Psychosocial stress enhances IgE-mediated triphasic cutaneous reaction in mice: Antagonism by Yokukan-san (a Kampo medicine) and diazepam

http://www.firstlight.cn 2006-03-03

Background: In the present study, we investigated the effect of social isolation stress on IgE-mediated triphasic cutaneous reactions after 2,4-dinitrofluorobenzene (DNFB) challenge in male BALB/c mice passively sensitized with anti-dinitrophenol (DNP) IgE antibody, and examined the effects of Yokukan-san (a Kampo medicine with antipsychotic action) and a reference drug (diazepam) on the stress-enhanced cutaneous reaction.

Methods/Results: In response to challenge with 0.01, 0.025 and 0.05% DNFB, triphasic skin reactions, including an immediate-phase response (IPR), a late-phase response (LPR) and a very late-phase response (vLPR) at 1 and 24 h and 8 days after antigen challenge, respectively, were increased in socially isolated mice compared with group-housed mice. Oral administration of Yokukan-san attenuated the isolation stress-exacerbated triphasic skin reactions in a dose-dependent manner, whereas it had no significant effect on cutaneous reactions in the unstressed group-housed mice. In contrast, intraperitoneal administration of diazepam, a classic benzodiazepine receptor agonist, suppressed the enhanced IPR and LPR in socially isolated mice but, surprisingly, stimulated vLPR in both stressed and unstressed mice, showing different efficacy to Yokukan-san. Moreover, the elevated locomotor activity in socially isolated mice was reduced by Yokukan-san and diazepam, while the isolation stress-induced aggressive behavior was normalized only by diazepam and not by Yokukan-san.

Conclusions: The results of the present study indicate that IgE-mediated triphasic cutaneous reactions were exacerbated by social isolation stress and suggest that Yokukan-san and diazepam antagonize isolation stress-induced cutaneous reactions partly through their sedative action on social isolation stress.

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