

孕期類鴉片藥物暴露對子代之行為影響

Behavioral Effects of Prenatal Exposure to Morphine, Methadone, and Buprenorphine in rats

江耀璋¹、陳紹祖²、洪采瑋³、何英剛¹、陳慧誠³

Yao-Chang Chiang¹, Shao-Tsu Chen², Tsai-Wei Hung³, Ing-kang Ho¹, Hwei-Hsien Chen³

¹ 中國醫藥大學附設醫院成癮醫學研究中心

¹ Center for Drug Abuse and Addiction, China Medical University Hospital

² 慈濟大學醫學系精神科

² Division of Psychiatry, School of Medicine, Tzu Chi University

³ 國家衛生研究院群體健康科學研究所精神與成癮醫學研究組

³ Division of Mental Health & Addiction Medicine, Institute of Population Health Sciences, National Health Research Institutes

Objectives : Methadone and buprenorphine maintenance treatment are widely used to treat pregnant women with a history of opioid dependence. This study compared the behavioral outcome of young rats exposed prenatally to morphine, methadone, and buprenorphine.

Methods : Female pregnant Sprague-Dawley rats were sub-grouped to receive (1) vehicle, (2) 2-4 mg/kg morphine (1 mg/kg increment per week), (3) 5 mg/kg on E3, then 7 mg/kg methadone, and (4) 3 mg/kg buprenorphine, subcutaneously, once or twice a day from E3 to E20. The behavioral experiments that included cognitive function, social interaction, anxiety-like, and depression-like behaviors were conducted on animals 8-12 weeks old (postnatal day 43-78) and with body weight between 250 and 350 g.

Results : Prenatal exposure to morphine, methadone and buprenorphine had no effect on the basal locomotor activity in the offspring, but resulted in cognitive impairment and social withdrawal in male and female rats. Prenatal morphine exposure produced a significant increase in the

anxiety-like behaviors in the light-dark transition and elevated plus maze tests in both males and females, whereas prenatal exposure to methadone and buprenorphine only increased the anxiety-like behaviors in females.

Conclusions : Prenatal exposure to opioids developed social deficit and cognitive impairment once these offsprings reached their adulthood and buprenorphine showed less severe effects than prenatal exposure to morphine or methadone on the offspring in all the behavioral manifestations observed in this study. In addition, gender effects were observed in certain behaviors. These findings suggest that the offspring of mothers under opioid maintenance therapy may increase the risk of cognitive impairment and social deficit. Female offspring might have a higher risk for anxiety-related disorders than males. **Acknowledgments:** The work was supported by the National Health Research Institutes (PHPP46-021), the Tzu Chi University (TCIRP100001-02Y1) and the China Medical University Hospital (DMR-101-117) in Taiwan.