

Relationships of Serum Lipids to Plaque and Tangle Frequency in the Very Old

Background and Importance

Despite many investigations, the role of serum lipids (total cholesterol = TC; low-density cholesterol = LDL; high-density cholesterol = HDL) in Alzheimer's disease (AD) of the elderly has not been established. This is unfortunate, since manipulation of serum lipids could be a means of influencing the onset and course of this progressive condition. Several reports, including those from our research group, noted positive relationships of serum lipids with AD or dementia or cognitive loss in very old populations. Higher TC and LDL have also been associated with more rapid cognitive decline in those who already have AD. However, many studies find no such associations and some even report negative associations of lipids with AD or dementia.

Aside from obvious demographic differences among the observed cohorts, several reasons for such discrepancies can be posited. For those studies that are clinically based (the large majority), identification of demented individuals within a population can vary widely, depending upon the psychometric tools employed; in addition, clinical methods often fail to distinguish the various dementing conditions from one another (e.g., AD vs vascular vs Lewy body dementias). These problems are evidenced by frequent clinical-pathological disagreement as to the presence and type of a dementing process. Such methodological limitations, individually and collectively, often lead to errors in assigning dementia presence and dementia type for subjects within a clinically observed cohort. For the very few studies that have used neuropathological tools to establish the presence and classification of specific dementia processes, other methodological variations may have affected outcomes and reduced comparability. Two pathologically-based studies (one from our group), using Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropathological criteria for the definition of AD and other dementing processes, report positive relationships of TC and LDL with AD, and no relationships of these lipids with dementing pathology other than AD. Other investigators, using different pathological criteria and/or different brain sites or different covariates, report somewhat dissimilar findings.

Most assumptions, definitions and procedural problems of these studies can be avoided by comparing serum lipids with the basic neuropathological "markers" for AD - plaques and tangles. Only one prior study has examined serum lipid values directly with plaque and tangle prevalence, and this was carried out in a community-based, all male population with a very low frequency of dementia. We are investigating a large nursing home (NH) population and comparing the relationships of serum lipids directly with neuropathological evaluations of these hallmarks of AD in the neocortex and the allocortex. [Multiple references available]

Objectives

To explore the role of cholesterol in Alzheimer dementia by establishing the association(s) of serum lipids directly with the basic (and original) markers of AD, brain plaques and tangles.

Methods

In collaboration with members of the NIH sponsored Alzheimer's Study Group (at Mount Sinai School of Medicine Departments of Pathology and Psychiatry), we have compiled a large, ongoing database over a number of years from the postmortem studies and clinical charts of residents at JHL. The database now includes information from about 500 autopsied JHL residents. [This pathological database is a rare resource, and shares information with research laboratories worldwide]. For over 350 of these autopsied JHL residents we also have information from JHL records as to serum lipids at admission as well as demographic data as to ages at admission and at death, length of stay, race, gender, and comorbidities. We have analyzed tissue of each resident for apoE genotype and also have the detailed neuropathological evaluations collected by leading experts in this field. The neuropathological studies include detailed, time-consuming observation (including actual counting) of the numbers of plaques and tangles in every area of the brain pertinent to AD.

Current Status

Extensive statistical analyses of the above information have been proceeding for some months, and are nearing completion. To this time, we appear to have established statistically significant positive correlations of serum total and LDL cholesterol with Alzheimer type plaques in all pertinent areas of the brain. The findings are strengthened by the relatively large sample size, by the high prevalence of dementia in this population, and by the expert, detailed neuropathological methods.

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