Acute, But Not Chronic, Exposure to D-Cycloserine Facilitates Extinction of a Conditioned Taste Aversion

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Abstract

D-cycloserine (DCS), the glutamate NMDA receptor partial agonist, has been reported to facilitate the extinction of learned fear. However, timing of DCS administration during extinction (EXT) processes is unclear, and whether DCS treatment is more effective in reducing Spontaneous Recovery (SR) than asymptomatic extinction (AE) has yet to be determined. We have previously shown that acute DCS exposure is more effective in reducing SR than chronic drug treatments; however, rapid reductions in DCS dose early in the EXT process may decrease its effectiveness as a facilitator of CTA extinction.

Methods


eighty-two naive adult male Sprague-Dawley rats were used.

Three SAC + LiCl pairings produced a significant Conditioned Taste Aversion (CTA) that was extinguished during EXT (Fig. 3). A second group of rats acquired a strong CTA, which was extinguished during EXT through exposure to the CS only (Fig. 4). A third group of rats acquired a strong CTA, which was extinguished during EXT through exposure to the CS only (Fig. 4).

Results

Conditional extinction processes may take a unique shape when the animal is first exposed to the US in the presence of the CS.

Figure 6: The procedure for training the CTA extinction procedure is shown in Table 1. The rats that received a CS-only (CSO) treatment, had a lower rate of extinction compared to the CS + US treatment group. * = Significantly lower (p<0.05) compared to the CS + US treatment group.

Summary & Conclusions

As reported previously (Mickley et al., 2009), the EU extinction procedure significantly reduced the time rats to achieve asymptomatic extinction of the CTA.

However, chronic DCS failures to shorten the time required to reach asymptomatic extinction when other EU treatments were employed. Acute DCS treatments, but not chronic DCS treatments, shortened the time to reach asymptomatic extinction. Moreover, acute DCS treatments were more effective in reducing SR of a CTA that were chronic drug treatments.

The timing of the acute DCS treatments during extinction did not affect the days required to achieve asymptomatic extinction but did fail to affect the SR of the CTA.

Acute DCS administrations later in EXT were more effective in reducing SR than were DCS doses given early in the EXT process.

Acute DCS administration given later in EXT training appears to be more effective at facilitating CTA extinction and reducing SR.

The data are consistent with others (Fernandez et al., 2008) indicating that multiple exposures to DCS can reduce its effectiveness as a facilitator of extinction learning.

Introduction

Fear can be acquired through a variety of routes, including contextual fear conditioning (Maren, 2003; Maren & Fanselow, 2002). Fear may be induced through various exposure therapies, which are thought to be effective in reducing fear responses by forming a negative association between the CS and the US. Fear extinction may be successfully achieved by manipulating the association through standard (AC) or alternate extinction procedures, which involve a number of factors (Maren & Fanselow, 2002).

The timeline of EXT-CTA extinction provides an indicator of the degree of successful extinction. The DCS extinction procedures do not affect the timeline of EXT.