Submitter Name: Marsida Kallupi
Submitted email: mkallupi@scripps.edu
PI Name: Olivier George
PI email: ogeorge@scripps.edu

Pharmacological treatments for opioid dependence in Heterogeneous Stock rats

Marsida Kallupi, Giordano de Guglielmo, Lisa Maturin, Molly Brennan and Olivier George[1]

[1]Department of Neuroscience; The Scripps Research Institute

Although the neurobiological target of opioids is well known, so far there is not such as a single treatment effective for all individuals with opioid dependence. The Guidelines for the Pharmacological Treatment of Opioid Dependence in the last decade, reviewed the use of FDA approved medicines such as methadone, buprenorphine and naltrexone in the treatment of people dependent on opioids, however, their effectiveness was not always promising. To address this issue, we used a unique outbred strain of rats (Heterogeneous Stock) that mimics the behavioral and genetic diversity found in humans and characterized by individual differences in addiction-like behaviors. HS rats were allowed to self-administered oxycodone 12h/daily for 14 days. The animals were screened for their addiction-like behaviors using an addiction index that incorporates the key criteria of opioid-use disorder: escalated intake, compulsive-like responding, and hyperalgesia. The results showed significant interindividual variability of oxycodone intake, motivation and withdrawal-induced hyperalgesia. Buprenorphine, methadone and naltrexone were tested using a latin-square design under a progressive ratio phase (PR) of reinforcement. We found that almost 40% of the population responded to all the three pharmacological approaches, while 30% of the population did not respond to any of the treatments. Future studies, will allow to identify genetic variants that predict the response to FDA-approved drug for 1) the treatment of opioid-use disorder, 2) the analgesic response to oxycodone (and possibly tolerance to it), and 3) the hyperalgesic response to opioid withdrawal. Such data will have considerable translational value for designing pharmacogenetic studies in humans.