THE INFRALIMBIC CORTEX AND THE HIPPOCAMPAL CA1-SUBICULUM ARE FUNCTIONALLY INVOLVED IN THE EXTINCTION OF COCAINE-CONTEXT ASSOCIATIONS IN MICE (C47)

Topic
AS08 Diseases of The Nervous System (including, infective and psychiatric)

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Abstract Body
Cocaine abuse is a health and social problem worldwide. Treatment seeking for cocaine use disorder is on the rise, and relapse prevention remains as a primary goal. Interventions based on extinction of cocaine-related associative memories are promising but so far have not been successful. In this sense, further research is needed to elucidate the neurobiological substrates of extinction learning. Here, we aimed to study the neural circuitry involved in extinction of cocaine-context associations in the Conditioned Place Preference (CPP) model. Adult C57BL/6J mice received habituation to the CPP apparatus followed by conditioning with increasing doses of cocaine (2, 4, 8 and 16 mg/kg/day). After testing for CPP acquisition, a group of mice was submitted to four sessions of forced extinction (CPP+EXT, n = 9) while another group was maintained at home-cage (CPP+ACQ, n = 6). Then, both conditions were retested for cocaine-CPP. Ninety minutes later, animals were perfused, and brains collected. Next, we analysed by immunohistochemistry the expression of c-Fos in a variety of addiction-related structures including the medial prefrontal cortex (prelimbic, infralimbic), the striatum (nucleus accumbens, caudate-putamen), the basolateral amygdala and the hippocampus. Our results indicated that both groups acquired cocaine-CPP, but only the CPP+EXT condition ceased to show preference for the cocaine-paired compartment during the CPP retest. Importantly, the CPP+EXT mice showed increased c-Fos expression in the infralimbic cortex (IL), and the hippocampal CA1-subiculum during the CPP retest, with no changes in the other brain areas examined. Multivariate analyses revealed a relationship between IL and CA1-subiculum activity and CPP extinction. This suggest that such structures are functionally involved in retrieval of extinction memory for cocaine-context associations, thus standing out as potential therapeutic targets. Funding: PID2020-113806RB-I00, 08-2021-AREA3, B1-2020_06, PREDOC_01094, PRE2018-085673, FPU20/00908, POSTDOC_ 21_00222. II Plan Propio de Investigación, Transferencia y Divulgación Científica de la Universidad de Málaga.