with some results in the nondemented elderly suggesting that homocysteine is associated with psychomotor rather than memory impairment.

P2-270 DEMENTIA PREVALENCE IN VERY LONG-TERM USERS OF ESTROGEN ALONE VERSUS ESTROGEN PLUS PROGESTIN

Diana Petitti[1], Galen Buckwalter[1], Valerie Crooks*[2], Vicki Chiu[1]. [1]*Kaiser Permanente Southern California, Pasadena, CA, CA, USA;* [2]*Kaiser Permanente Southern California, Pasadena, CA, USA. Contact e-mail: Valerie.C.Crooks@kp.org*

Background: In the Women's Health Initiative Memory Study (WHIMS), the risk of dementia in women assigned to PERT was increased compared with those assigned to placebo. We previously reported on dementia risk in users of hormone replacement therapy, combining users of estrogen alone (ERT) and estrogen plus progestin (PERT). **Objective:** We reanalyzed our data to assess the risk of dementia in ERT and PERT users separately. **Methods**: The study involved 3,924 women 75+ years who were members of the Southern California Kaiser Permanente Medical Care Program in 1998. Hormone use was determined based on computer-stored prescription data for 1992-1998. Cognitive function and dementia were assessed using the Telephone Interview of Cognitive Status supplemented by the Telephone Dementia Questionnaire and medical record review. **Results**: There were a total of 300 dementia cases; 207 were probable Alzheimer's Disease (AD) and 93 were dementia with known cause, mostly vascular dementia. The mean duration of hormone use was 29.1 years (± 11.8 SD) for ERT users and 21.6 years (± 11.1 SD) for PERT users. PERT users (N = 569) differed from ERT users (N = 1375) in age and education but not ethnicity. After adjustment for age, education, ethnicity, and medical history variables, the odds ratio (OR) for all dementia in ERT users compared with non-hormone users was 0.78 (95% C.I. 0.59,1.03); for PERT users compared with non-users of hormones, it was 0.90 (95% C.I. 0.61,1.32). The adjusted OR for probable AD in ERT users compared with non-users of hormones was 0.73 (95% C.I. 0.52, 1.02); for PERT users compared with non-users of hormones, it was 0.92 (95% C.I. 0.58, 1.44). The adjusted ORs for dementia with known cause, were 0.93 (95% C.I. 0.58, 1.49) in ERT users and 0.85 (95% C.I. 0.42, 1.72) in PERT users. **Conclusions**: In this study, unlike WHIMS, the ORs for all dementia, AD dementia, and dementia with known cause were not increased in PERT users. There was some hint that the OR for probable AD might be lower in ERT users but not in PERT users, but the confidence limits for the OR estimates for ERT and PERT overlapped.

P2-271 AMYLOID MEDIATES THE ASSOCIATION OF APOLIPOPROTEIN E ε4 ALLELE TO COGNITIVE FUNCTION IN OLDER PERSONS

David A. Bennett*[1], Julie A. Schneider[1], Robert S. Wilson[1], Julia L. Bienias[1], Elizabeth Berry-Kravis[1], Steven E. Arnold[2]. [1]*Rush University Medical Center, Chicago, IL, USA;* [2]*University of Pennsylvania, Philadelphia, PA, USA. Contact e-mail: dbennett@rush.edu*

Background: We previously provided evidence consistent with a sequence of pathological events whereby the effect of amyloid deposition on cognitive function is mediated by neurofibrillary tangles. **Objective(s):** Test the hypothesis that amyloid mediates the association of the apolipoprotein E ε4 allele with level of cognition. **Methods:** Subjects were 44 persons with clinical AD and 50 without dementia, who participated in the Religious Orders Study, underwent apolipoprotein E allele determination, cognitive testing about eight months prior to death, and brain autopsy. Percent area of cortex occupied by amyloid-beta and the density of tau-positive neurofibrillary tangles were quantified from six brain regions and averaged to yield summary measures of amyloid load and neurofibrillary tangles. Multiple regression analyses were used to simultaneously examine the effects of allele status on amyloid load and neurofibrillary tangles, and level of global cognition, controlling for age, sex, and education. **Results:** The apolipoprotein E ε4 allele was associated with the density of tangles ($p = 0.002$) in a regression model. When a term for amyloid was added to the model, the effect of the ε4 allele was reduced by more than 50% and was no longer significant ($p = 0.12$) consistent with amyloid mediating the effect of allele status on tangles. In subsequent regression analyses, the ε4 allele was associated with amyloid load ($p < 0.001$). However, when a term for tangles was added to the model, the effect of the ε4 allele was reduced but remained significant ($p = 0.02$). To confirm that amyloid mediates the effect of allele status on level of cognition proximate to death, we added a term for amyloid to a regression model examining cognition as a function of the ε4 allele. The ε4 allele was associated with a lower cognitive function score ($p = 0.04$). When a term for amyloid load was added to the model, the effect of the ε4 allele was reduced by nearly 60% and was no longer significant ($p = 0.41$) while the effect of amyloid was significant ($p = 0.001$). **Conclusions:** These findings are consistent with a sequence of pathologic events whereby amyloid deposition comes prior to tangles in the sequence linking the apolipoprotein E ε4 allele to level of cognition.

P2-272 PUBLICATION TRENDS IN ALZHEIMER DISEASE

Mikolaj A. Pawlak*, Wojciech Kozubski. *Department of Neurology; University of Medical Sciences, Poznan, Poland. Contact e-mail: mpawlak@am.poznan.pl*

Background: For more than sixty years since its first description by Alois Alzheimer in 1906 neurodegenerative disease named after him had not been attracting attention of researchers. However over the last four decades there has been a significant increase in both basic and clinical research on the subject. There are many causes for such renewed and growing interest. Better understanding of the underlying causes can help in predicting future developments. **Objective:** Documentation of publication trends in Alzheimer disease related articles in biomedical literature covering the period from 1962 to 2003. **Methods:** Search of The National Institute of Health MEDLINE database was conducted to retrieve the papers published between 1962 and 2003 containing MeSH keywords *"Alzheimer disease"* and its derivatives. Frequency of search terms in keywords and titles was analyzed by bibliometrics. **Results:** Over last four decades the number of publications concerning Alzheimer disease has rapidly increased. From single number of publications per year in 1950' it increased to 2611 papers in 2002. At the same time the number of papers with MeSH keyword *'dementia'* grew steadily from 57 in 1965 to 3957 in 2002. We also found that the nature of publications on Alzheimer disease has changed over this period of time from basic research to definition and criteria seeking papers and to analysis of diagnostic approach, therapeutic options and clinical trials. Pace of growth of Alzheimer publications compared to the rest of publications on dementia syndromes is substantially higher. **Conclusions:** We consider the

Abstract P2-272 – Table 1. Total publication count in 5 year periods

Year of publication	ACHEI in any and Alzheimer Disease in MeSH keyword	Alzheimer in MeSH keyword and Publication Type: Review	Dementia in MeSH keyword without Alzheimer Disease in MeSH keyword	Alzheimer in MeSH keyword	Dementia in MeSH keyword
65–69	0	0	620	2	622
70–74	0	0	1033	19	1052
75–79	0	26	1152	271	1423
80–84	0	84	1724	1148	2872
85–89	47	591	2856	4088	6944
90–94	181	1225	4157	6608	10756
95–99	385	1970	5423	9714	15137
00–02	361	1707	3964	7405	11369