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LOSING CONTROL: EXCESSIVE ALCOHOL SEEKING AFTER SELECTIVE INACTIVATION OF CUE-RESPONSIVE NEURONS IN THE INFRALIMBIC CORTEX

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The neurobiological mechanisms underlying craving and relapse into alcohol drinking are poorly understood. Human and animal studies implicate the prefrontal cortex in drug and alcohol addiction. So far the involvement of the infralimbic (IL) and prelimbic (PL) cortices, as parts of the medial prefrontal cortex in rats, has been shown for cocaine seeking. However, the role of IL and PL in alcohol seeking has not yet been established. Drug seeking can successfully be modeled in rats using the cue-induced reinstatement paradigm. The present study aimed to investigate the role of the IL in cue-induced reinstatement of alcohol seeking in rats. Selective inactivation of cue-responsive neurons within the IL was obtained by local Daun02 infusions in combination with a cFos-lacZ transgenic rat line that expresses β-galactosidase only in activated (cFos-expressing) neurons. β-galactosidase converts the inactive pro-drug Daun02 into the active form daunorubicin, thereby inactivating the neuron. Furthermore, we used constitutively β-galactosidase expressing pCAG-LacZ rats for a non-selective IL inactivation. We found, that inactivation of cue-responsive neurons in the IL cortex induced excessive alcohol seeking in cFos-lacZ rats. The observed effect was specific for cue-induced reinstatement of alcohol seeking and had no effect on stress-induced reinstatement of alcohol seeking. In contrast we found, that non-selective Daun02 inactivation of the IL in pCAG-LacZ rats had no effect on cue-induced reinstatement of alcohol seeking. Thus, our findings demonstrate an important role of the IL cortex in alcohol seeking behavior and support the hypothesis that this behavior is mediated by distinct neuronal ensembles.