

STRESS HAS A CAUSATIVE ROLE IN AD AND MILD COGNITIVE IMPAIRMENT (MCI)

Roger Bullock

UK

The key to this debate is the word causative. The burden of proof to prove causality is much higher than to have a strong correlation or association. It is clear that the ongoing effects of stress and the resultant hormonal imbalances produce physical effects that are easily measurable. Magri (2006) has shown hippocampal volume reduction using MRI that correlates to high cortisol/DHEA ratios. It also correlated with age associated cognitive decline. However hippocampal size is not the sole determinant of AD. People with chronic depression have smaller hippocampi for the same reason, often with no cognitive effects.

Last year the researchers in Gothenberg published results in a 35 year old follow up of 1500 women that showed 65% more dementia in those that had episodes of stress than those who did not. A powerful association, but still a relatively low incidence in the stressed women all the same and definitely not proof of cause.

The difficulty with proving cause in AD, is understanding what AD is in its own right. Stress is associated with over eating, alcohol and drug abuse and smoking. Taken one by one: over eating is usually of high carbohydrate comfort foods, with sugar now being implicated in neurodegeneration and oxidative stress. Alcohol may be protective in moderation, but not in long term overusage. Prescription drugs may affect cognition and smoking will contribute to vascular risk, which if the Nun study and various studies from the same researchers in Gothenberg is true, may be the most important contributor to developing dementia in the presence of AD pathology. So a compelling case can be made for how stress exacerbates other known risk factors, while adding to the bank of risk factors in its own right.

The final answer will have to come through well conducted prevention studies. However, these are difficult to do and control, given all the interactions. Clive Holmes started a prospective study in MCI last year - looking at physical and psychological outcomes. That may be a little late, as given the public fear of AD, how do you stop someone with MCI being stressed?

I think that stress is clearly a contributor to the more rapid degeneration of the brain in an interactive way with many other known risk factors. It is attractive to link the neuroendocrinology and the evidence of hippocampal shrinkage is interesting. The question in the debate is whether stress is causal. It is too early to say, but aggressively addressing stress at all stages of life can only be beneficial.