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大麻素WIN55, 212-2对双环己酮草酰二脲诱导的脱髓鞘模型髓鞘修复作用的研究(PDF)

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Title: Remyelination effect of cannabine WIN55,212-2 in cuprizone-induced demyelination mice

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关键词: 大麻素; 脱髓鞘; 运动功能; 髓鞘

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摘要: 目的　探讨大麻素WIN55,212-2对双环己酮草酰二脲（cuprizone，CPZ）诱导C57BL/6小鼠脱髓鞘模型的治疗作用。　方法　取6周龄C57BL/6雄性小鼠，分为正常组、第2周WIN55,212-2给药组与DMSO对照组、第4周WIN55,212-2给药组及DMSO对照组，每组10只。正常组每天喂养普通饲料，CPZ模型持续喂养含有0.25% CPZ的混合饲料，在第2周和第4周时进行WIN55,212-2注射，DMSO对照组则在相同条件下注射10%的DMSO，继续喂养CPZ混合饲料。于第3、5周末通过体质量变化观察整体状态；旋转棒实验观察小鼠运动功能，利用LFB和MBP免疫组化技术染色观察胼胝体区域髓鞘，GFAP染色观察星形胶质细胞。　结果　与DMSO对照组相比，WIN55,212-2给药组模型体质量下降趋势明显减缓($P<0.05$)；旋转棒实验中，WIN55,212-2给药组小鼠运动功能仍弱于正常小鼠，但是与DMSO对照组相比，WIN55,212-2给药组运动功能明显改善($P<0.01$)；LFB染色结果显示DMSO对照组髓鞘脱失明显，WIN55,212-2给药组介于正常与DMSO对照组之间，MBP染色进一步证实了这一结果；GFAP免疫组化实验结果显示DMSO对照组CPZ模型小鼠胼胝体区域GFAP阳性细胞广泛表达，而经过WIN55,212-2

治疗的小鼠GFAP表达量明显低于DMSO对照组(P<0.05)。　结论　大麻素WIN55,212-2可通过降低髓鞘的脱失和星形胶质细胞的活化，对脱髓鞘病变具有一定缓解的作用。

Abstract: Objective To determine the treatment effect of cannabine WIN55,212-2 (WIN) in cuprizone (CPZ)-induced demyelination model in C57BL/6 mice. Methods A total of 50 6-week-old male C57BL/6 mice were randomly divided into 5 groups, that is, normal group, the WIN treatment groups, and the corresponding DMSO groups. The mice of normal group were fed with normal lab chow everyday, and those of other groups were fed with normal lab chow containing 0.25% cuprizone. In 1 and 2 weeks after CPZ feeding, WIN dissolved in 10% DMSO was injected intraperitoneally at a dose of 1 mg/kg to the mice of WIN treatment groups, and 10% DMSO was given to the control group for 2 weeks. Overall functions of mice were observed by their weight. Their motor function was observed by Rotarod test. Luxol fast blue (LFB) staining and myelin basic protein (MBP)immunohistochemical staining were used to observe the myelination of corpus callosum, and GFAP immunohistochemical staining for astrocyte. Results The weight of WIN treatment groups was decreased slowly than the DMSO control group(P<0.05). Rotarod test found that the motor function was weak in WIN treatment groups than normal mice, but significantly improved than the DMSO control (P<0.01). LFB staining displayed that demyelination was very obvious in the DMSO control groups, and that in the WIN treatment groups was better than the DMSO groups, but worse than the normal control (P<0.05), and the same results were found in immunohistochemical assay for MBP (P<0.05). The expression of GFAP was widely in corpus callosum of the DMSO control groups, but it was significantly lower in the WIN treatment groups (P<0.05). Conclusion Cannabine WIN alleviates demyeination through attenuating the myeline loss and astrocyte activation.

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