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• 中文摘要

由於甲基安非他命對於中樞神經系統的神經毒性，會透過降低血清素傳導系統的活性及提高興奮性氨基酸接受器之亞型 NMDA (N-methyl-D-asparate) 接受器的活性來產生。有證據顯示安非他命也會對肝醣合成酶激酶(GSK-3beta)的活化產生影響 GSK-3beta 是早期胚胎發育和神經細胞發展很重要的酶，其活性的改變會導致腦神經功能的變化。而 GSK-3beta 的活化也受到腦中血清素及 NMDA 接受器的調控。本研究計畫主要的目的，在於建立一個胎兒時期長期暴露於甲基安非他命的幼年動物模式並偵測幼鼠腦中血清素及 NMD 接受器的表現量及 GSK-3beta 的活化是否會受到甲基安非他命的影響。我們以翻身反射及學習測試來偵測幼鼠行爲發展的影響以西方點默法來定量幼鼠七天、十四天及三十天時其大腦皮質、海馬迴及紋狀體中血清素接受器 5-HT1A、1B、2A、2B 的表現量以及 NMDA 接受器亞型蛋白 NR1、NR2A、NR2B 的表現量。並且定量 GSK-3beta 的表現量以及其絲氨酸 9 磷酸化的情形。結果發現甲基安非他命組其出生後一週內體溫較控制組低且一個月內其體重增加也較低。而在甲基安非他命組於七天大時海馬迴之 NR1 及 NR2A 均較同年齡之控制組低但是 NR2B 並無顯著差異。而甲基安非他命組於十四天及三十天大與控制組間無明顯差異。相反的甲基安非他命組於七天、十四天及三十天大時海馬迴之磷酸化 pGSK-3β/GSK-3β 比例均較同年齡之控制組高。本計劃結果將有助於進一步瞭解甲基安非他命影響胎兒腦部發育的機制，並且提供未來在藥物治療上以 NMDA 接受器的拮抗劑、血清素再吸收抑制劑或選擇性 GSK-3beta 抑制劑在治療產前甲基安非他命對幼鼠發育發展所造成影響上的可能性的重要評估

• 英文摘要

Methamphetamine (MAMP) is one of the leading abused drug in Taiwan society. There is increased incidence of children born to mother addicted to MAMP, suggesting that the potential risk of abnormal neuropsychological development in these children. To identify the impact to neural

development especially in the neuroplasticity of hippocampus, we determined the physical growth and body temperature in the rats born to dams rats received daily subcutaneous injection of MAMP (5 mg/kg) (MAMP group rats) or normal saline (control group rats) . We also used immunoblotting assay to determine the expression of NMDA receptor subunits, NR1,NR2A and NR2B in the hippocampus of these rats on day 7 , 14 and 30. The results showed that the rats born to MAPH-addicted rats had lower body temperature during the fist week after birth, and had lower body weight gain during the first postnatal month as compared to that of control rats. In addition, the expression of NR1A and NR2A of MAMPH group on day 7 is significantly lower that of control rats. However the expression of NR2B was not difference between these two groups of rats. On the contrary, the ratio of pGSK-3β/GSK-3β is significantly increased in MAPH group on day 7, 14 and 30. These results suggest that prenatal exposure to MAMPH could induce an subunit-selective down regulation of NMDA receptor with an increased in the GSK-3β activation in the hippocampus, an important region for the developmental of learning and memory in the developing rats.