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Modic改变动物模型的建立及其评估

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The establishment and evaluation of animal model for modic changes

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摘要 目的 采用终板钻孔髓核置入建立兔Modic改变动物模型，并通过影像学、组织学和分子生物学等进行评估，探讨建立Modic改变动物模型的可行性及Modic改变的形成机制。方法 54只新西兰大白兔(体重2.5~3.0 kg，雌雄各半)随机分为髓核置入组、肌肉置入组和对照组，每组各18只。髓核置入组行腰椎前外侧手术入路暴露L_{4-5}、L_{5-6}椎间盘右前外侧，使用16 G骨穿针在L5-6椎间盘紧邻骶板的椎体处钻孔，深度约3 mm；利用5 ml空针刺入L4-5椎间盘中，抽取髓核并将其推入至椎体的钻孔内；肌肉置入组行相同手术显露及钻孔方法在L5-6椎间盘紧邻骶板的椎体处钻孔，取少量椎旁肌肉置入椎体的钻孔内；对照组行相同手术显露及钻孔方法，但不置入任何组织。止血、冲洗后，缝合各层组织和皮肤。术后12、16和20周行MR检查后各组动物处死6只，取标本进行大体形态学和组织学（HE染色）观察造模形成情况，实时荧光定量RT-PCR及Western blot观察造模部位炎症因子的表达。结果 术后12周、16周和20周，MRI显示髓核置入组T_1加权像可见有低信号出现，T_2加权像则显示低信号的背景下出现了不同程度的混杂高信号，而对照组及肌肉置入组均未见明显信号改变。大体观察及组织学观察结果也证实髓核置入组髓核置入部位出现组织的异常增殖。RT-PCR及Western blot检测显示髓核置入组IL-4、IL-17及IFN-γ的高表达现象，髓核置入组均高于肌肉置入组和对照组，且基本与术后时间呈正相关。肌肉置入组与对照组比较差异无统计学意义。结论 终板钻孔髓核置入法可以成功建立Modic改变的动物模型，自身免疫因素很有可能在Modic改变中发挥着重要的作用。

关键词： 椎间盘退行性变 模型, 动物 白细胞介素4 白细胞介素17 干扰素γ

Abstract： Objective To investigate the possibility of establishing a Modic changes (MCs) animal model, and explore the pathogenesis of MCs through imaging, histology and molecular biology experiments. Methods Fifty four New Zealand rabbits (weight 2.5-3.0 kg， half male and half female) were randomly divided into 3 groups: sham group (n=18), muscle embedment group (n=18) and NP embedment group (n=18). In NP embedment group, the L4-5 and L5-6 discs were exposed by the lumbar anterolateral surgical approach. A 16 G needle was used to puncture the L5-6 vertebral body close to the epiphyseal plate. The depth of the drilling was approximately 3 mm. A 5 ml syringe was then put into the L4-5 intervertebral disc and extracted the NP, which was injected into the drilled hole of the vertebral body. The muscle embedment group and sham group shared the same operating procedures and drilling methods with the NP embedment group. Some pieces of muscle acquired from paraspinal muscles were put into the drilled hole in muscle embedment group, while nothing was put into the drilled hole in sham group. After that, the bleeding stopping, tissue washing and suture were done in all groups. 12 weeks, 16 weeks and 20 weeks after the surgery, MRI scan was applied to each group. All the specimens were tested by HE staining, real-time fluorescence quantitative PCR and Western blot to observe the expression of inflammatory cytokines. Results After modeling for 12 weeks, 16 weeks and 20 weeks, MRI showed low signal changes on T1WI and mixed high signal in the context of low signal changes on T2WI in the NP embedment group. However, the muscle embedment and sham group showed no significant signal changes. Gross observation and HE staining confirmed that there was abnormal tissue proliferation in the imbed site of the NP embedment group. RT-PCR and Western blot showed high expression of IL-4, IL-17 and IFN-γ in the NP embedment group, which were positively correlated with the length of the

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postoperative period. There was no significant difference between the muscle embedment group and sham group. Conclusion The puncturing of vertebral body close to endplate and putting nucleus into it can create an animal model of MCs. Autoimmune factors may play an important role in MCs.

Key words: Intervertebral disc degeneration Models, animal Interleukin-4 Interleukin-17 Interferon-gamma

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