participants reported their history of depressive episodes and, if relevant, the number of episodes. Volumetric assessment of the hippocampus was performed using a 3-dimensional MRI sequence. Total hippocampal volumes were calculated with correction for head size and gender. Subjects with volumes below the 25th percentile of the distribution were defined as having a small hippocampus (n=128). All subjects were followed for development of AD. The diagnosis of AD was made according to internationally accepted criteria. **Results:** A history of depressive episodes was reported by 142 (27.8%) subjects, with 85 reporting one episode and 50 reporting 2 or more episodes. Logistic regression analyses adjusted for age, gender, education, memory complaints, and MMSE score, showed that subjects with a history of depression were less likely to have a small hippocampus than those without such a history (OR 0.63; 95%CI 0.38-1.05). The OR of having a small hippocampus associated with 1 episode versus none was 0.74 (95%CI 0.41-1.33) and 2+ versus none 0.42 (95%CI 0.18-0.98) (p-trend 0.03). After an average of 6 years of follow-up, 34 subjects developed AD. Cox regression analyses with adjustment for the same covariates showed that subjects with a history of depression had an increased risk of AD (HR 2.42; 95%CI 1.15-5.10). The HR of AD associated with 1 episode versus none was 2.14 (95%CI 0.81-5.64), and 2+ versus none 2.54 (95%CI 0.90-7.16) (p-trend 0.04). **Conclusion:** This study suggests that elderly with a history of depressive episodes are less likely to have a small hippocampus, whereas prospectively they have an increased risk of AD. If replicated, future research should investigate what mechanisms may underly these seemingly contradictory associations.

P1-221 ASSOCIATION BETWEEN DEMENTIA AND CANCER

Ilaria Guidi, Daniela Galimberti, Andreea Dobreea, Barbara Corrà, Marco Tiriticco, Laura Perego, Ferruccio Bonino, Nereo Bresolin, Elio Scarpini, *University of Milan, Ospedale Maggiore, Milan, Italy. Contact e-mail: ilaguidi@libero.it*

Background: The relationship between cancer and dementia is still poorly understood. Recent studies showed that cancer survivors frequently experience short-term cognitive deficits, but it is unknown whether these deficits last or whether they worsen over time, as well as the cause of this association. **Objective(s):** To evaluate whether patients with a diagnosis of dementia have a higher frequency of malignant neoplasia in their clinical history, and if there is an association between cancer history and dementia subtype. **Methods:** Medical history of 470 consecutive subjects evaluated in our Centre for Cognitive Disturbances were retrospectively examined to determine how many of them were cancer survivors. 200 had Alzheimer's disease (AD), 89 Mild Cognitive Impairment (MCI), 49 Vascular Dementia (VaD), 25 tauopathies (21 Frontotemporal dementia, 3 Progressive Supranuclear Palsy, 1 Corticobasal Degeneration), 28 other dementias. 79 subjects had neither cognitive impairment nor other neurological diseases. Frequency of cancer in these different groups was compared by Chi-Square. **Results:** 59 out of 470 subjects were long-term survivors (cancer diagnosis from at least 5 years) and 6 were short-term survivors. A medical history of cancer were present in 12 healthy subjects (15.1%), 30 AD (15%), 7 MCI (7.8%), 7 VaD (14.2%), 6 patients with tauopathies (24%), 3 patients with other dementias (10.7%). No significant differences in the frequency of cancer was observed between healthy aged and demented people. However, a trend towards a higher percentage of cancer history in patients affected by tauopathy compared with other dementias was observed. Stratifying by type of neoplasia or age at cancer occurrence, no significant differences were observed. Notably, 6 MCI patients were short-term survivors. **Conclusions:** In our population, no significant association between dementia and cancer history was found. Nevertheless, the observed higher prevalence of cancer history in patients with tauopathies needs to be further studied in larger populations. The possible biological mechanism underlying this association could be linked to microtubule and cytoskeleton role in intracellular signaling, cell shape and replication. The higher prevalence of short-time survivors among MCI patients confirms the previous demonstration of a major risk of cognitive impairment in patients with cancer, possibly due to the therapy.

P1-222 APOE4 LIPOPROTEIN 4 REDUCES RISK OF DEMENTIA FROM HIGH SENSITIVITY C-REACTIVE PROTEIN

Mary N. Haan[1], Allison Aiello[1], William J. Jagust[2], [1]*University of Michigan, Ann Arbor, MI, USA;* [2]*University of California, Berkeley, CA, USA. Contact e-mail: mnhaan@umich.edu*

Background: Inconsistent evidence exists for an association of C-reactive protein (CRP) with dementia. ApoE lipoprotein genotype (4 allele) is associated with increased risk of dementias. Recent work suggests that CRP levels are lower in the presence of E4 allele. This analysis investigates whether E4 status modifies the association between c-reactive protein and incidence of dementia and cognitive impairment without dementia (D/CIND). **Methods:** The association of CRP to 4.5 year incidence of D/CIND was examined in a cohort of 1,789 Mexican Americans. Dementia and CIND (n=71) were ascertained by neuropsychological, clinical exams and expert adjudication. APOE, baseline CRP (mg/L) and fasting LDL values were available for 1,059 subjects; 63 were APOE4+. The associations between CRP and D/CIND incidence were tested in proportional hazards models with age at diagnosis as the time variable and including serial adjustment for APOE, LDL, baseline age, gender. Interaction terms for E4 with CRP and LDL were included. **Results:** CRP was significantly lower in those with an E4 allele (adjusted means: 1.82 vs. 3.12, p=0.005). CRP was significantly lower in demented cases with E4 compared to those without E4 (means: 0.64 vs 3.4, p=0.007). Presence of at least one APOE4 allele was associated with an increased risk of D/CIND (HR: 2.13, p=0.05) in a model with age and LDL. CRP was not associated with D/CIND risk in a model including APOE, LDL, age (HR: 1.03, p=0.76). Risk of D/CIND from CRP was lower in those E4+ than in those E4- (HR: E4+ 0.28: HR: E4-: 0.72, p = 0.04). Adjustment for LDL decreased the risk by 36%. **Conclusions:** In the presence of an E4 allele, higher CRP is protective for D/CIND; lower CRP increases risk. LDL adjustment indicates CRP may act in this association by lipid pathways. These results have implications for therapies in AD that affect CRP levels such as estrogens and statins.

P1-223 ACTIVE INSULIN DEGRADING ENZYME IN LIPID RAFTS: RELEVANCE FOR Aβ DEGRADATION IN THE BRAIN

Ayelen Bulloj[1,2], Maria Celeste Leal[1], Laura Morelli[1], Huaxi Xu[3], Eduardo Castaño[1], [1]*Fundacion Instituto Leloir, Buenos Aires, Argentina;* [2]*The Burnham Institue, La Jolla, CA, USA;* [3]*The Burnham Institute, La Jolla, CA, USA. Contact e-mail: abulloj@yahoo.com.ar*

Background: Newly generated amyloid β peptide (Aβ) is rapidly cleared from the brain and this process may be defective in Alzheimer's disease (AD). Insulin degrading enzyme (IDE) is a major brain protease capable of degrading Aβ but little is known about the sub-cellular compartment where IDE-Aβ interaction occurs. It has been proposed that Aβ generation and its oligomerization in AD takes place in membrane regions enriched in cholesterol and glycosphingolipids defined as *lipid-rafts.* We hypothesize that membrane -rather than cytosolic- IDE isoforms are critical in keeping the levels of soluble brain Aβ within a physiological range. **Objective(s):** 1. To investigate if proteolitically active IDE is associated with lipid rafts. 2. To study the interaction of this IDE isoform with Aβ. **Methods:** 1. Preparation of membrane homogenates from cells and brain, alkaline treatment and IDE detection by western blot. 2. Isolation of lipid rafts from N2a cells, rat and human brain by Triton X-100 treatment and sucrose gradient flotation. 3. Detection of IDE in lipid rafts of living cells by immunofluorescence (IF) using cholera toxin subunit B (CTB) and 1C1 anti-IDE monoclonal antibody. 4. Depletion of cellular cholesterol with methyl β-cyclodex-