New study challenges accepted approaches to research in senile dementia

7 November 2011

Impacting millions of families and devouring billions of dollars globally, Alzheimer's disease is the focus of exhaustive research to find a cure. Although intensely investigated over the last three decades using cutting-edge technologies, the "pathogenic cause" of Alzheimer's disease has not been found. While many research "breakthroughs" have been claimed and high-profile drugs trials carried out, why does the promised "cure" still seem to elude scientists?

In an effort to address this question, Ming Chen, PhD, Huey T. Nguyen, BS, and Darrell R. Sawmiller, PhD, Aging Research Laboratory, R&D Service, Bay Pines VA Healthcare System and University of South Florida, undertook an independent and systematic analysis of the underlying research assumptions against the established scientific principles. This analysis led them to hypothesize that perhaps the main problem is the research community's perception of the disease.

In an article scheduled for publication in the December issue of the *Journal of Alzheimer's Disease* the authors suggest that when the National Institutes of Health separated out dementia from other senile conditions and redefined it as a distinct and "curable" disease -- Alzheimer's - in the 1970s, it opened a Pandora's box and may have misdirected research for decades. It triggered the search for pathogenic factors and cures, and disregarded the role of demographic change and its diverse end results in the elderly.

The authors argue that senile disorders - diseases occurring after age 60 and eventually affecting the majority of the elderly, such as tooth, hearing or memory loss - are caused by aging, thus differ fundamentally from distinct diseases by origin, study paradigm and intervention strategy.

Moreover, the authors contend that a central regulator in cognition ? the Ca2+ signaling system ? has been misconceived by institutional thinking that favors a "cure" for senile dementia. The dominant hypothesis, although unproven, is that Ca2+ levels rise throughout the aging process, leading to cell death, and thus research has focused on calcium antagonists to lower those levels. This viewpoint has been promoted by policy makers, and the subject of a number of high profile clinical trials, but to date no positive results have emerged.

In contrast, the authors propose that declining functionality of Ca2+ signaling as a result of the aging process, among a myriad of other age-related changes, leads to cognitive decline. Therefore Interventions for senile dementia could activate Ca2+ function by promoting energy metabolism and also by Ca2+ agonists such as caffeine and nicotine. At the same time, risk factors play a key role. "Aging and Ca2+ deficits set the stage for senile dementia, but do not always lead to senile dementia in real life," explains Dr. Chen. "Lifestyles and other risk factors are the key. So we think that senile dementia may be explained by 'advanced aging plus risk factors.' This model points to a new direction for prevention. This means we must support the elderly in healthy lifestyles. And we should develop medications to extend the lifespan of old neurons, rather than looking for ways to inhibit far-fetched 'pathogenic' factors."

"The model implies that senile dementia is, by and large, a lifestyle disease," says Dr. Chen. "This view, in fact, has been shared by many in the medical and clinical community, but contrasts sharply with current dominant theories in the Alzheimer research field, which assume a linear and 'cause and effect' mechanism. Since they have not taken into account the fundamental roles of aging and risk factors, it is clear that these theories, though highly appealing to the public and researchers alike, are of little relevance to the scientific nature of senile dementia."

"The two overwhelming concepts, senile dementia as a distinct disease and the Ca2+ overload hypothesis, have effectively blocked any meaningful progress in senile dementia research, and have inhibited the self-correcting mechanism of science," concludes Dr. Chen. "An independent scrutiny on the field may be helpful."

"Although incurable", Dr. Chen is optimistic. "Our research, if guided by correct theories, will produce medications to help delay dementia to a certain extent ? similar to the drugs that delay or ameliorate atherosclerosis and osteoporosis today."

Provided by IOS Press