causing mutation identified to date). *LRRK2* may be involved in the pathogenesis of several disorders since autopsy results of mutation carriers revealed diverse brain pathologies including pathology resembling Alzheimer Disease (AD). The domain structure of the *LRRK2* protein suggests a wide variety of functions that could be responsible for the pleomorphic brain neuropathology of mutation carriers. Intriguingly *LRRK2* is mapped to a chromosome 12 locus, linked to late-onset familial AD and thus *LRRK2* represents a good positional and functional gene candidate for AD. **Objective(s):** To elucidate the genetic contribution of *LRRK2* in a Canadian PD dataset and to conduct association studies to test the hypothesis that four common coding *LRRK2* polymorphisms might be associated with increased susceptibility to AD. **Methods:** We are using our DNA microarray system to perform a complete mutational survey of *LRRK2* in a PD dataset consisting of 72 probands of families with PD. The genotypes for four common *LRRK2* single nucleotide polymorphisms were obtained in three independent late-onset AD datasets: North American sporadic case-control set (243 AD cases and 252 normal controls); and two expanded groups of AD families (124 North European and 118 Caribbean Hispanic pedigrees). **Results:** For the AD association studies we selected four coding variations, located in three different functional *LRRK2* domains (LRR, Ras, WD40): L953L (rs7966550)-14kb-H1398R (rs7133914)-11kb-G1624G (rs1427263)-45kb-T2397M (rs3761863). The results of the microarray screen for mutations in PD and the association studies in AD are currently under analysis and will be presented.

P3-172 GENE-INFECTION INTERACTION AND RISK OF DEMENTIA

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Background: Several studies have suggested that latent infections, such as cytomegalovirus (CMV), may be causally associated with diseases that have an inflammatory component, including dementia and cardiovascular disease. Genotype APOE lipoprotein allele 4, in particular, may increase vulnerability to infection with several pathogens. **Objective:** This study examines whether presence of APOE4 modifies the association between CMV incident dementia and cognitive decline. **Methods:** Baseline serum samples from an ongoing cohort of 1,204 Mexican Americans aged 60+ were analyzed for APOE and IgG antibody levels to CMV. Over a 4 year period, participants were annually screened for global cognition using the modified mini mental state exam (3MSE) and were diagnosed for incidence of dementia or cognitive impairment with no dementia (CIND). The association between CMV and dementia or CIND incidence was examined in proportional hazards (PH) models with age at diagnosis as the time variable. Effects of CMV on repeated measures of the 3MSE were assessed using a linear mixed model. All models included control for gender, age, and education. Effect modification by E4 of the association between CMV and incident dementia/CIND was assessed with a multiplicative interaction term added to the PH model. **Results:** Mean CMV IgG antibody values (optical density units) varied by APOE (mean E2/2=6.04; E2/3=4.77; E2/4=6.17; E3/3=4.97; E3/4=5.37; E4/4 =5.27). CMV antibodies were significantly higher among those with at least one E4 allele (means: 5.47 vs. 4.95, p=0.02) even after controlling for age, gender, and education. Higher levels of CMV were not associated with dementia/CIND incidence (HR=1.18, 95%CI: 0.78-1.77) but were significantly associated with decline in 3MSE scores over four years (slope= -0.013, p=0.001). The rate of dementia/CIND associated with CMV was 4 times higher among those with at least one E4 allele compared to those E4 negative (HR E4+: 4.05, p=0.22 vs HR E4-: 1.12, p=0.59), but was not statistically significant. **Conclusions:** CMV antibody levels are not associated with a statistically significant increased rate of dementia/CIND diagnosis, but higher CMV antibody levels are associated with decline in 3MSE scores over four years. Moreover, apoE4 genotype appears to modify the relationship between CMV and dementia/CIND incidence.

P3-173 APOLIPOPROTEIN E FREQUENCY IN POSTERIOR CORTICAL ATROPHY AND TYPICAL ALZHEIMER'S DISEASE

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Background: Typical Alzheimer's disease (AD) is characterized by early episodic memory loss, whereas Posterior Cortical Atrophy (PCA) is characterized by visual agnosias, with a relative sparing of episodic memory early in the disease course. The majority of cases of PCA share pathological features with those of typical AD. A well defined risk factor of typical AD is the presence of the apolipoprotein E (APOE) 4 allele. **Objective(s):** To compare the APOE 4 allele frequency in typical AD and PCA. **Methods:** We conducted a case control study in which the APOE status was determined on 22 patients who fulfilled clinical criteria for PCA, were longitudinally assessed in our Alzheimer's Disease Research Centre and had stored DNA. These patients were matched for age at onset and sex to 37 cases of typical AD diagnosed by the NINCDS-ADRDA criteria, and 38 controls. The APOE4 allele frequency was compared using a chi-square test. Furthermore, the PCA cases were stratified by age at onset > 60 to access for possible interaction. **Results:** There was no difference in years of education, or disease severity based on the MMSE, between the cases with PCA and typical AD. The mean age at onset was 60 years in both groups. The APOE4 allele frequency was 29.5% for PCA, 47.0% for typical AD, and 7.9% for controls. There was no difference in APOE 4 allele frequency between the cases of PCA and typical AD (p=0.47), or between PCA and controls (p=0.12). However, there was a difference between typical AD cases and normal controls (p =0.004). There was no difference when the PCA cases were stratified by age at onset > 60. **Conclusions:** We did not find any evidence for a difference in the APOE 4 allele frequency between PCA and typical AD.

P3-174 THE REGIONAL DISTRIBUTION AND MAGNITUDE OF THE PATHOLOGY IN ALZHEIMER DISEASE CORRELATE WITH THE REGIONAL PATTERN AND INTENSITY OF THE AMINERGIC INNERVATION OF THE FOREBRAIN

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Background: A fundamental, yet unexplained feature in Alzheimer disease (AD) is the selective vulnerability ("pathoklisis"). The allocortex including limbic nuclei, the neocortical association areas, the truncothalamic nuclei, the upper raphe nuclei and the locus ceruleus belong to the most severely affected brain regions. Conversely, the cerebellar cortex and its deep nuclei, the thalamic relay nuclei, many brainstem nuclei, as well as the cranial and spinal motor nuclei show little, if any, pathology. **Objective(s):** The aim of the present investigation was to examine semiquantitatively on the basis of data from the literature whether the magnitude of the ascending neuroaminergic innervation and receptor distribution might correlate with the regionally distinct distribution and severity of the pathology in the AD brain. Four aminergic systems with ascending projections, the cholinergic, serotoninergic, noradrenergic, and histaminergic systems, known to sustain severe pathology themselves in AD, were included in the evaluation. **Methods:** Neuroamine transmitter (NAT) levels and the expression of NAT receptors were evaluated for 235 CNS regions and nuclei semiquantitatively from data provided by more than 350 original papers, monographs and book articles. In order to standardize the very heterogeneously, i.e., both numerically or alpha-numerically, documented data values for pooling, a five category evaluation score was used. Categorization was accomplished by "numerical coding of semantics": Seman-