The role of 5-HT_{2B}-receptor in the modulation of macrophages-induced Th17-immune response in multiple sclerosis.

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Introduction: fluoxetine is a selective serotonin reuptake inhibitor, which also has an immunomodulatory effect and may modulate Th17-cells, which plays a crucial role in the pathogenesis of multiple sclerosis (MS). This study aimed to clarify the influence of fluoxetine on macrophages-induced Th17-immune response and the involvement of 5-HT_{2B}-receptor in this modulation in (MS).

Methods: sixteen MS patients and twenty-five healthy subjects were examined. To study the effect of fluoxetine on macrophages-induced Th17-immune response, monocyte-derived macrophages were incubated in the presence of fluoxetine and / or agonist/antagonist of 5-HT_{2B}-receptor whereafter interferon-γ (IFN-γ) and lipopolysaccharide (LPS) were added to the cultures. Then, LPS-activated macrophages were co-cultured with autologous $CD4^+$ T cells. The levels of IL-6, IL-17, and IFN-γ in culture supernatants were assessed by ELISA.

Results: fluoxetine suppressed IL-6 production by LPS-activated macrophages and their ability to induce IL-17 and IFN-γ production by $CD4^+$ T-cells in both groups ($p<0.001$). Blockade of 5-HT_{2B}-receptor decreased the inhibitory effect of fluoxetine on the ability of macrophages to induce cytokine production by $CD4^+$ T-cells in both groups ($p<0.05$), while activation of 5-HT_{2B}-receptor did not affect the inhibitory effect of fluoxetine. The direct activation of 5-HT_{2B}-receptor (without pretreatment with fluoxetine) on macrophages with a specific agonist reduced the ability of macrophages to induce IL-17 and IFN-γ production by $CD4^+$ T-cells in both groups ($p<0.05$), while blockade of 5-HT_{2B}-receptor had no effect on macrophages.

Conclusions: these data suggest an anti-inflammatory role for fluoxetine in MS, which could be mediated by the suppression of macrophages-induced Th17-immune response via 5-HT_{2B}-receptor activation.

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