

[1]陈通,龙志敏,汪克建,等.丙戊酸钠对APP/PS1转基因小鼠自主活动及脑形态结构的影响[J].第三军医大学学报,2012,34(09):870-873.

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丙戊酸钠对APP/PS1转基因小鼠自主活动及脑形态结构

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Title: Effect of valproic acid on autonomous behaviors and cerebral morphology and structure in APP/PS1 double transgenic mice

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关键词: [丙戊酸钠](#); [自主活动](#); [神经元](#); [阿尔茨海默病](#)

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摘要: 目的 研究丙戊酸钠 (valproic acid, VPA) 对APP/PS1双转基因阿尔茨海默病 (Alzheimer' s disease, AD)模型小鼠自主活动及脑组织形态结构的影响,探讨VPA对AD的保护作用及可能机制。 方法 将3月龄APP/PS1双转基因小鼠及同窝野生型小鼠分为VPA处理组和生理盐水对照组,运用VPA[30 mg/ (kg·d)]和等量生理盐水腹腔注射4周。旷场实验观察各组小鼠的自主活动能力;尼氏染色、透射电镜观察各组小鼠脑组织的病理改变。 结果 行为学结果显示:与野生型小鼠相比,AD模型小鼠自主活动明显减少 ($P<0.05$);野生型小鼠VPA处理组与对照组自主活动无明显差异 ($P>0.05$);而AD模型小鼠VPA处理组比对照组的自主活动明显减少 ($P<0.05$)。尼氏染色显示:AD模型小鼠脑内神经元密度显著低于野生型小鼠。AD模型小鼠中,对照组脑内神经细胞明显肿胀,尼氏小体明显减少而致细胞质淡染,神经细胞密度降低 (85.2 ± 13.3);而VPA处理组脑内神经元肿胀程度明显减轻,神经元数量显著回升 (116.9 ± 16.2 , $P<0.05$),但VPA不影响野生型小鼠脑内的神经元数量及形态(VPA处理组: 142.2 ± 24.4 vs生理盐水对照组: 136.7 ± 23.1 , $P>0.05$)。电镜结果显示AD模型小鼠对照组脑内神经元细胞核、线粒体及神经毡肿胀明显,突触结构稀疏;而AD模型小鼠VPA处理组脑内神经元细胞核、线粒体及神经毡的水肿明显减轻,突触结构清晰。 结论 VPA可显著减少APP/PS1双转基因AD模型小鼠的自主行为,显著减轻躁狂症状;VPA可改善APP/PS1双转基因小鼠脑内神经细胞的形态结构,减少肿胀的神经元并抑制神经元数量的减少。

Abstract: Objective To investigate whether valproic acid (VPA) can affect autonomic activity and cerebral morphology and structure in the APP/PS1 double transgenic Alzheimer' s disease(AD) mouse model, so as to explore the neuroprotective effect of VPA on AD. Methods Three-month old APP/PS1 double transgenic AD model mice and its wild-type littermates were randomly divided into two groups (VPA-

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treated group and saline-treated group), VPA [30 mg/ (kg·d)] and the same amount of normal saline were peritoneally injected into mice for 4 weeks. Open field test was used to examine autonomous behaviors of AD model and wildtype mice. Nissl staining and transmission electron microscopy (TEM) were applied to observe the morphological structures in the brains of AD model mice. Results Open field test revealed that the autonomic activities of AD mice showed an obvious decrease when compared to wild-type mice ($P<0.05$), the autonomic activities of VPA-treated mice were decreased significantly compared with the saline-treated controls ($P<0.05$), while the autonomic activities of both VPA-treated and saline-treated wild-type mice showed no difference. Nissl staining showed that neuronal cells in the brain of AD model mice were greatly decreased compared with wild-type mice. Furthermore, neuronal cells in the brain of saline-treated AD model mice were severely reduced in number (85.2 ± 13.3), and a large number of neurons became swollen and round, the nuclei were slightly stained, and the cytoplasm was pale in which Nissl bodies were reduced significantly. Administration of VPA notably suppressed the enhanced neuronal swelling and rescued the neuronal loss (116.9 ± 16.2 , $P<0.05$). VPA did not exert effect on the morphology and number of neuronal cells in the brain of both saline-treated and VPA-treated wildtype mice (142.2 ± 24.4 vs 136.7 ± 23.1 , $P>0.05$). TEM revealed that the cytoplasm, nucleus, part of mitochondria and neuropil in AD mice became obviously swollen, which were partially rescued by VPA. Meanwhile, the structure of synapse became clearer in VPA-treated mice. Conclusion VPA reduces the autonomous behavior and relieves manic symptoms in AD model mice. VPA may not only change the morphology of neuronal cells, but also rescue the neuronal loss in the brains of AD model mice.

参考文献/REFERENCES

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