



Changes in the immune system in depression and dementia: causal or co-incidental effects?

Leonard BE.

Pharmacology Department, National University of Ireland, Galway, Ireland. belucg@iol.ie

It is now widely accepted that psychological stress and psychiatric illness can compromise immune function. Furthermore the mechanisms whereby such changes occur are probably associated with the activities of the cytokines and other inflammatory mediators of the immune system which are known to initiate changes in behaviour. This review aims to summarise the experimental and clinical evidence that implicates the pro-inflammatory cytokines in the pathological changes seen in major depression and in Alzheimer's disease (AD). In major depression, evidence is provided to show that both activation (e.g., macrophage activity, acute phase proteins) and inhibition (e.g., natural killer cell activity) of the immune system occur. Many of the behavioural changes seen in depression are simulated by three pro-inflammatory cytokines (IL-1, IL-6 and TNF-alpha), which may produce their impact on the brain by activating cyclooxygenase, nitric acid synthase and corticotrophin releasing factor. Effective antidepressant treatments largely attenuate the immune changes thereby raising the possibility that the normalisation of central biogenic amine function that are conventionally implicated in the cause of depression may be secondary to those of the pro-inflammatory cytokines. With respect to AD, while the cause(s) are unknown, there is both experimental and clinical evidence to suggest that inflammatory processes in the brain caused in particular by TNF-alpha together with the subsequent rise in free radicals, are instrumental in causing the pathological changes which underlie the disease. Evidence in favour of the inflammatory hypothesis is supported by the finding that nonsteroidal anti-inflammatory drugs slow down the progression of the disease. Although, more research is needed into the inter-relationships between the various pro-inflammatory cytokines and the behavioural changes invoked in major depression and AD, the immunological hypothesis has been important in stimulating new concepts regarding the causes of the pathological changes in these diseases and how effective drug treatments may attenuate them.

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