459 THE ASSOCIATION BETWEEN SECONDARY PATHOLOGY AND FUNCTIONAL DISABILITY IN DEMENTED SUBJECTS

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Dementia has been recognized as the strongest determinant for developing functional disability. But dementia patients typically present with concomitant illness. The objective of the current study was to examine the associations between specific diagnosed pathologies and specific functional disability in individual domains necessary for daily autonomous function. Using data on nearly 2900 subjects from the clinical examination of the 1991 Canadian Study of Health and Aging, multiple logistic regression models accounting for specific conditions and impairments that have demonstrated consistent associations with the development of physical disability in older people were estimated for disability in each of several domains (bathing, dressing, grooming, toileting, urinary and stool incontinence) assessed using the CAMDEX. The presence of a gait disorder, a history of falls, and current depression were significantly associated with disability in bathing. Among these, only the presence of a gait disorder was significantly associated with disability in any other domains (in dressing, grooming, toileting, and urinary incontinence). Diabetes was significantly associated with disability in dressing. Cardiac symptoms were significantly associated with disability in dressing, grooming, and toileting. In each case, it appeared to be protective against disability in that particular domain. Respiratory complaints were significantly associated with disability in dressing, urinary incontinence, and stool incontinence, while malignancies were significantly associated with disability in dressing and grooming. Chronic conditions are increasingly frequent in old age, many of which are associated with a likelihood of disability. When older persons present with possible cognitive problems, it is actually the disability that families are complaining of. Estimating the specificity and strength of secondary disease-disability associations in demented people is of practical importance because coexisting medical conditions may cause "excess disability" in patients with dementia that may be reducible by treatment and rehabilitation.

460 COGNITIVE FUNCTION IN THE OLDEST OLD: WOMEN PERFORM BETTER THAN MEN

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Objective:The incidence of dementia is higher in women than in men. Limited formal education has been associated with poor cognitive function and susceptibility of dementia. If limited formal education is associated with dementia, we would expect women to have a poorer cognitive function than men. Our aim was to explore whether limited formal education can explain the higher incidence of dementia in older women. Design:The Leiden 85 plus Study is a population-based study investigating all 85-year old inhabitants of the city of Leiden. From September 1997 until September 1999 a total of 599 participants were visited at their place of residence. The response rate was 86%. Main outcome measures:The Mini-Mental State Examination was completed by all participants. Cognitive speed and memory were determined with four neuro-psychological tests in participants with a Mini-Mental State Examination score of 19 points or higher. Results:The proportion of women with limited formal education was significantly higher than that of men (70% versus 53%, p=0.001). Despite this difference in formal education, women had better scores for cognitive speed and memory than men ($p<0.05$). After adjustment for differences in limited formal education, the odds ratio for women to have a higher cognitive speed than men was 1.6 (95% CI; 1.0 to 2.5), and for them to have a better memory the odds ratio was 1.7 (95%CI; 1.1 to 2.7). Conclusion: Among the oldest old, cognitive function of women was better than that of men. Therefore, less formal education alone can not explain the higher incidence of dementia in women compared to men. It is more likely that biological mechanisms, such as atherosclerosis, account for the differences in cognitive function between the sexes.

461 MILD MEMORY IMPAIRMENT AND MEDICAL CARE: RESULTS FROM A POPULATION-BASED STUDY

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Mild memory impairment may be associated with an increased risk of medical care and greater health care costs. To investigate this question, a multi-ethnic cohort of 1190 older adults without dementia was identified from a population-based study (Washington Heights-Inwood Columbia Aging Project). All subjects completed a full battery of cognitive evaluations in 1996 or earlier and survived through 1996. Subjects with Medicare (1996, n=811) and NYC Medicaid claims (1996-1998, n=560) were then identified and examined relative to performance on tests of memory (a factor-analytic derived composite of seven tests). In multivariate models that adjusted for age, gender, and education, mean [median] Medicare charges in 1996 were $7713 [$7505], $7930 [$7726], and $5848 [$5677] for subjects with the lowest, middle, and highest memory test performance, respectively ($p < .001$ by Kruskal-Wallis [K-S] test of median scores). Mean [median] annual Medicaid costs by memory tertile were $16,115 [$15,794], $10,651 [$10,313], and $7552 [$7197] ($p < .001$ by K-S test). Memory tertile groups did not differ in number of comorbid conditions. Low memory scores were associated with risk of incident dementia after 1996 (half of 59 subjects diagnosed with dementia during follow-up were in the lowest memory score tertile). Removing these subjects from analyses eliminated cost differences in Medicare but not Medicaid claims, suggesting that low memory performance in non-demented elders may be an independent risk factor for medical care costs that are captured in the Medicaid system.

462 THE ASSOCIATION BETWEEN DEMENTIA AND MID-LIFE RISK FACTORS

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Objective: Previous studies of Alzheimer's disease (AD) and other dementia have identified an association between these conditions and education, smoking, alcohol use, and co-morbid disorders, such as hypertension and diabetes mellitus (DM). We investigated the association of mid-life risk factors with the development of dementia, as detected 25 years later. Method: Study subjects were the 1,774 Japanese men and women participating in the Adult Health Study (AHS) of the Radiation Effects Research Foundation. The AHS consists of atomic bomb survivors and their controls. Based on DSM-IV, 114 subjects were diagnosed with dementia in examinations conducted between 1992-97. The number of cases of AD and vascular dementia (VaD) were 51 and 38, respectively. Information regarding education, physical activity, dietary habits, systolic blood pressure (SBP), total-cholesterol, body mass index, and history of DM were obtained in 1968-70. Sex, age, and radiation dose were also considered as explanatory variables. We evaluated the risk factors of dementia, AD, and VaD using logistic regression analysis. Results: The prevalence of dementia increased with increasing age, lower attained education, higher SBP in middle age, and a higher intake of salt in middle age. Odds ratios of AD for age (in 5-year increments), attained education (in 3-year increments), history of DM, and a lower intake of salt were 2.54, 0.42, 3.09, and 0.53, respectively. Odds ratios of VaD for age (in 5-year increments), sex (women to men), SBP (in 10 mmHg increments), and a greater intake of milk were 1.33, 0.61, 1.33, and 0.35, respectively. Conclusion: In addition to age, sex, and education, dietary habits and a history of diseases in middle age were associated with the development of dementia.

Poster Presentation: Genetic Studies II

463 ASSOCIATION STUDIES OF NOVEL POLYMORPHISMS IN BACE AND BACE2

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The release of amyloidogenic amyloid-β peptide (Aβ42) from amyloid-β precursor protein (APP) requires cleavage by β- and γ-secretases. Mutations in these enzymes that increase Aβ42 production would be expected to increase the risk for Alzheimer's disease (AD). Four groups have identified a candidate for the "β-site APP-cleaving enzyme " (BACE), also known as "Asp2" because the enzyme is a transmembrane aspartic protease. This enzyme maps to chromosome 11q23-24. Its homologue, BACE2 (Asp1), is mapped to chromosome 21q22 which includes the Down Syndrome region. Thus mutations or other polymorphic variants that alter the level of expression or activity of BACE and/or BACE2 may be risk factors for AD. We sequenced BACE cDNA from brain tissue of those with pathologically confirmed AD and elderly controls to look for polymorphisms in the coding sequence. We found one polymorphism at nucleotide 1239 where G is changed into C (from sequence Genbank:AF190725). The polymorphism was confirmed by PCR amplification and restriction enzyme digestion (Hph 1). In BACE2, two polymorphisms have been found by sequencing 8 exons using genomic DNA from 15 individuals, including 7 cases of familial dementia. We identified a C/T substitution in exon 6 at nucleotide 1200 (from sequence Genbank:AF050171) which can be screened with a BspM I digestion. An intronic C/T substitution was found at 10 bp 5 of exon 4 which was confirmed with by EcoN I digestion. No pathogenic mutations were observed in BACE2 in 5 individuals from FAD kindreds. Preliminary data in a small number of individuals failed to show differences in allele or genotype frequency between AD