

Clot formation as a potential diagnostic tool and therapeutic target for Alzheimer's disease

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Research Abstract

Alzheimer's disease (AD) is the leading cause of dementia in the elderly. Accumulating evidence links AD with vascular risk factors. These correlations, together with profound alterations of cerebrovascular structure and function present in AD, suggest a "vascular

hypothesis”, where vascular pathology eventually leads to neurodegeneration and subsequent cognitive decline. A decrease in cerebral blood flow has been reported in AD patients and, moreover, a correlation between the level of cerebral hypoperfusion and the degree of dementia has been identified. Several pieces of evidence indicate that there is an increased obstruction of the cerebral blood vessels in the AD brain, that could strongly affect the overall cerebral circulation. For example, a significant reduction in the number of functional intracortical microvessels in aged AD mice has been described. Furthermore, in vivo clot formation experiments in AD mice showed not only that the AD brain is more prone to clot, but also once the clot has been formed it is more resistant to degradation. Also, the number of spontaneously stalled brain capillaries is significantly increased in AD mouse models, which can provoke an important decrease in the downstream cerebral blood flow.

These obstructions in AD cerebral vessels could initiate and/or aggravate the brain hypoperfusion and inflammation present in the AD brain. Cerebral hypoperfusion seems to be a good indicative for dementia conversion, which suggests that the occlusion of vessels might be happening at very early stages of the disease, many years before the clinical manifestation of AD. Therefore, I propose to develop an in vivo noninvasive imaging method to identify these occlusions since it might prove a useful tool to identify patients at very early stages of the AD pathology. Also, I will analyze whether the use of new effective anticoagulants with lower risk of intracranial bleeding could be a potential therapeutic strategy as treatment for AD.

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