

Psychopharmacology Unit, Dorothy Hodgkin Building, Bristol, UK. Ben.Watson@bristol.ac.uk

Introduction
Cue exposure therapy has been advocated as a potentially effective means of treating addictive behaviors (1). Strategies that enhance learning may improve the outcome of cue-exposure therapy. D-cycloserine, a licensed antibiotic with partial NMDA receptor agonistic properties, has been shown to facilitate extinction of learned fear in rats (2), and improve extinction of fear in patients with height phobia undergoing cue exposure therapy (3). This pilot study used a cue-exposure paradigm, salient for an individual’s alcohol drinking to see if D-cycloserine could reduce objective and subjective responses (craving) to these cues.

Methods
Subjects
- 16 abstinent, alcohol dependent individuals
- Mean age = 44.1 (±8.6)
- 11 Male, 5 Female
- No major concurrent medical or psychiatric disorder

Design
- A double-blind, placebo controlled, parallel group pilot study.

Procedure
- Randomization to either single dose (250mg) D-cycloserine or placebo.
- 3 separate testing sessions, separated by at least 1 week.
- 2 hours post drug administration subjects exposure to a series of 4 alcohol cues over 60 minutes (see below).
- Debriefing by an addiction psychiatrist after each testing session.

Outcome measures taken at baseline & before & after cue-exposures:
- Change in Alcohol Urge Questionnaire (AUQ) scores.
- Change in Finapres assessment of cardiovascular response (BP & HR).
- Change in Visual analogue scales (VAS) scores:
  - “At this moment how Relaxed/Tense/Anxious/Sad/Mouthwatering do you feel?”

Results
- No statistical difference in the outcome measures (AUQ, Finapres, VAS) were found between the D-cycloserine and placebo groups.

- The range of measurable response to cue-exposure varied greatly between subjects.
- Over half of subjects showed small changes in AUQ score in response to the cue exposures with 5 out of 16 subjects showing no change at all (3 from D-cycloserine group, 2 from placebo group).
- Changes in subjective responses measured with VAS were consistent with AUQ scores.
- Changes in objective cardiovascular responses were generally consistent with anecdotal clinical observation of signs of distress e.g. facial expressions/sweating). This raises the issue of what exactly craving is and how best to measure it given its possible cognitive, emotional and physiological components.

Conclusion
We have used the cue exposure paradigm safely in this group. An expected reduction in craving scores over the 3 testing days was seen, but no detectable effect of D-cycloserine. Future studies should examine carefully the inclusion criteria and measures of alcohol craving employed. The high proportion of subjects with little or no subjective response raises the question of whether “non-responders” be excluded at screening. In addition, there were a few subjects who didn’t show a response on the AUQ to cue-exposure, yet did show a cardiovascular response (this was consistent with anecdotal clinical observation of signs of distress e.g. facial expressions/sweating).

References