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Neonatal opioid withdrawal primes the somatosensory system

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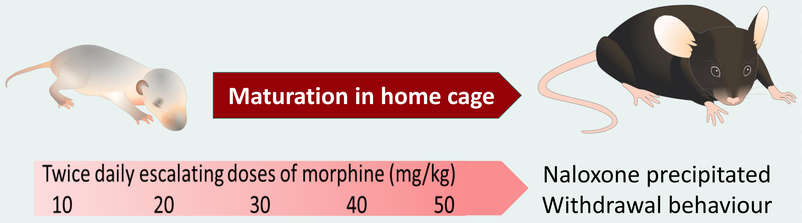
Introduction: Opioid abuse and misuse have increased greatly over the last decades across the adult population, including pregnant women. When a child is born to an opioid dependent mother, the infant will likely undergo withdrawal. The high degree of central nervous system plasticity directly after birth ensures opioid withdrawal can affect long-lasting changes in the somatosensory circuit, responsible for touch and pain processing and effectiveness of analgesics.

In the present study, we examined the neuro-developmental consequences of neonatal opioid withdrawal on the mechanical sensitivity and repeated withdrawal in adulthood.

Methods: Escalating doses of morphine were administered from postnatal day (P)5 to P10; Naloxone precipitated withdrawal assessment at P10. Mice aged in their home cages. In adulthood (8-10 weeks of age), mechanical sensitivity was assessed with Von Frey filaments. To assess the response to repeated morphine withdrawal, escalating doses of morphine were given over 5 days, and naloxone precipitated withdrawal behaviour was assessed.

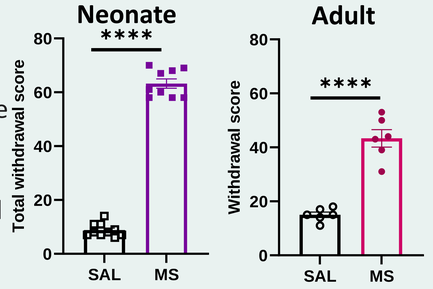
Table 1: Behavioural outcome measures

Neonate: Rolling, Headshakes; Belly press; Chewing/licking; Wet-dog shakes; rearing; line crossing; tremors; tail erection
Adult: Headshakes; full body shakes; licking/grooming; tremors; jumping; teeth chattering; salivation; piloerection

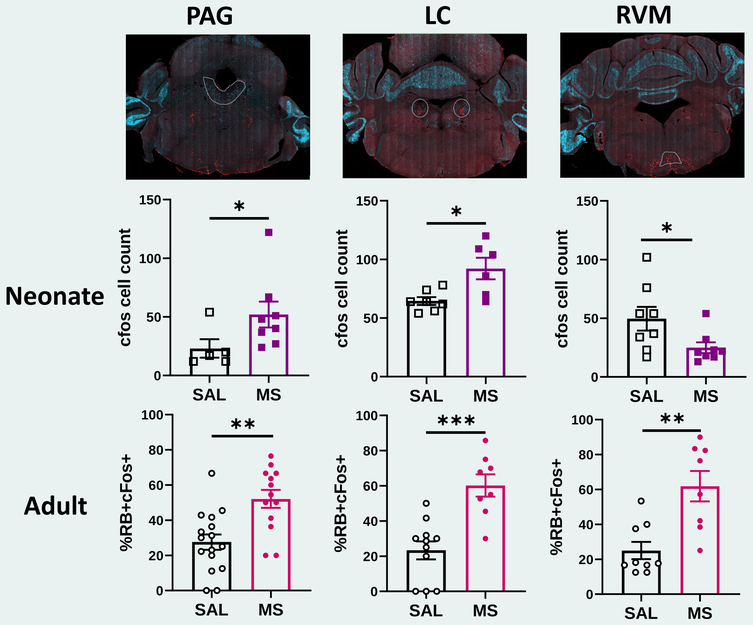


Key result 1: Neonatal withdrawal shows a distinct behavioural and neuronal activation profile

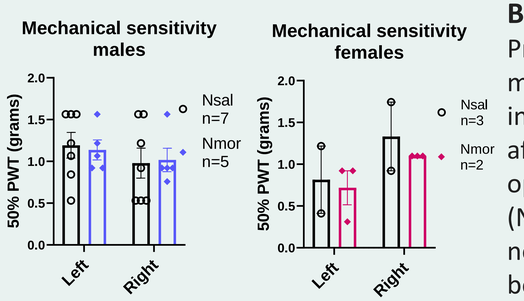
Behaviour: Naloxone precipitated robust opioid withdrawal behaviour in both neonatal and adult mice exposed to morphine (MS), as compared to saline (SAL) treated controls. Behavioural outcomes differs at neonatal age (see table 1).



Neuronal activation: While the periaquaductal grey (PAG) and locus coeruleus (LC) show an increased neuronal activation similar to adults, the rostroventral medial medulla (RVM) shows a decrease in neuronal activation unique to neonatal withdrawal.

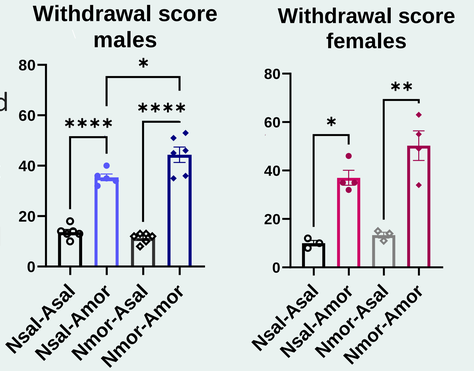


Key result 2: Repeated withdrawal in adulthood increases withdrawal behaviour score, while baseline mechanical sensitivity is unaffected



Baseline sensitivity: Preliminary data shows mechanical sensitivity in adulthood is not affected by neonatal opioid withdrawal (Nmor) as compared to neonatal saline (Nsal) in both male and female mice.

Repeated withdrawal in adulthood: Repeated withdrawal in adulthood led to robust withdrawal behaviour in all groups; but males who underwent neonatal opioid withdrawal showed a stronger withdrawal response.



Conclusion: Neonatal opioid withdrawal affects the neurodevelopment of the opioidergic system lasting into adulthood, affecting withdrawal outcomes in adulthood

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