

ALZHEIMER DISEASE

Inflammation speeds up cognitive decline in AD

People with mild to severe Alzheimer disease (AD) who sustain infections that cause acute systemic inflammation have markedly increased levels of tumor necrosis factor (TNF). They also show twice the rate of cognitive decline to people without systemic inflammation, conclude researchers who followed 300 community-based patients with AD. “Systemic inflammation is associated with an increase in long-term cognitive decline in patients with AD, and this might be caused by specific inflammatory mediators such as TNF,” notes lead author Clive Holmes.

Blood tests and cognitive assessments were performed at 2, 4 and 6 months, and both patients and caregivers were quizzed to pinpoint patients showing acute inflammatory signs. Patients who already had chronic inflammation and high TNF levels at baseline showed a rate of cognitive decline that was 10 times that of

AD patients who had neither chronic nor acute inflammation. In fact, patients with low levels of serum TNF throughout the study period showed virtually no cognitive decline during that time.

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“We have known for some time that acute infections can cause a short-term deterioration in cognitive decline by causing delirium. This study is showing that acute infections can cause a long-term decline in the absence of delirium and, in addition, that these effects are especially bad when there is evidence that chronic inflammation is already present,” explains Holmes.

TNF is a proinflammatory cytokine produced by macrophages that activates a central innate immune response. Although conflicting evidence exists on the role of TNF in the brain—studies show both beneficial and harmful effects—its role in AD seems to be predominantly destructive. Studies in animal models have demonstrated that TNF stimulates the production of cytotoxic inflammatory mediators that accelerate neurodegeneration, particularly if chronic inflammation is already present. Blocking TNF could reduce this effect; “we definitely want to investigate if measures that can control systemic inflammation can slow down progression of cognitive decline in this disease,” comments Holmes.

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