

Title: Introducing White Noise Training for Cocaine Self-Administration, Extinction, and Cue-Induced Reinstatement in Adolescent and Adult Male Wistar Rats.

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Introduction: Some data suggest that drug intake and relapse are worse after adolescent-onset of drug use, compared to adult onset. We have reported, however, that adolescent and adult male rats self-administer cocaine at similar levels and that adolescents show less robust reinstatement of drug seeking after abstinence. The present study replicated and extended this work by testing whether rats acquire lever-pressing using a new negative reinforcement technique, white noise training, and testing whether age differences occur in cocaine self-administration, extinction, or reinstatement, when cocaine is paired with the aversive white noise stimulus.

Methods: Adolescent and adult male Wistar rats (postnatal days 24 and 73) were implanted with intravenous (i.v.) catheters, and allowed to acquire lever pressing in four 2-hr daily sessions, during which pressing turned off an otherwise constant 80 dB white noise stimulus, on a fixed ratio (FR) 1 schedule of negative reinforcement. In the next two sessions, lever-pressing not only turned off the noise but also produced i.v. cocaine (0.37 mg/kg). For the next eight sessions, noise was not constant but rather was presented with cocaine infusions. Finally after a 1-, 14-, or 30-day forced abstinence, rats were tested in five 1-hr extinction sessions and one 1-hr cue-induced reinstatement test. Blood samples were collected, rats perfused, and brains removed for analysis of neuronal activation.

Results:

Removal of a white noise stimulus negatively reinforced the acquisition of lever pressing, although adults pressed more than adolescents until cocaine was added. On the switch to white noise paired with cocaine, both age groups decreased responding, but reached stable cocaine intake at a rate that was notably higher than the reinforced lever-pressing during white noise training. After abstinence, extinction pressing was more robust in adults vs. adolescent-onset groups and increased across abstinence periods more quickly among adults. Adults reinstated at higher levels, regardless of abstinence period.

Conclusion: This study provides a new approach to lever-press training, shows similar persistence of cocaine intake in the presence of an aversive stimulus across age groups, and supports previous reports that adolescent-onset of cocaine self-administration does not necessarily increase vulnerability to the enduring effects of cocaine.