

Huang-Lian-Jie-Du decoction alleviates depressive-like behaviors in dextran sulfate sodium-induced colitis mice via Trem2/Dap12 pathway

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Abstract:

Introduction: Huang-Lian-Jie-Du decoction (HLJD), a traditional Chinese medicine prescription. Our study aimed to explore the effect and the underlying mechanism of HLJD treatment on colitis-induced depression and the involvement of the inflammatory factors and microglial-activated related genes.

Materials and Methods: The chronic colitis model was established by treating male mice with 1% dextran sulfate sodium (DSS) for 8 weeks. One week after DSS-treated, HLJD decoction

was administered orally with 2 and 4 g/kg daily for 7 weeks. Behavior tests and TUNEL staining were then assessed. The expression of inflammatory-related genes and microglial dysregulation were measured by RT-PCR and the expression of Trem2, Dap12 and Iba1 were assessed by immunofluorescence methods.

Results: Depressive-like behaviors were observed in mice treated with DSS, which suffered colitis. Compared to normal control (NC-V) mice, the density of TUNEL+ cells in the habenula (Hb), hippocampus (HIP), and cortex were significantly higher in colitis (DSS-V) mice, especially in Hb. Compared to NC-V and several brain regions, the expression levels of the *Il-1 β* , *Il-10* and *Dap12* mRNA were significantly increased in the lateral habenula (LHb) of colitis mice. Moreover, the expression of Trem2, Dap12 and Iba1 were increased in LHb of DSS-V mice. HLJD treatment could alleviate depressive-like behaviors, reduce the density of TUNEL+ cells in Hb and the expression of *Il-6*, *Il-10* and *Dap12* mRNA in LHb of DSS-V mice. The overexpression of Trem2, Dap12 and Iba1 in LHb of DSS-V mice were reversed after HLJD treatment.

Conclusions: These results reveal LHb is an important brain region during the process of colitis-induced depression. HLJD treatment could alleviate depressive-like behaviors in colitis mice via inhibiting the Trem2/Dap12 pathway in microglia of LHb, which would contribute to the precise treatment. It provides a potential mechanistic explanation for the effectiveness of HLJD treatment in colitis patients with depression.

References:

1. Zheng JY, Li XX, Lin WY, et al. Huang-Lian-Jie-Du decoction alleviates depressive-like behaviors in dextran sulfate sodium-induced colitis mice via Trem2/Dap12 pathway. *J Ethnopharmacol.* 2023 Oct 28;315:116658. doi: 10.1016/j.jep.2023.116658