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Identification of individual differences in response to methadone, buprenorphine, and naltrexone in animal models of opioid use disorder

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Current medications for opioid use disorder include buprenorphine, methadone and naltrexone. While these medications show significant efficacy in reducing craving, there are substantial individual differences in response to these treatments in humans. The reason for such difference is poorly known.

Here, we tested the hypothesis that similar individual differences may be observed in a large population of heterogenous stock rats, that have been breed to maximize genetic diversity, using a behavioral paradigm relevant to opioid use disorder.

Three hundred rats were given intermittent (5d/week) and extended access (12h/day) to oxycodone self-administration for three weeks to establish oxycodone dependence and escalation of intake. We then measured the effect of buprenorphine (0.5mg/kg), methadone (3mg/kg) and naltrexone (3mg/kg) on the motivation to take oxycodone using a progressive ratio schedule of reinforcement. We found that 65 % of rats decreased their motivation to take oxycodone with at least one treatment. There were substantial individual differences in response to each treatment, with individuals being sensitive to one, two, or all three medications. Buprenorphine and naltrexone were associated with the highest number of responsive animals, and around 8% of individuals were responsive to all three medications.

These results demonstrate individual differences in response to medications to treat opioid use disorder in a genetically diverse population of rats. To unveil the genetic, cellular and molecular basis of these differences, we created the Oxycodone Biobank (www.oxycodonebiobank.org), from which investigators can request biological samples, including brains, blood, urine, liver, kidney and other organs.