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Effects of interleukin (IL) 6 and IgG1 on the formation of gonadotropin-releasing hormone (GnRH) neuron migratory pathway in mice

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The development of GnRH system during early stages of ontogenesis can be perturbed by various negative factors, including infections. Maternal immune activation induced by infections leads to elevated synthesis of proinflammatory cytokines, especially IL-6, and retarded intranasal migration of GnRH neurons from olfactory placodes to forebrain [4], that results in long-term effects on reproductive ability [1]. Currently, attempts are being made to neutralize increased levels of proinflammatory cytokines by IgG [3].

This study was aimed to define the effects of IL-6 and IgG1 on the migratory route formation of GnRH neurons in mouse embryonic nasal placodes.

Nasal placodes were prepared from Balb/c mouse embryos on day 11.5, and cultured in serum-free medium (control) for 5 days at 37°C, according to previously described protocol [2]. Olfactory placodes were cultured (1) with IL-6 (10 ng/ml), (2) with IL-6 and IgG1 (5 ng/ml each) and (3) with IgG1 (10 ng/ml). On day 5, the explants were processed for immunohistochemistry with anti-peripherin antibodies. Axonal outgrowth was measured using fluorescent microscope and ImageJ software.

The axonal growth was suppressed by IL-6 twofold and stimulated by IgG1 fivefold. After the simultaneous co-culture of olfactory placodes with IL-6 and IgG1 suppressive effect of IL-6 was abolished by IgG1 and fiber length reached that in the control group.

Thus, disorders of the migration route formation of GnRH neurons the prenatal induced by IL-6 lead to a slowdown in the migration of neurons to the hypothalamus, thereby disturbing the development and functioning of reproductive axis. IgG could exhibit anti-inflammatory effect, which leads to a decrease in the synthesis of proinflammatory cytokines and an improvement of the fetal development.

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