(一)Dextromethorphan 對於預防幼鼠嗎啡脫癮症狀的作用 (二)長期給予母鼠嗎啡對其所生幼鼠腦中 NMDA 受體表現的影響 (三)長期給予母鼠嗎啡對其所生幼鼠腦中 spectrin 的表現以及分解作用的影響

（一） Effect of dextromethorphan in preventing the morphine withdrawal syndrome in the neonatal rat （二） Effect of chronic treatment of morphine on the expression of the NMDA receptor in the developing rat brain. （三） Effect of chronic tre

中文摘要

嗎啡在臨床上是一種強而有效的止痛劑，但是在長期的濫用下會導致耐藥性以及依賴性的產生。懷孕婦女長期使用嗎啡，其所生幼兒會有嗎啡脫癮症狀，以及長期行為與學習異常，顯示了嗎啡對於腦部發育有一定程度的影響。因此對於預防新生兒嗎啡脫癮症狀以及瞭解嗎啡對於發育中的腦部所造成的毒性作用是非常重要的一個工作。本實驗室曾經發現長期給予懷孕母鼠嗎啡會導致其新生幼鼠在 naloxone 的誘發下產生嗎啡脫癮症狀，而直接給予此幼鼠 dextromethorphan 可以抑制脫癮症狀的產生；另外也發現初生幼鼠在出生後第 14 天腦中大腦皮質以及海馬迴之 N-methyl-D-aspartate receptor（NMDA receptor, 是一種興奮性氨基酸接受體之一）的密度有短暫性的下降。這種下降可能是由於 NMDA 受體各亞型的表現量下降或者是神經細胞突觸的減少所造成的。因此本研究利用此動物模式探討（1）給予懷孕母鼠 dextromethorphan 是否可以預防新生幼鼠產生的嗎啡脫癮症狀；（2）是否這些幼鼠腦部 NMDA 受體各種亞型表現會有異常；（3）是否這些幼鼠腦中與神經突觸發育有關的細胞骨架 spectrin 的表現會有異常。結果發現，給予懷孕母鼠 dextromethrorphan 可以預防幼鼠經 naloxone 所誘發的嗎啡脫癮症狀。我們也發現在幼鼠出生後第 7 天以及第 14 天其腦部各腦區的 NMDA 受體各個亞型會有短暫性的減量調控，在大腦皮質中為 NR1A, NR2A, NR2B, NR2C；在海馬迴中為 NR2A、NR2B 以及 NR2C 在紋狀體中，NR1A, NR2A, NR2B, NR2C。而我們也發現在幼鼠出生後各個天數其腦部各腦區的 spectrin 有明顯的下降，在大腦皮質中，α-spectrin 在幼鼠出生後第 7 天、第 14 天以及 30 天，而 β-spectrin 則在第 7 天與 14 天；在海馬迴中，α-spectrin 在幼鼠出生後第 7 天，而 β-spectrin 在幼鼠出生後第 7 天；在紋狀體中，α-spectrin 在幼鼠出生後第 7 天，而 β-spectrin 在幼鼠出生後第 7 天、第 14 天、第 60 天。而 spectrin 的崩解產物在各天數並沒有變化。

由此可知，dextromethorphan 可以有效的預防長期嗎啡成癮幼鼠經 naloxone 所引發的脫癮症狀。另外長期給予母鼠嗎啡確實會導致其所生幼鼠腦中的 NMDA 受體各種亞型發生減量調控以及會導致幼鼠腦中 spectrin 的崩解作用會增加。

英文摘要

It has been reported that infants born to morphine or heroin addicted women have high incidence of neonatal abstinence syndrome and abnormal neuropsychological performance. Preventing of neonatal abstinence syndrome and defining the neurotoxicity of morphine in the developing brain are important works. Our previous studies found that dam rat injection of dextromethorphan can attenuate the naloxone induced withdrawal syndrome. We also found that ontogenic expression of the NMDA receptor in this rats is different to that of control rat by lacking an overshooting of NMDAreceptor density on PND14. It is possible that this transient change is due to decrease in the subtype of the NMDA receptor or a decrease in the numbers of the synapse that containing the NMDA receptor. We used the same morphine treatment animal modal to further explore（1）whether prenatal treatment with dextromethorphan on the dam rats could prevent the morphine withdrawal syndrome in their off springs.（2）whether morphine treatment could induce a change in the NMDA receptor subunits in the developing rat brain（3）whether morphine treatment will change the the expression and degradation of the spectrin in the developing rat brain. We found that pre-treatment with dextromethorphan on the dam rats can prevent morphine withdrawal syndrome in the neonatal rat born to morphine treated dam rat. The expression of NMDA receptor subunit in the cortex, hippocampus and striatum of morphine group rats is decreased at PND14 as compare to that of control group. In the cortex, NR1A, NR2A, NR2B, NR2C are decreased on PND7 and PND14； in the hippocampus, NR2A, NR2B, NR2C are decreased on the PND7 ； in the striatum, NR1A, NR2A, NR2B, NR2C are decreased on PND7 and PND14. We also found that the expression of spectrin in the rat brain of morphine rats is decreased as compare to that of control group. In cortex α-spectrin decreased on PND7, PND14, PND30, andβ-spectrin decreased on PND7, PND14. In the hippocampus the α-spectrin decreased on PND7 andβ-spectrin on PND7. In the striatum the α-spectrin decreased on PND7 andβ-spectrin decrease on PND7, PND14, PND60.