Dementia Update

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With the accumulation of scientific knowledge and discovery, the focus is being shifted away from the symptomatic stages of dementia towards the preclinical state. It is particularly true of Alzheimer's disease (AD). Repeated failures of 'disease-modifying' drug trials and better understanding of pathophysiology of AD have led to the idea that if we do not detect and intervene very early in the disease process of AD, we do not have much chance of success in staving off the disease. Alzheimer's disease is widely regarded as the neurodegenerative brain disorder caused by accumulation of β-amyloid, regardless of clinical status, representing a continuous process of synaptic and neuronal deterioration. The distinction between brain aging and AD is somewhat blurred and remains controversial. "Suspected Non-Alzheimer Pathology" (SNAP) encompasses individuals with biomarker evidence of neurodegeneration in the apparent absence of elevated β-amyloid accumulation and takes up about a quarter of the cognitively normal elderly population. The concept of the non-amyloid (or amyloid-independent) pathway leading to neurodegeneration is intriguing in terms of clinical implications for a new therapeutic target.

In the present state of knowledge, β-amyloidosis is necessary but not sufficient to cause AD dementia. There is growing body of evidence that β-amyloidosis and neurodegeneration (tau accumulation, more specifically) arise independently and, at some point in preclinical stage, chronically high levels of β-amyloid and neurodegeneration interact to facilitate neurodegeneration.

The emerging theme in the field of dementia is the contribution of vascular brain injury (VBI) to the development of dementia. VBI has been considered as taking on a secondary role in what causes dementia in AD. Recent studies suggest that vascular damage and amyloid plaques occur independently in early stages of AD and some VBI may play a bigger role than amyloid in producing cognitive decline. It is currently unclear whether VBI plays a critical role in the pathogenesis of AD, or if VBI is a 'second hit' providing an independent mechanism which increases neural burden, the rate of cognitive decline, and the probability of the development of dementia.

There is increasing evidence that subjective cognitive decline (SCD) in people with unimpaired performance on cognitive tests may represent the first manifestation of AD. Research criteria for SCD are proposed by the SCD working group to reach consensus on a conceptual framework. Patients with SCD may be an excellent population to study earliest stages of AD and enrich subjects for AD drug trials.