Alzheimer’s Disease, is a Cure Possible?

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There is an enormous amount of research in progress worldwide in the search for a cure of Alzheimer’s disease (AD) undertaken at very great cost. It is therefore timely to take stock and review these efforts in the light of the reality of the neuropathology of AD. AD is the commonest cause of dementia which is estimated to affect 6% of the population at the age of 60 years and rises one percent by every year of age from then on by the age of 80 years 26% will be affected. AD therefore poses a gigantic problem medically, socially and economically becoming more so as life expectancy increases. This is reason why so much time, effort energy and money is spent on trying to find a cure. However the idea that a cure is possible flies in the face of reality because by the time cognitive decline is clinically manifest the cerebral cortex is in a state of advanced atrophy with whole populations of neurons having been lost. Unfortunately a great deal of the research on AD seems to overlook or be unaware of this fact. The dementia of AD is due to the degeneration and loss of neurons, a process which begins in the hippocampus of the temporal lobes extending to the frontal lobes and from there to other parts of the brain. Degenerating neurons contain neurofibrillary tangles composed of tau protein accompanied by the interstitial deposition of amyloid plaques. The outfall of neurons is the result of an as yet unknown mechanism but with a hint that the etiology may involve altered glucose metabolism [1]. The senile plaques characteristic of AD are composed of Amyloid beta (Aβ) peptide. Some theories of pathogenesis maintain that the Aβ amyloid is toxic to neurons but this effect has not been convincingly substantiated scientifically in vivo. A cure for AD requires the replacement of functioning neurons in the cerebral cortex together with their dendrites and axons. Simple replacement of lost neurons by differentiated stem cells will not be sufficient to restore lost intellectual functions because the appropriate network of neuronal circuits would need also to be reproduced. Although brain development mainly takes place during childhood the fine architecture continues to alter and modify throughout life according to use. It is these continuously changing neuronal connections and their networks which underlie the modalities of consciousness, self-awareness, personality, memory, emotion, cognition, language, other learned activities and manual skills. Because Alzheimer’s disease is a global disorder affecting all of the cerebral cortex, a cure would require a very large number of neurons to be put in their proper place including their networks. Immunologically compatible stem cells transplanted into the cerebral cortex may differentiate into neurons but they would also need to re-create the complex circuits of neurites and synapses arranged in exactly similar fashion to those which have been lost. Therefore a more realistic approach rather than a cure would be the prevention of AD. It is a remarkable finding, in recent years that the lifestyle changes which aid in the prevention of coronary heart disease also apply to the brain. Regular physical exercise is the most important of these factors followed by a healthy natural diet rich in antioxidants [2]. It is possible that the basic cause of AD will be discovered in the near future and clues to this most desirable outcome are the known genetic risk factors such as the APOE4 genotype and the TOMM40 genotype which
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are known to predispose to the disease [3, 4]. If and when the molecular etiopathogenesis of AD is discovered in it should be possible to arrest its progression this being the best outcome one may expect in the light of the neuropathology of AD.

References


