

Social housing promotes recovery of wheel running depressed by inflammatory pain and morphine withdrawal in male rats



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Introduction

When opioid use transitions to dependence, part of why people continue use is to stave off withdrawal symptoms. Reducing opioid withdrawal severity is therefore a key factor to reduce morbidity and mortality caused by the opioid crisis.

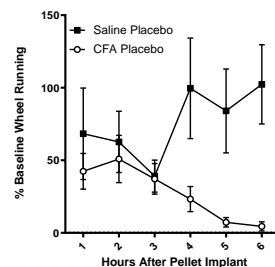
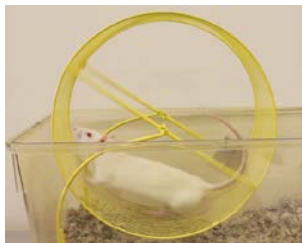
- Socialization can reduce heroin self-administration in rats, (Venniro et al., 2018).
- Social support in humans correlates with sobriety adherence during recovery from alcohol, opioid and nicotine use (Havassy et al., 2017).
- Numerous rodent studies show social housing can reduce pain, which may suggest that social housing may reduce the aches that accompany opioid withdrawal (Devor et al., 2007; Raber et al., 2002).

Primary aim of this study: to investigate if social housing could attenuate opioid withdrawal symptoms as assessed by daily wheel running

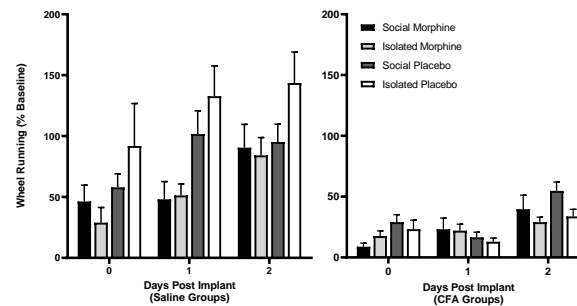
Methods

- Male Sprague-Dawley rats (n = 87, n per group = 9-12) were housed with a dual cage paradigm: a wheel cage for the first 6 hours of dark time and a home cage. Social rats shared a home cage with one other rat receiving the same treatment, isolated rats had their own home cage.
- After one week of habituation, rats received a subcutaneous implantation of either two 75mg morphine pellets or 2 placebo pellets of equal size and an injection in the right hindpaw of either 0.1 mL saline or CFA (to induce hindpaw inflammation). Pellets were removed after 3 days to induce withdrawal.
- Rat's daily activity was converted to % of baseline, baseline being defined as the day before implant. All data presented are means +/- SEM, * indicates $p < .05$

Recovery from implant surgery lasts approximately 3 hours

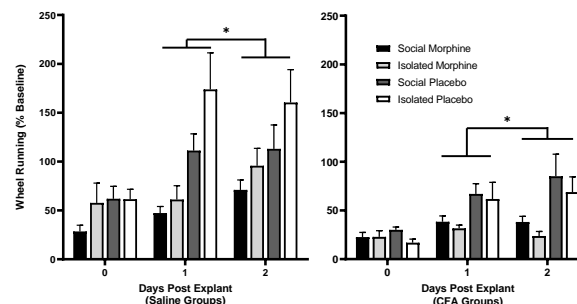


Isolated rats recovered faster from surgery



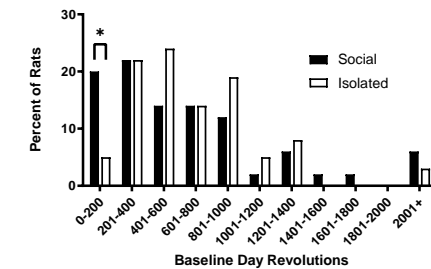
- CFA reduced mean percent of baseline activity to under 30% in all groups.
- Morphine implantation further decreased wheel-running.
- Morphine pellets depressed wheel running for 2 days in pain free rats, running recovered by day 3 indicating development of tolerance.

Social housing mediates recovery only with pain



- Wheel running was significantly lower in pain free rats undergoing morphine withdrawal compared to placebo on days 2 and 3 after explant surgery ($F(1, 33) = 11.648, p < .002$).
- Social rats had more severe wheel running depression following explant than isolated rats, with or without withdrawal.
- Social rats with hind paw inflammation had higher levels of wheel running compared to individually housed rats ($F(1, 65) = 4.933, p = .03$).

Baseline wheel-running was negatively skewed



- There was no significant difference in mean baseline between social and isolated rats. However there was a significant difference in the proportion of social and isolated rats that did not meet the running criterion of 200 revolutions: 10/50 social, 2/37 isolated (Chi square = 3.802, $p = 0.05$).

Discussion

Social housing facilitated recovery of wheel running depressed by hind paw inflammation, with morphine or placebo treatment. Social housing exacerbated depression of wheel-running caused by spontaneous morphine withdrawal in pain free rats.

These findings suggest that the facilitation of recovery from opioid withdrawal in socially housed rats is a result of pain inhibition.

Future directions: Research has shown that social amelioration of pain is greatest in rodents when one is in pain and the other is pain-naïve. We intend to extend this to opioid withdrawal, house a rat undergoing withdrawal with an opioid-naïve rat.

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