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論文名稱:	猪胚胎中腦組織與大鼠嗅覺髓鞘細胞共同移植於巴金森氏症大鼠模式
論文名稱(外文):	Co-grafting Rat Olfactory Ensheathing Cells and Porcine Mesencephalic Tissue in Parkinsonian Rats
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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:	2011
畢業學年度:	99
語文別:	中文
論文頁數:	57
中文關鍵詞:	巴金森氏症、異種移植、嗅覺髓鞘細胞
外文關鍵詞:	Parkinson's Disease、Xenograft、Olfactory Ensheathing Cells
中文摘要:	巴金森氏病是因黑質紋狀體的多巴胺神經元缺失所造成的神經退化性疾病，在臨床上以神經幹細胞進行替代被視為是可行且有希望的療法。而利用人類胎兒組織進行異體移植有實行與倫理道德的問題，爲了避免這些爭議，以猪胚神經組織為來源進行異種移植是一種可行的方式。嗅覺髓鞘細胞會分泌多種生長因子可對多巴胺細胞有神經保護效果。本研究的主要目的是建立以幹細胞替代療法為策略治療巴金森氏病。由猪胚分離之中腦幹細胞與出生後 3 天之仔鼠分離出的嗅覺髓鞘細胞共同移植到巴金森氏病大鼠的紋狀體。再以阿樸嗎啡引發的旋轉評估大鼠的行為，並利用酪胺酸羥化酶作為多巴胺神經元的指標進行免疫組組織化學染色。結果顯示經過阿樸嗎啡引發的旋轉大於每分鐘四轉的巴金森氏病大鼠之多巴胺神經元幾乎完全被破壞。將出生後 3 天之仔鼠分離出的嗅覺髓鞘細胞以免疫螢光染色測定細胞純度為 89 %。手術控制組與嗅覺髓鞘細胞移植組之巴金森氏病模式大鼠分別經行為測試與免疫組組織化學染色後，旋轉行為沒有改善，多巴胺神經元亦無回復。在大鼠胚胎中腦組織與嗅覺髓鞘細胞共同移植組、猪胚中腦組織移植組和猪胚中腦組織與嗅覺髓鞘細胞共同移植組的旋轉行為回復與手術控制組相比有顯著差異。而經由免疫組織化學染色後進行多巴胺神經纖維密度

定量發現有中腦組織移植之三組與手術控制組相比酪胺酸氫化酶表現皆有顯著差異。而在的免疫組織化學染色中可以發現猪胚中腦組織與嗅覺髓鞘細胞共同移植組的免疫反應較猪胚中腦組織移植組輕微。本實驗證實以猪胚細胞作為異種移植來源並輔以嗅覺髓鞘細胞治療巴金森氏症大鼠是可行的方式。

外文摘要: Parkinson’s disease (PD) is a neurodegenerative disease characterized by a loss of dopaminergic neurons in the nigrastriatal pathway. Neuron stem cells (NSC) have been considered as an appropriate alternative source of cells for clinical application and offer a promising future for cell replacement therapy in PD. However, there are major practical and ethical issues using human fetal allograft for these trials. To overcome those issues, porcine fetal neural tissue has been considered as an alternative source for human xenografts in neurodegenerative disorders. Olfactory ensheathing cells (OEC) express a variety of growth factors that may exert a neuroprotective effect on dopaminergic cells. The purpose of this study is to establish a therapeutic strategy for Parkinson’s disease using stem cell replacement therapy. Porcine midbrain stem cells isolated from E26 pig and OEC from P3 rat will be co-grafted into striatum of parkinsonian rats. Behavioral studies will be assessed by apomophine induced contralateral rotations. Tyrosine hydrosylase, the marker of dopamine neurons, will be determined by immunohistochemical study. The preliminary results indicate that the dopamine neurons were almost complete destroyed in parkinsonian rats whose rotations more than 4 turns per minute. OEC from P3 were determinated with immunofluorescent stain and the purity was 89%. The sham group and cell-transplantation groups were followed behavioral test and immunohistochemical study and these data show that the behavior did not improved after OEC grafted and there was no TH neurons recovery. But there is a significant decrease ($p < 0.05$) in rotation behavior in rat midbrain-OEC cografted, porcine midbrain, and porcine midbrain-OEC cografted groups and TH neuron were observed at striatum. Quantification of TH-IR neuron density data shows there are significant expression of TH neurons between the three midbrain-grafted groups and sham group. The immune response occurred in transplantation area in porcine midbrain-OEC cografted group is minor than those of porcine midbrain grafted group, maybe OEC have ability to modulate immune response. As a result, porcine embryo midbrain tissue and cografteS OEC is a nice source as xenograft therapy for Parkinsonian rats.