thus, any factors which may affect the occurrence and magnitude of these phenomena merit scrutiny (e.g., Brooks & Bouton, 1993, 1994; Urcelay, Wheeler, & Miller, 2009). In the present study, we focused on extinguishing behavior by gradual fading.

According to Bouton (1991, 1994, 1997, 2004), the underlying mechanism of extinction learning is the acquisition of inhibition rather than unlearning of conditioned excitation, and background contexts work by retrieving, signaling, or setting the occasion for the appropriate excitatory or inhibitory association. Specifically, the inhibitory association is gated by the extinction context and a release from that context would reduce activation of the inhibitory association and result in a relapse of responding. According to Rescorla (2001, 2002), the amount of inhibitory learning positively correlates with the response frequency during extinction. If we combined these two theories, any procedures that attenuate the occurrence of

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a conditioned response during extinction should decrease inhibitory learning, and in turn, reduce the probability of relapse. One such procedure involves exposing animals to a series of gradually strengthening excitors (Smith & Guthrie, 1921; Guthrie, 1952). Such a progressive schedule evokes a small response not only in the early stage of extinction training with a threshold stimulus, but also in the late stage, with a stimulus of the original intensity. Thus, response extinction can be accomplished with decreased expression of the original response throughout the extinction training process. Assuming that response expression is necessary to produce inhibitory learning (Rescorla, 2001, 2002), extinction without responding should be based on an inhibition-free suppression process, such as unlearning of the conditioned association (see also Terrace, 1972, for a similar concept of inhibition-free discrimination learning in instrumental conditioning). If the conditioned association is truly eliminated rather than suppressed, by any inhibitory process in the extinction phase, then limited relapse of responding should be expected during testing.

Notably, there have been several reports about partial renewal of spider fear in college students by changing contexts after exposure to a series of progressively increasing fear-evoking stimuli (e.g., Mineka, Mystkowski, Hladek, & Rodriguez, 1999; Mystkowski, Craske, & Echiverri, 2002; Mystkowski, Echiverri, Labus, & Craske, 2006; Rodriguez, Craske, Mineka, Hladek, 1999). They suggest that the progressive extinction schedule did not completely prevent the renewal effect. However, we cannot conclude that the progressive schedule is ineffective in reducing fear renewal, because these studies did not assess fear renewal after extinction treatment with an original stimulus of the same strength.

In addition to the method of exposing animals to a series of gradually strengthening excitors, concurrent presentation of any stimuli-evoking antagonistic reactions is also effective in weakening responses to the target excitor without evoking an inhibitory process (Guthrie, 1952). These two methods are, respectively, referred to as toleration and interference (Poppen, 1970). Their combination underlies many practical procedures, including systematic desensitization therapy (Wolpe, 1958, 1961). Another example of such a combination can be seen in some stimulus fading studies. For example, by using an interlocking device, Öst (1978) gradually brightened (or faded in) a phobic picture up to the full strength and dimmed (or faded out) a pleasurable picture down to zero illumination for treatment of a patient with phobia.

The present study was initially designed to find an effective procedure for reducing the renewal effect. In this study, we adopted a generalized bait-shyness paradigm, where oral intake of toxic lithium chloride (LiCl) solution yields conditioned aversion in rats to other salty, but safe, liquids such as sodium chloride (NaCl) solution (Balagura & Smith, 1970; Balagura, Brophy, & Davenport, 1972; Nachman, 1963; Smith & Balagura, 1969). Lately, this conditioning paradigm has been used for a variety of experimental purposes (e.g., Arriola, Alonso, & Rodríguez, 2014, 2015; Baird, John, & Nuyen, 2005; Loy & Hall, 2002; Nagaishi & Nakajima, 2008; Nakajima & Nagaishi, 2005), partly because it better mimics natural conditions compared with conventional conditioned taste aversion, which is induced by an intraperitoneal (i.p.) injection of LiCl after the target taste intake (see Arriola, Alonso, Vázquez, & Rodríguez, 2015, for a discussion of this procedure).

In the first set of experiments, aversion of rats to a salty taste induced by ingestion of the LiCl solution in one context was extinguished by repeated exposure of animals to an NaCl solution of constant concentration or by gradually fading an NaCl-sucrose mixture in another context. In the end, the rats were tested with the NaCl solution in the original context. Their performance was compared with that of control rats that were tested in the same, unchanged context. As explained below, the results of the first experiment (Experiment 1A) were unexpected, and thus, the experiment was repeated twice with some minor modifications (Experiments 1B and 1C). Contrary to our expectation, all of these experiments (1A, 1B, and 1C) yielded numerically larger renewal effects after graded, rather than constant, extinction treatment. Hence, in Experiments 2 and 3, we compared the extent of spontaneous recovery and reacquisition between graded and constant extinction groups, respectively. In general, responding extinguished by the graded procedure was more susceptible to relapse than conventionally extinguished responding.

Experiments 1A, 1B, and 1C

Several studies have reported that taste aversion acquired by rats following ingestion of a target taste accompanied by a LiCl injection, which was subsequently extinguished by a mere exposure to the target taste alone, could be renewed by changing background contexts (e.g., Bernal-Gamboa et al., 2012; Fujiwara et al., 2012; Revillo, Castello, Paglini, & Arias, 2014; Rosas & Bouton, 1997, 1998; Rosas, García-Guetiérrez, & Callejas-Aguilera, 2007). To the best of our knowledge, however, there have been no published studies on the renewal of taste aversion acquired by rats in the generalized bait-shyness paradigm. In the present study, acquisition of salty taste aversion was induced by the ingestion of a toxic 0.15 M LiCl solution by thirsty rats in Context A. Taste aversion was then extinguished by the presentation of a safe NaCl solution in Context B. Testing was carried out in Context A with the NaCl solution. The rats' performance was compared with the control animals that received all of the acquisition, extinction, and test treatments in Context A.

Our principal goal was to determine whether the magnitude of the renewal effect would decrease if the NaCl concentration was gradually increased from 0.05 to 0.15 M and an added interfering sweet taste was gradually faded out.

Material and methods

Subjects

Experimentally naïve male albino Jbc:Wistar rats were purchased from a local breeder at the age of 8 weeks and maintained on an ad libitum food schedule in individual hanging cages at the vivarium on a 16/8 h light/dark cycle (lights on