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• 中文關鍵字	花生四烯酸；神經毒性；缺氧；缺血缺氧腦病變；缺血
• 英文關鍵字	Arachidonic acid；Neurotoxicity；Hypoxia；Hypoxia ischemia encephalopathy (HIE)；Ischemia
• 中文摘要	過去研究顯示花生油酸在缺氧-缺血性腦病變扮演重要的病理機制。我們在本實驗中,以初級大腦細胞培養確定缺氧下神經細胞壞死與花生油酸產生的關係以及花生油酸是否可產生類似缺氧性神經細胞壞死。在缺氧引起神經細胞壞死伴隨 LDH 的釋放以及花生油酸的釋放。這些變化可以爲 NMDA 接受器的拮抗劑 D-APV 所阻斷。加入花生油酸可以加速缺氧引起神經細胞壞死以及伴隨的 LDH 釋放。花生油酸可以獨自產生引起神經細胞壞死伴隨 LDH 釋放。這種細胞毒性可以部分被 Lipooxygenase 的抑制劑 NDGA 所抑制,但 Cyclooxygenase 以及 Epioxygenase 的抑制劑則無抑制作用。我們進一步偵測在有窒息的新生兒及無窒息的新生兒其腦脊髓液中花生油酸的含量。我們發現有嚴重窒息的新生兒其花生油酸含量較有輕度窒息或無窒息的新生兒高。本研究證實在缺氧-缺血性腦病變神經細胞壞死花生油酸及其下游代謝物的產生是重要的神經毒性物質。
• 英文摘要	Both arachidonic acid (AA), an important oxygenated polyunsaturated fatty acid in cell membrane, and N-methyl-D-aspartate (NMDA) receptor, one of glutamate subtype receptor, have been implicated in neonatal hypoxia-ischemia encephalopathy (HIE). We further investigate the role of AA on the hypoxia-ischemia induced neurotoxicity in both of animals and humans. We demonstrated that hypoxia could induced neuronal cell death, LDH release and AA release in primary cortical cell cultures. AA could enhance the hypoxia-induced cell death. AA alone also produced neuronal cell 1 death in concentration-dependently manner. Nordehydroguiaretic acid (NDGA), the inhibitor of lipooxygenase, could partially protect the neuronal death. However, aspirin, indomethacin and micronazol did not have any effect. We further determined the AA level in CSF samples from 15 control newborns and 12 asphyxiated newborns. The severe asphyxiated newborn have a higher AA level in CSF than that of control or mild asphyxiated

patients. This study indicated that AA contribute to the hypoxia-ischemia induced neurotoxicity to a significant extent. Development of selective inhibitor for the lipooxygenase may be of useful for clinics in treating the hypoxia-ischemia encephalopathy.