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Effects of antidepressants and cyclooxygenase-2 inhibitor on cytokines and kynurenines in stimulated in vitro blood culture from depressed patients.

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1. Abstract

BACKGROUND:

Immune activation induces a pro-inflammatory state, which enhances the tryptophan degradation into kynurenine (KYN). The involvement of kynurenines has been shown in patients with major depression. Here, the effects of anti-inflammatory medication and antidepressants on cytokines and tryptophan metabolite changes in blood culture with immune challenge [bacterial mimetic lipopolysaccharide (LPS)] were investigated.

MATERIALS AND METHODS:

A total of 21 depressed patients and 38 matched controls were recruited. Whole blood cultures were stimulated with LPS and drugs were added (celecoxib, venlafaxine, reboxetine, imipramine and fluoxetine). Cytokines and kynurenines were analysed.

RESULTS:

After stimulation with LPS, the interferon-γ and interleukin (IL)-10 secretions were significantly higher in controls than in patients ($p = 0.045$, $p = 0.032$), respectively. Adding imipramine and celecoxib abolished the significance for IL-10. Challenge with LPS induced the kynurenine pathway in each group. Regarding the ratio KYNA/KYN, which indicated how much of KYN formed is further catabolised into the neuroprotective arm, the controls' blood cultures showed a significantly higher ratio ($p = 0.045$).

DISCUSSION:

Stimulation with LPS induced increased production of pro-inflammatory and anti-inflammatory cytokines in both groups, but higher responses in controls. This lower production of cytokine responses in depressed patients indicates that their immune cells are in a refractory phase, induced by a pre-existing pro-inflammatory state. For kynurenines, the whole metabolism was enhanced by LPS; however, an imbalance to neuroprotective metabolites was observed just in control blood. A drug effect could only be shown for imipramine and celecoxib, which were beneficial in terms of re-balancing the immune function but not in re-balancing neuroactive metabolites.