罗 婧,胡昔权,张丽颖,李莉莉,郑海清,张青杰.运动训练对脑梗死大鼠侧脑室室管膜下区内源性神经干细胞迁移的影响及其机制[J].中国康复医学杂志,2014,(4):299~305

运动训练对脑梗死大鼠侧脑室室管膜下区内源性神经干细胞迁移的影响及其机制

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基金项目：国家自然科学基金资助项目（81071607）；广东省科技计划项目（2009B030801149，2011B060300013）

DOI：

摘要：

摘要 目的：研究运动训练对脑梗死大鼠侧脑室室管膜下区（SVZ）内源性神经干细胞迁移的影响，并观察基质细胞衍生因子-α（SDF1-α）/趋化因子（CXCR4）信号通路在其中的作用。方法：成年Wistar大鼠81只，采用线栓法制作大脑中动脉阻塞再灌注模型，随机分为运动训练组（E，n=18）、运动训练+AMD3100组（EA，n=18）、对照组（C，n=18）、对照+AMD3100组（CA，n=18）和假手术组（S，n=9）。E和EA组从术后第3天起每天予以跑笼运动训练；EA和CA组于术后第2天起隔天注射AMD3100；C、CA和S组则置于普通笼内饲养，不予以任何针对性措施。所有大鼠在造模术后第7、14、21d进行神经功能评分（mNSS），并采用免疫荧光法观察大鼠梗死侧SVZ、纹状体、梗死周围皮质BrdU和Dcx双阳性细胞数，以及梗死边缘区SDF-1α及其受体CXCR4的表达情况。结果：在造模术后第14天和第21天，E组的mNSS评分均明显优于其他各组（P<0.05）。免疫荧光结果显示：术后第7、14、21天，E组BrdU和Dcx双阳性细胞及SDF-1α、CXCR4阳性细胞在相应区域的表达均多于C组（P<0.05）、CA组（P<0.001）和S组（P<0.001）。此外，术后第14天和第21天，E组的BrdU和Dcx双阳性细胞数在各个区域的表达也明显多于EA组（P<0.05），E和EA组的SDF-1α、CXCR4阳性细胞在梗死边缘区的表达差异无显著性意义（P>0.05）。结论：运动训练促进脑梗死大鼠神经功能的恢复，其机制可能与运动训练上调SDF-1α/CXCR4的表达，进而促进SVZ的内源性神经干细胞迁移有关。

关键词：脑梗死 运动训练 内源性神经干细胞 基质细胞衍生因子-1α/趋化因子

Effects of stromal-derived factor-1α/chemokine receptor 4 pathways in physical exercise on migration of endogenous neural stem cells from subventricular zone in rats with focal cerebral infarction

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Abstract:

Abstract Objective: To examine whether physical exercise can improve functional recovery by enhancing neural stem cells (NSCs) migration from subventricular zone (SVZ) through stromal-derived factor-1α (SDF-1α) /chemokine receptor-4 (CXCR4) pathways in rats after ischemic stroke. Method: Eighty-one adult Wistar rats after transient middle cerebral artery occlusion (tMCAO) were randomly divided into five groups: physical exercise group (E, n=18), physical exercise combined with AMD3100 injection group (EA, n=18), Both of these two groups were given running exercise daily at 3 days after MCAO. Control group (C, n=18). control combined with AMD3100 injection group (CA, n=18) and sham-operated group (S, n=9), which all were fed in standard cages without any special training exercise. The rats were sacrificed on the 7th, 14th, 21st day after evaluating the neurological function with modified neurological severity score(mNSS). Bromodeoxyaridine (BrdU) and doublecirtin (Dcx) double-positive cells were observed in the ipsilateral SVZ, striatum and peri-infarct cortex. SDF-1α and CXCR4 were checked in the peri-infarct region. Result: The mNSS score in E group was much better than that in other groups (P<0.05) at the 14th days and 21st days after MCAO (P<0.05). Immunofluorescence analysis showed amount of BrdU and Dcx double positive cells and SDF-1α, CXCR4 positive cells displayed a significantly higher expressions in E group than that in C group (P<0.05), CA group(P<0.001) and S group (P<0.001) at each time points and that in EA group at the 14th and 21st days (P<0.05) after MCAO in the corresponding regions. In addition, physical exercise significantly increased the amount of SDF-1α and CXCR4-positive cells but no significant difference(P>0.05). Conclusion: Physical exercise can enhances neurological function possibly by mediating endogenous NSCs migration from SVZ to the peri-infarct region via SDF-1α/CXCR4 pathways in rats after ischemic stroke.

Keywords:cerebral infarction physical exercise endogenous neural stem cell stromal-derived factor-1α/chemokine receptor 4

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