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論文名稱(外文):	Establishment of Parkinsonian Swin Model
指導教授:	劉江川、王順德
學位類別:	碩士
校院名稱:	國防醫學院
系所名稱:	生物及解剖學研究所
論文出版年:	1997
畢業學年度:	85
語文別:	中文
論文頁數:	78
中文關鍵詞:	巴金森氏症、蘭嶼
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中文摘要:	巴金森氏症是一種退化性的神經疾病，一般的症狀為行動遲緩、肌肉僵直以及靜止時不自主的顫抖。而神經系統中主要的退化部位為黑質緻密部的多巴胺神經元，導致黑質-紋狀體系統中多巴胺釋放量不足，在巴金森動物模式中，以含有多巴胺神經元的胚胎腹側中腦組織進行移植，可以減少藥物誘發旋轉行為以及改善其運動功能。目前胚胎移植已經進行人類臨床試驗，雖然在治療上已有進步，但尋求更有效的治療方法，改進現有的動物模式仍是當今重要課題。本實驗的目的即是試圖建立一個非靈長類的大動物模式，期望此動物模式可以對人類的巴金森氏症的基礎研究有所貢獻。我們選取台灣蘭嶼豬 (Sus vittatus) 做為實驗動物，它有下列優點：1) 來源充足；2)其多巴胺神經系統與人類相似；3) 平均生命週期為八年，遠較嚙齒動物長，適合進行長期追蹤與評估。在本實驗中，我們以藥物誘導旋轉行為，正電子電腦斷層掃描術 (positron emission tomography; PET) 及免疫組織化學染色法，評估蘭嶼豬是否可以做為巴金森氏症動物模式，首先，以 6-Hydroxydopmine 做為神經毒素，在核磁共振掃描術的引導下，單側注入內側前腦束來破壞黑質多巴胺神經元，使紋狀體多巴胺釋放減少，1-2 個月後，由肌肉注射安非他命，發現動物出現向破壞側旋轉的現象，平均旋轉次數為 260.86±86.4（轉/小時，mean±s.e.m. ；n=7），而 PET 結果顯示破壞紋

狀體中，再吸收 6-Flouro-DOPA 的功能明顯降低，以免疫組織化學染色法進行觀察，則發現破壞側之黑質及紋狀體區域中，TH-陽性的細胞本體及神經末稍大部份都消失。而 GFAP 免疫染色中，則可見到破壞側紋狀體的反應性星狀膠細胞有增生的現象，與以往學者在大白鼠的實驗中結果相符。進行移植時，將豬胚胎中腦黑質組織植入破壞側紋狀體中，之後，每月肌肉注射安非他命以進行觀察，發現蘭嶼豬的旋轉行為逐漸減少，PET 結果則顯示移植區的 6-Flouro-DOPA 再吸收功能有恢復的現象，動物犧牲後進行免疫組織化學染色，發現紋狀體移植區域有許多 TH-陽性細胞本體及纖維，顯示所移植之多巴胺神經元存活良好。從 GFAP 免疫染色結果中，則觀察到移植區域之星狀膠細胞有神經膠樣變性 (gliosis) 現象。綜合以上結果，證明蘭嶼豬確實可以做為巴金森氏症動物模式。

外文摘要: Parkinson's disease (PD) is a progress neurodegenerative disorder characterized by the motor disturbances such as bradykinesia, muscular rigidity and resting tremor. The principal lesion is the progress loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), that results in profound dopamine deficiency in the nigrostriatal system. Grafts of fetal ventral mesencephalon containing dopaminergic neurons, can reduce rotational behavior and cause improvements in other functional measures of experimental models of PD. Despite the successful progress reported, there are lots of problem remaining to be resolved. To establish an effective, permanent treatment, and improvement on animal models is still needed. The swine (Sus vittatus) is an ideal experimental animal for studying neural transplantation because the source is abundant, their dopaminergic system is very similar to human's and life span is much longer than small animal. The purpose of this experiment is to establish a non-primate big animal model that it will be used for further basic investigation in clinical treatment of human PD. In this study, 6-OHDA were unilaterally injected into medial forebrain bundle under MRI guiding to eliminate the dopamine content of corpus striatum in swine. The degree of dopamine depletion was tested by amphetamine-induced rotation, 6-Fluoro-DOPA PET scan and immunocytochemistry. In swine, 6-OHDA unilateral lesioned swine could develop amphetamine induced ipsilateral rotations. PET study found that 6-Flouro-DOPA uptake was significantly decreased at the 6-OHDA lesion side. Immunocytochemical study showed that TH immunostaining was significantly decreased both at ipsilateral striatum and SNpc. Increasing GFAP immunostaning represented reactive astrocytes at the striatum lesion site. Swine fetal ventral mesencephalic tissue of E22-26 (CRL: 2.0cm) was grafted into dopamine-denervated striatum under MRI guiding. All swines that received grafts, the rotational behavior decreased beginning in second or third month. PET scan showed that 6-Flouro-DOPA uptake increased at the grafted area. TH immunostaining indicates that grafts survive in the host striatum. The results suggest swine can be another animal model for Parkinson's disease study.