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THE EFFECT OF ANTIDEPRESSANTS ON INFLAMMATORY MARKERS IN ANIMAL MODELS OF DEPRESSION

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Considering the evidence that pro-inflammatory cytokines play a causal role in depressive illness, the ability of antidepressants to induce anti-inflammatory effects is a subject of considerable interest. In an in vivo context we observe that antidepressants that enhance noradrenaline availability are the most effective anti-inflammatory agents; a fact consistent with the established anti-inflammatory actions of noradrenaline. Specifically, we have observed that noradrenaline reuptake inhibitors (NRIs) inhibit microglial activation and inhibit expression of pro-inflammatory cytokines (IL-1beta and TNF-alpha), iNOS, and inflammatory chemokines (IP-10 and RANTES) in rat brain following a systemic inflammatory challenge. These in vivo anti-inflammatory actions of NRIs are mimicked by in vitro exposure of primary glial cells to noradrenaline, but not by in vitro exposure of glial cells to the drugs themselves. These data suggest that NRIs promote an anti-inflammatory environment in rat brain in vivo by increasing noradrenaline availability at glial cells. We have also observed that even in the absence of any overt inflammation, chronic treatment with the NRI reboxetine promotes an anti-inflammatory phenotype in the CNS characterised by reduced expression of pro-inflammatory cytokine IFN-gamma, and increased expression of the anti-inflammatory cytokine IL-10. Current experiments are focused on the activation of the inflammatory response system in animal models of depression secondary to inflammation. The models are used subsequently to assess the anti-inflammatory effects of antidepressants in vivo.

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