

论著

脑源性神经营养因子对细胞外蛋白水解酶激活作用的研究

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摘要

目的: 研究脑源性神经营养因子 (BDNF) 对细胞外蛋白水解酶表达和激活作用的影响。方法: 体外分离并培养人脐静脉内皮细胞 (HUVEC), RT-PCR法检测HUVEC基质金属蛋白酶MMP-2、MMP-9和基质金属蛋白酶组织抑制剂TIMP-1、TIMP-2 mRNA的表达, 明胶酶谱检测MMP-2和MMP-9蛋白酶活性, 纤维蛋白酶谱检测尿激酶型纤溶酶原激活剂 (uPA) 蛋白酶活性, Western blotting检测uPA、纤溶酶原激活剂抑制剂 (PAI)、TIMP-1及TIMP-2表达。结果: 在对HUVEC增殖无明显促进作用的浓度范围内, BDNF可促进无血清培养的HUVEC MMP-2和MMP-9 mRNA表达, 并可促进MMP-2和MMP-9酶原的激活产生活性明胶酶, BDNF对TIMP-1和TIMP-2的表达无明显影响。BDNF以浓度和时间依赖性方式上调HUVEC uPA和PAI-1的表达, 并可促进uPA的活性。结论: BDNF可激活MMPs和uPA/PAI相关的蛋白级联。

关键词 [脑源性神经营养因子; 细胞外蛋白水解酶; 脐静脉内皮细胞](#)

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Effects of brain-derived neurotrophic factor on extracellular proteolytic enzymes

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Abstract

<P>AIM: To investigate the effects of brain-derived neurotrophic factor (BDNF) on extracellular proteolytic enzymes including matrix metalloproteinases (MMPs) and serine proteases, in particular, the urokinase-type plasminogen activator (uPA)-plasmin system in a human umbilical vein endothelial cell (HUVEC) model.
METHODS: The HUVEC was activated with different doses of BDNF (25-200 μg/L) for different time period (6-48 h). Reverse transcriptase-polymerase chain reaction (RT-PCR) was used to assay MMP-2, MMP-9, TIMP-1, and TIMP-2 mRNA in HUVEC. The cultured conditioned medium was analyzed for MMP and uPA activity by gelatin zymography and fibrin zymography, respectively. uPA, PAI-1, TIMP-1, and TIMP-2 were quantified by Western blotting analysis.
RESULTS: The stimulation of serum-starved HUVECs with BDNF caused marked increase in MMP-2 and MMP-9 mRNA expression and induced the pro-MMP-2 and pro-MMP-9 activation without significant differences in

扩展功能

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proliferation. However, BDNF had no effect on TIMP-1 and TIMP-2 production. BDNF increased uPA and PAI-1 production in a dose dependent manner up to 100 µg/L, while effects of 200 µg/L were approximately equal to those of 100 µg/L. BDNF stimulated uPA and PAI-1 production beyond that in control cultures from 12 h until 48 h after BDNF addition. Protease activity for uPA was also increased by BDNF in a dose dependent manner. CONCLUSION: BDNF activates MMP and uPA/PAI-1 proteolytic network in HUVEC.

Key words [Brain-derived neurotrophic factor](#) [Extracellular proteolytic enzyme](#) [Umbilical vein endothelial cells](#)

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