

# 温阳解郁颗粒调控 NLRP3/ASC/Caspase-1 通路对大鼠的抗抑郁作用机制研究<sup>△</sup>

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**摘要** 目的 通过NOD样受体热蛋白结构域相关蛋白3(NLRP3)/凋亡相关斑点样蛋白质(ASC)/胱天蛋白酶1(Caspase-1)通路探讨温阳解郁颗粒的抗抑郁作用机制。方法 采用慢性不可预知温和应激(CUMS)结合孤养的方法构建抑郁大鼠模型,造模持续42 d。实验设置空白组、模型组、MCC950(NLRP3炎症小体抑制剂)组(10 mg/kg)、氟西汀组(阳性对照,2.08 mg/kg)和温阳解郁颗粒低、高剂量组(3.78、7.56 g/kg),每组10只。从实验第22天起,氟西汀组和温阳解郁颗粒低、高剂量组大鼠灌胃相应浓度药物并腹腔注射等体积生理盐水,MCC950组大鼠腹腔注射相应浓度MCC950并灌胃等体积蒸馏水,空白组和模型组大鼠灌胃等体积蒸馏水并腹腔注射等体积生理盐水,每天1次,连续21 d。每周进行1次行为学考察。末次给药后,检测大鼠海马组织中ASC、离子钙结合适配器分子1(Iba1)、白细胞介素1 $\beta$ (IL-1 $\beta$ )、IL-18含量以及NLRP3、分化簇68(CD68)、Caspase-1、B细胞淋巴瘤2(Bcl-2)、Bcl-2相关X蛋白表达情况和神经元凋亡情况。结果 末次给药后,与模型组比较,温阳解郁颗粒高剂量组大鼠旷场活动时间显著延长( $P<0.05$ ),新环境进食潜伏期显著缩短( $P<0.05$ );海马组织中ASC、Iba1、IL-1 $\beta$ 、IL-18含量以及NLRP3、Caspase-1、CD68蛋白表达和神经元凋亡阳性率均显著降低/下调( $P<0.05$ ),Bcl-2蛋白表达显著上调( $P<0.05$ ),神经元凋亡阳性细胞密度显著减小( $P<0.05$ )。结论 温阳解郁颗粒通过抑制NLRP3/ASC/Caspase-1通路,减轻小胶质细胞介导的神经炎症,抑制海马神经元凋亡,从而发挥抗抑郁作用。

**关键词** 温阳解郁颗粒;抑郁症;NLRP3炎症小体;凋亡相关斑点样蛋白;胱天蛋白酶1;神经炎症;神经元

## Mechanism of Wenyang jieyu granules regulating NLRP3/ASC/Caspase-1 pathway on antidepressant effect in rats

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**ABSTRACT** **OBJECTIVE** To explore the antidepressant mechanism of Wenyang jieyu granules (WYJYG) via the NOD-like receptor thermal protein domain associated protein 3 (NLRP3)/apoptosis-associated speck-like protein containing a CARD (ASC)/Caspase-1 pathway. **METHODS** A rat model of depression was established by chronic unpredictable mild stress combined with single-housing for 42 consecutive days. The experiment set up blank group, model group, MCC950 (NLRP3 inflammasome inhibitor) group (10 mg/kg), fluoxetine group (positive control, 2.08 mg/kg), low-dose WYJYG (3.78 g/kg) and high-dose WYJYG group (7.56 g/kg), with 10 rats in each group. From the 22nd day of the experiment, rats in the fluoxetine group, low-

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dose and high-dose WYJYG groups were intragastrically administered with the corresponding drugs and intraperitoneally injected with an equal volume of normal saline. Rats in the MCC950 group were intraperitoneally injected with MCC950 at the corresponding concentration and intragastrically administered with an equal volume of distilled water. Rats in the blank group and model group were given an equal volume