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Long-term treatment with isorhynchophylline reverses chronic unpredictable mild stress-induced depressive-like behaviors via increasing expression of neurotrophins in the rat brain

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Isorhynchophylline (IRN), an oxindole alkaloid, has been identified as the main active ingredient responsible for the biological activities of *Uncaria rhynchophylla*. Previous studies in our laboratory have shown that IRN has anti-depressant-like effects in mice. The present study aimed to investigate the molecular mechanisms underlying the antidepressant-like action of IRN by measuring neurotrophins including brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) in the non-stressed and Chronic Unpredictable Mild Stress (CUMS)-treated rats. IRN (20 or 40 mg/kg/day) was administered by oral gavage to rats for 5 weeks. The results showed that CUMS caused depression-like behaviors in rats, as indicated by the significant decreases in sucrose consumption and duration of immobility (assessed by forced swim test). In addition, it was found that BDNF contents in the hippocampus and frontal cortex were significantly decreased in the CUMS-treated rats. CUMS treatment also significantly decreased the level of NGF in the frontal cortex of the rats, while markedly enhanced the level of corticosterone in serum of rats. Daily intragastric administration of IRN (20 or 40 mg/kg/day) during the five weeks of CUMS significantly reversed the behavioral and biochemical changes induced by CUMS. Treating non-stressed animals with IRN (40 mg/kg) for 5 weeks also significantly increased BDNF contents in the hippocampus and frontal cortex, and NGF contents in the frontal cortex of rats, but not change was observed in the level of corticosterone in serum of rats. The results suggest that the antidepressant-like action of IRN is mediated, at least in part, by increasing the expression of BDNF and NGF in the selective brain tissues.

Biography

Xian Yan-Fang, a Postdoctoral Fellow at School of Chinese Medicine, The Chinese University of Hong Kong, obtained her PhD degree in 2013 from The Chinese University of Hong Kong. She has rich experience in studying the Chinese medicines and neuroscience. Her team has investigated the neuroprotective effects of Chinese medicines and natural products for more than 10 years. She has published 14 original research articles based on her experimental findings in various SCI-listed academic journals as the first author. In this study, she aimed to examine the anti-depressant-like effect of isorhynchophylline (IRN) in Chronic Unpredictable Mild Stress (CUMS)-treated rats and explore the molecular mechanisms in the hippocampus and frontal cortex of rats. The results showed that IRN treatment could reverse the behavioral and biochemical changes induced by CUMS. The results from the present proposed study would form foundation that may lead to future clinical trial of IRN on depression.

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