

Inflammatory response to infection and injury may worsen dementia

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Inflammation in the brain resulting from infection or injury may accelerate the progress of dementia, research funded by the Wellcome Trust suggests. The findings, published this week in the journal *Biological Psychiatry*, may have implications for the treatment and care of those living with dementia.

Systemic inflammation – inflammation in the body as a whole – is already known to have direct effects on brain function. Episodes of delirium, in which elderly and demented patients become extremely disoriented and confused, are frequently caused by infections, injury or surgery in these patients. For example, urinary tract infections, which are typically bacterial, appear to be particularly potent inducers of psychiatric symptoms.

Until now, there had been little research into the impact of systemic inflammation on the progress of dementia and neurodegenerative diseases. However, with over 700,000 people currently living in the UK with dementia – a figure set to rise with our ageing population – scientists are keen to understand more about the mechanisms behind such diseases.

Now, in a study to mimic the effect of bacterial infection in people with dementia, Dr Colm Cunningham and colleagues at Trinity College Dublin, in collaboration with Professor Hugh Perry at the University of Southampton have shown that the inflammatory response to infection in mice with prior neurodegenerative disease leads to exaggerated



symptoms of the infection, causes changes in memory and learning and leads to accelerated progression of dementia.

"Our study clearly shows the damaging effect of systemic infection or inflammation in animal models of dementia," says Dr Cunningham, a Wellcome Trust Research Career Development Fellow.

In previous studies, Dr Cunningham and colleagues showed that infection-induced inflammation can exacerbate nerve cell damage in animal models of dementia. Now, the team has shown that just one episode of systemic inflammation could be sufficient to trigger a more rapid decline in neurological function.

"Doctors and carers need to pay increased attention to protect people with dementia from potential causes of systemic inflammation," says Dr Cunningham. "These include preventing infection, protecting them against falls and carefully weighing up the risk-benefit ratio of non-essential surgery."

Dr Cunningham believes the research may provide clues for helping slow down the progression of neurodegenerative diseases in humans. Although long-term use of non-steroidal anti-inflammatory drugs to treat conditions such as rheumatoid arthritis offers modest protection against the development of Alzheimer's disease, actually treating Alzheimer's patients with these drugs has not had a significant impact on disease progression.

The researchers found that systemic inflammation leads to the production of a protein known as IL-1 β by microglia, the brain's resident immune cells, in the hippocampus region of the brain. This region is involved in memory and learning. The protein is known to exacerbate nerve cell damage in stroke. Inflammatory mediators such as IL-1 β are routinely produced in the blood in response to inflammatory stimuli and



prior studies by colleagues in Southampton have shown a correlation between elevated blood IL-1 β levels, recent infection and subsequent cognitive decline.

"The recognition that relatively banal systemic inflammatory events can interact with and exacerbate neurodegenerative processes in the brain opens up potential avenues of treatment for patients with dementia," he says.

Rebecca Wood, Chief Executive of the Alzheimer's Research Trust, commented:

"This is really interesting research leading to a significant step forward in our understanding of dementia. Inflammation has been implicated in dementia for some time, which is why falls are of such concern, but this also shows that the dementia is increased by another common problem of ageing - urinary tract and other infections. It also demonstrates how important it is to lower our dementia risk through maintaining good overall health.

"In the UK, 25 million of us know a close friend or family member with dementia, but research into the condition is severely underfunded. We need far more research like this if we are to reduce dementia's impact on our society."

Source: Wellcome Trust

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