糖尿病用藥梵蒂雅可減緩實驗小鼠之癲癇行為反應

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摘要

癲癇乃大腦神經元一連串不正常放電所致，無論在未開發、開發中或已開發國家中，其癲癇患者皆占該國人口的一定比例。然而為何癲癇患者的腦部更易受到其他傷害或罹患神經其他相關疾病的問題，卻仍然困擾著生物醫學研究者。這些問題很可能是因為癲癇造成大腦處在長期或慢性發炎所致，因此探討癲癇產生後大腦皮質之發炎相關基因表現的研究，便是刻不容緩的方向之一。近年來已有相當文獻發現糖尿病用藥梵蒂雅之相關藥物具有抗發炎反應，而具實用性潛力。本研究計畫的主要目的，為探討糖尿病用藥梵蒂雅是否具有抑制化學物戊四唑所造成雄性小鼠的癲癇反應程度，並進一步偵測小鼠大腦皮質的發炎物質基因表現量是否因而改變。結果顯示單一次腹腔注射戊四唑於雄性小鼠後，隨著戊四唑劑量的增加，雄性小鼠的癲癇反應程度亦隨之增加，甚至在高劑量下，實驗動物會死亡。然而在注射化學物戊四唑的同時，給予雄性小鼠口服不同劑量的梵蒂雅，並無法立即降低癲癇反應，亦無影響大腦皮質的介白素-1 貝他的基因表現量；但是倘若先行讓雄性小鼠口服梵蒂雅兩天後，再給予化學物戊四唑的注射時，則實驗動物的癲癇反應程度下降，同時大腦皮質的介白素-1 貝他基因表現量亦出現下降的情形。因此這些結果證實糖尿病用藥梵蒂雅確實可降低戊四唑誘發實驗小鼠的癲癇反應與大腦皮質的發炎物質基因表現量，但投予時間的正確性影響藥物作用極大。

關鍵詞：大腦、神經發炎、介白素、癲癇反應、小鼠

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Anti-diabetes drug, Avandia, attenuate the seizure response induced by pentylenetetrazole (PTZ) in mice.

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Abstract

Epilepsy is a common health problem throughout the world influencing near 1% of human population. Epilepsy is defined by the recurrent and spontaneous seizures and caused by the chronically lower threshold of seizure. Recently increasing interest in the inflammatory role on the pathogenesis of epilepsy has been proposed. Therefore, it is an urge to investigate whether the expression levels of inflammatory- related gene were increased after seizure. Furthermore growing evidence showed that anti-diabetes drug, rosiglitazone (Avandia) might have anti-inflammatory effects. The present study aims to determine whether the PPARγ agonist, Avandia, was able to attenuate the seizure induced by pentylenetetrazole (PTZ) and affected the expression levels of inflammatory gene in the cortex of male mice. We found that the PTZ dose-dependently induced seizure responses, causing death at high dosages above 60 mg/kg. Co-treatment of Avandia did not affect the seizure response induced by the PTZ and the levels of *IL-1β* mRNA expression in the cortex were not changed in this co-treatment paradigm. However, pre-treatment of Avandia two days before PTZ administration significantly attenuated the PTZ-induced seizure responses and decreased the levels of *IL-1β* mRNA expression in the cortex. In summary these data suggest that preconditioning with the anti-diabetes drug, Avandia, attenuates PTZ-induced seizure responses and expression of inflammatory gene expressions in cortex in mice, whereas Avandia cotreatment is without such effects.

Keywords: brain, neuroinflammation, interleukin, seizure response, mice