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# 丙戊酸钠通过p21调控大鼠神经干细胞的增殖 [\(PDF\)](#) 分

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Title: Sodium valproate inhibits proliferation in rat neural stem cells through p21 pathway

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关键词: 丙戊酸钠; 脊髓; 神经干细胞; 增殖; p21

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摘要: 目的 探讨丙戊酸钠(sodium valproate, VPA)对体外培养的成年雌大鼠脊髓神经干细胞(neural stem cells, NSCs)增殖的影响。 方法 采用不同浓度的VPA( $10^{-5}$ 、 $10^{-4}$ 、 $10^{-3}$ 、 $10^{-2}$ 、 $10^{-1}$ 、1、10 mmol/L)作用于NSCs, CCK-8法检测在不同时间点(0、24、48、72 h)对细胞增殖的影响; VPA( $10^{-5}$ 、1 mmol/L)作用于NSCs 48 h后, 流式细胞仪测定细胞周期分布, PCR测定p21在基因水平的表达, Western blot测定p21在蛋白质水平的表达。 结果 CCK-8检测显示, 当VPA浓度 $>10^{-5}$  mmol/L时, 体外培养的成年大鼠脊髓NSCs的增殖受到明显抑制, 且具有时间依赖性。流式细胞仪细胞周期检测显示, 同样浓度下, VPA可阻滞NSCs由G<sub>0</sub>/G<sub>1</sub>期向S期转换, 表现为G<sub>0</sub>/G<sub>1</sub>期细胞增多, S期细胞减少, G<sub>2</sub>/M期细胞减少。PCR检测发现VPA可促进p21基因水平的表达。

Western blot检测发现VPA可促进p21蛋白质水平的表达, 各组间差异均有统计学意义( $P<0.05$ )。 结论 VPA可能通过促进p21表达, 使NSCs阻滞于G<sub>0</sub>/G<sub>1</sub>期, 最终抑制NSCs增殖。

Abstract: Objective To determine the effect of sodium valproate (VPA) on the proliferation and cell cycle in adult female rat spinal neural stem cells (NSCs). Methods Cell proliferation was assessed by CCK-8 assay after the cells were treated with VPA at different concentrations of  $10^{-5}$ ,  $10^{-4}$ ,  $10^{-3}$ ,  $10^{-2}$ ,  $10^{-1}$ , 1 or 10 mmol/L for 0, 24, 48 or 72 h. After NSCs were treated with VPA at a

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dose of  $10^{-5}$  and 1 mmol/L for 48 h, cell cycle was analyzed by flow cytometry and the expression of p21(cyclin-dependent kinase inhibitor) was detected by PCR and Western blot analysis. Results CCK-8 staining colorimetry showed that the proliferation of NSCs was markedly inhibited in a time-dependent manner when the concentration of VPA was more than  $10^{-5}$  mmol/L. Flow cytometry indicated more cultured NSCs were arrested in the  $G_0/G_1$  phase and fewer at the S phase after being treated with VPA, which indicated that VPA arrested the transition of NSCs from  $G_0/G_1$  phase to S phase. PCR and Western blot analysis indicated that VPA enhanced the expression of p21 at mRNA and protein levels( $P<0.05$ ). Conclusion VPA may arrest NSCs at  $G_0/G_1$  by increasing the expression of p21, and then finally inhibit the proliferation of NSCs.

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