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

University of South Australia

THE UNIVERSITY of ADELAIDE

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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-1B*) ✓
  - 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:
  - = ↑ management of the infant by potentially ↓ morphine administered to control NAS.

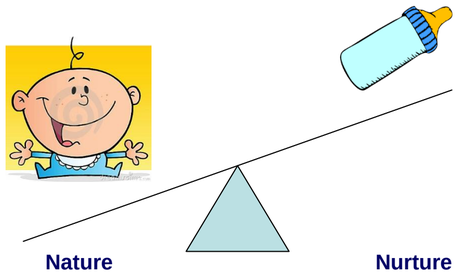
Aim

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

Nature vs Nurture

Dependence = genetics + environment

!!!!! Uniqueness of current study



Genotyping for *OPRM1* and *IL-1B*

- Infant buccal swab: DNA isolated from cheek cells, genotyped
- Genetic markers:
  - *OPRM1* A118G: Wild-type (WT) associated with ↑ response to opioids
  - Immune response, *IL-1B* -31 promoter mutation: Wild-type (WT) associated with ↑ IL-1β expression

Infant characteristics

Maternal methadone dose at delivery: mg (median (range))	120 (20-220)
Gestational age: weeks (median (range)) • Premature (n (%))	39 (35-41) 2 (8)
Gender male (n (%))	14 (54)
Birth weight: g (median (range)) • Low birth weight (n (%))	2963 (2157-3883) 5 (19)
Exposure to (n (%)): • Benzodiazepines • Nicotine	 11 (42) 15 (83)
Adjunctive phenobarb (n (%))	6 (23)

- 71 methadone exposed infants; 46 with NAS; 26 with genetic & morphine treatment data.
- No difference in *IL-1B* or *OPRM1* genotypes between infants with & without NAS, OR (p):

  IL-1B: 1.9 (0.21)

  OPRM1:0.23 (0.24)

Morphine Treatment

IL-1B -31 Infant genotype (morphine (mg), median (range))					
WT (n=21)	> 1 Var (n=5)	WT (n=21)	> 1 Var (n=5)	WT (n=20)	> 1 Var (n=5)
0.15 (0.1-0.4)	0.2 (0.14-0.3)	0.3 (0.17-0.66)	0.28 (0.23-0.68)	33.8 (14.3-79.3)	34.8 (26.7-91.8)
Initial morphine (p=0.06)		**Max morphine (p=0.94)**		**Total morphine (p=0.67)**	

OPRM1 A118G Infant genotype (morphine (mg), median (range))					
WT (n=24)	> 1 Var (n=2)	WT (n=24)	> 1 Var (n=2)	WT (n=23)	> 1 Var (n=2)
0.17 (0.1-0.4)	0.22 (0.13-0.3)	0.29 (0.17-0.68)	0.24 (0.18-0.3)	34.8 (14.3-91.8)	25.4 (19.4-31.5)
Initial morphine (p=0.73)		**Max morphine (p=0.39)**		**Total morphine (p=0.38)**	

Conclusion

- Despite impact of *IL-1B* and *OPRM1* genetic variability on opioid response in adults, this was not observed in infants.
- Limitation: small sample size to date.
- This study of possible impact of *IL-1B* and *OPRM1* genetic variability on NAS is ongoing, and could lead to tools to predict NAS incidence & severity.

References

Backstad, B., et al. Eur Addict Res, 2009. **15**(3): p. 128. Bell, G L. and K. Lau. Ped Clin North Am, 1995. **42**(2): p. 261. Blinick, G., E. Jerez, & R.C. Wallach. JAMA, 1973. **225**(5): p. 477. Blinick, G., et al. Am J Obstet Gynecol, 1976. **125**(2): p. 135. Brown, E.R. & B. Zuckerman. Ped Annal, 1991. **20**(10): p. 555, 561. Coller, J.K., et al. Int J Clin Pharm Therap, 2007. **45**(7): p. 410. Coller, J.K., et al. Clin Pharm Therap, 2006. **80**(6): p. 682. Coller, J.K., et al. Pharmacogenom Personal Med, 2009. **2**: p. 9. Connaughton, J.F., et al. Am J Obstet Gynecol, 1977. **129**(6): p. 679. Doberczak, T.M., et al. Obstet Gynecol, 1993. **81**(6): p. 936. Finnegan, L.P. and S.R. Kandall, in *Substance Abuse*, J.H. Lowinson, et al., Editors. 1997, Williams and Wilkins: Baltimore. p. 513. Grimmer, I., et al. Euro J Pediatr, 1999. **158**(8): p. 653. Hutchinson, M.R., et al. Scientific World J, 2007. **7**: p. 98-111. Johnson, K., A. Greenough, & C. Gerada. Addiction, 2003. **98**(6): p. 785. Kaltenbach, K., V. et al. Obstet Gynecol Clin North Am, 1998. **25**(1): p. 139. Kandall, S.R., et al. Early Hum Dev, 1977. **1**(2): p. 159. Lim, S., et al. Am J Obstet Gynecol, 2009. **200**(1): p. 70 e1-5. Liu, L., et al. Pharmacogenetics Genomics, 2009. **19**: p. 869-876 Silver, H., et al. J Perinatol, 1987. **7**(3): p. 178. Somogyi, A.A., D.T. Barratt, and J.K. Coller. Clin Pharm Therap, 2007. **81**(3): p. 429. Strauss, M.E., et al. Am J Obstet Gynecol, 1974 **120**(7): p. 895. Winklbaur, B., et al. Addiction, 2008. **103**(9): p. 1429.

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