and then induced expression for 2 months. This treatment dramatically reduced the severity of phenotype. **Conclusions:** In sum, these data demonstrate that timing of transgene expression is an important influencing agent on phenotypic outcome in these mice and that there may be significant difference between timing of peak levels of transgene expression, even if variables such as background and promoter are controlled. Our results have implications for the assessment of neurodegenerative phenotypes in other TDP-43 models of disease.

ORAL SESSIONS: O4-08
EPIDEMIOLOGY AND PREVENTION: PREVENTION AND RISK

O4-08-01 IDEA DENSITY IN EARLY LIFE IS ASSOCIATED WITH APOE-ε4 BUT AFFECTS THE RISK OF ALZHEIMER'S DISEASE INDEPENDENTLY

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Background: In the Nun Study, low idea density (ID), a measure of the semantic content of writing samples from early adult life, strongly predicted dementia and Alzheimer pathology in late life (JAMA 1996). Recently, in persons at risk for familial AD, ID was reported to be associated with APOE genotype, but not with FAD mutations (Dementia Geriatr Cognitive Disorders, 2011). We used Nun Study data to examine the association of APOE genotype with ID and to assess whether ID has an effect on dementia and Alzheimer pathology independent of APOE-ε4. **Methods:** Idea density was measured by experts blinded to clinical and pathological status from autobiographical essays written by 226 Catholic sisters at a mean age of 22 in the early 20th century. The association of APOE-ε4 status with the lowest tertile of ID (vs. the upper two tertiles) was assessed by logistic regression adjusted for grammatical complexity, age and educational status at the time of writing. Possible mediation by ID of the effect of APOE-ε4 on dementia and neuropathologic AD at autopsy was evaluated by adding ID to a model predicting these outcomes from APOE-ε4. All models were adjusted for grammatical complexity of the essay, attained education, age and educational status at the time of writing, and age at final examination or death. **Results:** Individuals in the lowest tertile for ID were 2.2 times more likely to carry an ε4 allele [95%CI:1.1-4.5]. APOE-ε4 was associated with both dementia [OR=2.7,95%CI:1.4-5.4] and neuropathologic AD [OR=13.5,95%CI:3.9-47.1]. Addition of ID to these models had little effect on these associations [dementia: OR=2.2,95%CI: 1.1-4.6; neuropathologic AD: OR=11.4,95%CI:3.2-39.8]. In addition, ID had a significant independent association with dementia [OR =5.0,95%CI:2.5-10.1] and neuropathologic AD [OR=3.4,95% CI:1.3-8.6] in the same models. **Conclusions:** Individuals carrying an e4 allele were more likely to have low idea density at an average age of 22. However, low idea density was associated with an increased risk of dementia and neuropathologic AD independent of APOE genotype. Idea density in early adult life is a strong predictor of dementia and neuropathologic AD and may be related to cognitive reserve as well as to genes associated with AD expression including APOE.

O4-08-02 ELEMENTARY EDUCATION PROTECTS AGAINST DEMENTIA: A CLINICOPATHOLOGICAL STUDY

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Background: Previous studies have shown that high levels of education protect against dementia and Alzheimer's disease (AD) related pathology. Evidence of the effects of elementary education against AD and other non-AD neuropathologic lesions is lacking. We conducted a clinicopathological study to determine whether elementary education could contribute to cognitive reserve and modify the prevalence of dementia independent of neuropathologic findings. **Methods:** In this case-control study, 571 individuals, ≥50 years of age from the Brain Bank of the Brazilian Aging Brain Study Group were included. Subjects were classified as normal cognition if: CDR=0 and IQCODE<3.41 (n = 335) and demented when presented CDR ≥1 and IQCODE≥3.41 (n = 236) through a post mortem evaluation. Neuropathologic examinations were performed using immunohistochemistry. Multivariate logistic regression models were conducted to assess if the association between dementia and years of education was independent of sociodemographics and neuropathologic lesions. Years of education were categorized into three levels (unschooled, which was taken as the reference group, 1-4 years of formal education and > 4 years of education). **Results:** Individuals who received formal education had lower prevalence of dementia when compared to the individuals with no formal education (N=112) after adjustment for sociodemographics, history of stroke and neuropathologic features including neuritic plaques, neurofibrillary tangles, lacunar infarctions, small vessel disease, and Lewy bodies (1-4 years: OR=0.55, 95%CI 0.32-0.97; > 4 years: OR=0.28, 95%CI 0.12-0.61; $P = 0.001$). **Conclusions:** A few years of education contributes to cognitive reserve and is associated with lower prevalence of dementia, independently of sociodemographics and neuropathologic lesions.

O4-08-03 HOW CAN ELDERLY APOE-ε4 CARRIERS REMAIN FREE FROM DEMENTIA?

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Background: Although APOE-ε4 allele is a well-established genetic risk factor for Alzheimer's disease (AD), not all APOE-ε4 carriers develop dementia. We sought to identify factors that may counteract the increased risk of dementia due to the ε4 allele. **Methods:** A cognitively intact cohort (n = 932, age ≥75 years) was followed for 9 years to detect incident dementia cases diagnosed according to international criteria. At baseline, information on education, participation in leisure activities, and vascular risk factors (e.g., blood pressure, heart disease, stroke, and diabetes) was collected through structured interview and clinical examinations. APOE allelic status was determined using a standard procedure. Data were analyzed using Cox proportional hazard models. **Results:** During the follow-up, 324 subjects developed dementia, including 247 AD cases. The hazard ratio (HR, 95% confidence interval) of dementia related to any APOE-ε4 was 1.39 (1.11-1.76), while the risk was diminished when ε4 carriers had high education or no vascular risk, or were physically, mentally and socially active. Among the ε4 carriers, the multi-adjusted HRs of high education, high level of leisure activities, and absence of any vascular risk factor were 0.59 (0.40-0.87), 0.49 (0.29-0.85), and 0.61 (0.41-0.90) for dementia, respectively. These three factors postponed dementia onset by more than 1.2 years. **Conclusions:** High education, active leisure activities, or maintenance of vascular health may counteract the risk of dementia due to the APOE-ε4 allele, and postpone the dementia onset in a way that ε4- and non ε4-carriers have similar dementia-free survival time.

O4-08-04 COFFEE CONSUMPTION AND THE RISK OF DEMENTIA IN THE OLDEST-OLD: THE MONZINO 80-PLUS STUDY

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Background: Coffee is a widely popular beverage worldwide. Recent findings have suggested that its consumption could have neuroprotective effects, but very few prospective studies have investigated the relationship between coffee consumption and dementia and no data are available in the oldest-old. Objectives: To investigate the association of long-term