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Neonatal abstinence syndrome in methadone exposed infants: Role of genetic variability

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Neonatal abstinence syndrome (NAS) in methadone exposed infants: role of genetic variability


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**Opioid dependence in pregnancy**

- Methadone (MD):
  - Currently the only FDA/TGA “approved” opioid substitution therapy during pregnancy.
  - Advantages: ↓ obstetric complications, ↑ prenatal care, ↑ maternal nutrition, ↓ drug seeking environment.
  - Disadvantages: Neonatal Abstinence Syndrome (NAS).

**Understanding opioid dependence**

- ↓ understanding of opioid dependence in adults.
- ↑ inter-individual variability in response to MD:
  - Impact of genetic variability.
  - Drug targets/receptors (OPRM1)?
  - Drug transporters (ABCB1)?
  - Metabolising enzymes (CYP2D6)?
- Immune response (IL-1β)?
  - Glial activation → release of immune mediators incl. proinflammatory cytokines interleukin-1 beta (IL-1β), creates proinflammatory environment → neuronal excitability to ↑ opioid reward and dependence.

**Genetic variability and NAS**

- Despite ↑ knowledge on the impact of genetic variability on MD response, the underlying mechanisms explaining NAS largely undefined:
  - ? genetic variability.
- By assessing genetic variability in mothers and infants, the association between genetic variability and NAS could be used as a predictive tool:
  - o = ↑ management of the infant by potentially ↓ morphine administered to control NAS.

**Aim**

- Investigate the impact of IL-1B -31 and OPRM1 A118G genetic variability on NAS incidence (treatment required) & severity (dose of morphine).