

Editorial

Extinction of Drug-Seeking Behavior

Some of the key defining characteristics of drug addiction (substance dependence) is the persistence of drug-seeking behavior despite attempts at abstinence, adverse health and legal consequences, and impaired social, occupational or academic functioning [1]. From a behavior modification standpoint, *extinction* refers to the gradual and intentional reduction of a maladaptive behavior, such as drug-seeking or drug self-administration behavior. From a cognitive-behavioral therapeutic perspective, *extinction* refers to a gradual and intentional reduction in psychological and/or physiological responses, such as autonomic nervous system activation and drug craving, to drug-associated stimuli. In the latter sense, extinction is essentially a “desensitization” process that is performed *via* cue exposure therapy (CET). During CET, addicts are presented with pictures of or actual physical exposure to drug-related stimuli such as drug paraphernalia (i.e., crack pipes), drug-related olfactory stimuli (i.e., the aroma of alcohol or cigarette smoke), or even drug self-administration contextual environments. Over time, the conditioned psychological and physiological responses to drug-associated stimuli extinguish. Similar cue exposure therapy procedures, such as exposure plus response prevention, are successfully used for the treatment of anxiety disorders including disabling phobias, obsessive-compulsive disorder, and post-traumatic stress disorder.

Unfortunately, the success rates of cue exposure therapy in preventing relapse in former addicts are modest at best [2]. Most addiction counselors, psychiatrists, and other treatment professionals attribute the meager success rate of cue exposure therapy to the context specificity of extinction. That is, while an addict might become desensitized to the craving evoked by handling a pack of cigarettes in a therapist’s office, this extinction of cue-induced drug craving fails to generalize to other contexts, such as actual “real world” environments which the addicts encounter in their everyday lives. Similar problems of context specificity have often impeded the successful extinction of maladaptive responses to fear- and anxiety-provoking situations or stimuli. As a result of the relatively poor outcomes that have resulted from extinction-based approaches, increased knowledge about the neural substrates that underlie extinction, an active form of learning, is greatly needed in order to improve existing behavioral modification and cognitive-behavioral therapies for the treatment of drug addiction.

In this special issue of *The Open Addiction Journal*, five papers on the topic of Extinction of Drug-Seeking Behavior are presented. First, *Widholm* provides a detailed theoretical framework of basic Pavlovian conditioning and learning phenomena that are involved in addictive processes. In addition, common “threats” to successful extinction of drug-seeking behavior, such as context specificity, spontaneous recovery, cue or context-evoked reinstatement, and rapid reacquisition, are also reviewed. Second, *Cleva* and *Gass* provide a comprehensive summary of current knowledge of the neuroanatomical and neurobiological substrates of extinction in the context of drug addiction. Next, *Janak* and *Chaudri* provide a review of animal studies that have examined the role of context in the reinstatement of alcohol-seeking behavior, along with potential underlying neurochemical substrates including dopaminergic and opioidergic neurotransmission. *LaRowe* and *Kalivas* present novel data on the effects of chronic administration of N-acetylcysteine on extinction responding in rats with a history of cocaine self-administration. N-acetylcysteine is a cystine pro-drug that activates the glial cystine-glutamate exchanger, and in animal studies this compound has been shown to normalize extracellular glutamate levels in the nucleus accumbens during cocaine withdrawal and prevent reinstatement of cocaine-seeking behavior. In human studies, N-acetylcysteine has been shown to reduce reactivity to cocaine-associated cues. Finally, *Martin*, *LaRowe* and *Malcolm* provide a timely and much needed analysis of recent clinical studies

that have employed cue exposure therapy methods in an effort to reduce drug craving and drug-seeking behavior. Unfortunately, in agreement with a 2002 meta-analysis [2], the studies reviewed by Martin and colleagues show that cue exposure therapy does not appear to have substantial efficacy in the prevention of relapse. These authors stress the need for more extensive clinical trial networks and improved methodological innovations, such as virtual reality-based therapies, in improving the clinical outcome of cue exposure therapy in the treatment of drug addiction.

REFERENCES

- [1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed, text revision (DSM-IV TR). Washington DC: American Psychiatric Press 2000.
- [2] Conklin CA, Tiffany ST. Applying extinction research and theory to cue-exposure addiction treatments. *Addiction* 2002; 97: 155-67.

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