frontal pcorrected = 0.06, temporal pcorrected = 0.04, occipital pcorrected = 0.03). PDMCI showed significantly larger bilateral temporal and occipital, and left frontal horn radial distance relative to PDCN (left: frontal pcorrected = 0.01, temporal pcorrected = 0.01, occipital pcorrected = 0.0004; right: temporal pcorrected = 0.005, occipital pcorrected = 0.03). Between the two PDMCI subtypes nonamnestic PDMCI subjects showed more significant and pronounced (up to 30%, p < 0.01) ventricular enlargement spanning all parts of the lateral ventricle while amnestic PDMCI subjects showed ventricular changes localized to the left occipital horn (up to 20%, p = 0.03).

Conclusions: We found subtle but significant hippocampal changes in PDCN and nonamnestic PDMCI as well as extensive enlargement of the lateral ventricles in both PDCN and PDMCI. Hippocampal atrophy and lateral ventricular enlargement show promise as sensitive biomarkers for tracking PD and PDD progression.

P1-050 PROTEASE-SENSITIVE PRIONOPATHY IN A COGNITIVELY NORMAL 93-YEAR-OLD
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Background: Protease-sensitive prionopathy (PSPr) is a recently described novel prion disease biochemically characterized by abnormal prion protein (PrP) sensitive to proteases resulting in a distinct profile on Western blot. Clinically, cases reported to date have presented with behavioral and psychiatric difficulties with an average age of onset of 62 and with a mean disease duration of 20 months. Most PSPr-affected subjects are homozygous for valine at codon 129 (VV) and have no mutation in the PrP gene.

Methods: The individual was clinically examined between 1996-2002, including semi-structured interviews, Clinical Dementia Rating (CDR) and Mini-Mental State Exam (MMSE) assessments, and retrospective postmortem dementia interview of surviving family. After death, the brain was examined and processed using standard neuropathologic methods and tau, beta amyloid, and PrP immunostaining. DNA was extracted from frozen brain tissue for sequence analysis. Frozen brain tissue was also used for Western blot analyses. Results: This individual was cognitively intact during her initial assessment (CDR 0; MMSE 30) at age 87 and remained cognitively unchanged until her death at age 93 (CDR 0). As a result, no ancillary studies were conducted including EEG, CSF, and imaging. Furthermore, no neurologic abnormalities associated with prion disease were observed. At autopsy, unfixed brain weight was 1180 grams and noted to have mild frontal atrophy; however, the basal ganglia and cerebellum were unremarkable. Neuronal loss, gliosis, and spongiform change were evident in the deeper cortical layers but were absent in the cerebellum. There was weak PrP immunostaining in the cortex and none in the cerebellum. DNA sequence analysis ruled out the presence of a pathogenic mutation in the coding region of the PrP gene and determined the codon 129 genotype as homozygous for methionine (MM). Western blot analysis confirmed the diagnosis of PSPr.

Conclusions: To our knowledge, this is the first description of PSPr in a case lacking clinically detectable dementia and advanced age at the time of death. This case report adds to the growing pathological spectrum of prion diseases. Support: P50 AG005681, P01 AG003991 (NG, NJC, JCM); The Patrick Yobs Gerstmann-Straussler-Scheinker Grant (GP); P01 AG014359, CDC UR8/CCU515004 and the Charles S. Britton Fund (PG)

P1-051 DIETARY FAT AND CHOLESTEROL CAUSES NEURONAL ENDOSONAL ABNORMALITIES AND BASAL FOREBRAIN CHOLINERGIC NEURODEGENERATION IN WILD-TYPE MICE
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Background: Cholesterol and metabolic syndrome are risk factors for Alzheimer’s disease pathobiology. Neuronal endocytic defects have been observed at early stages of Alzheimer’s disease and Down syndrome (DS), and can be modulated by cholesterol levels. Methods: Wild-type mice were fed a high fat/cholesterol diet for 4 weeks starting at 8 months of age. We have characterized and quantitated neuronal early endosomes and basal forebrain cholinergic neurons (BFCN) after dietary treatment. In order to evaluate the effect of high fat/cholesterol on nerve growth factor (NGF) retrograde transport to the medial septal nucleus, 125I-NGF was injected into the hippocampus, and its delivery to the medial septal nucleus was measured. Results: Rab5 immunolabeling detected altered early endosome morphology in pyramidal neurons of the cingulate cortex revealing that dietary high fat/cholesterol in wild-type mice leads to an increased number of large endosomes per neuron (n = 4.5 ± 0.67) when compared to those in mice fed a basal diet (n = 1.7 ± 0.35; p = 0.001). A similar endosomal phenotype is observed in a DS mouse model, the Ts(Rb12.1716)2CJc, as has been reported for the related Ts65Dn DS mouse model. Dystrophic neurites and reduced density of BFCNs, a neurodegenerative phenotype that is known to result from endosomal pathology in Ts65Dn mice, were detected by choline acetyltransferase immunolabeling after 4 weeks of dietary high fat/cholesterol. Preliminary findings indicate defective retrograde transport of NGF, with only ~20% as much NGF transported to the basal forebrain 20 hours after injection into the hippocampus in mice on high fat/cholesterol diet. Gene dosage of amyloid precursor protein affects endosome morphology. Accordingly, we have examined the transgenic mouse that over expresses the human London V717I mutation of amyloid precursor protein, and determined that it also has neuronal endosomal alterations, as well as BFCN degeneration. Conclusions: Dietary hyperlipidemia intake alone is sufficient to lead to endosomal pathology and basal forebrain cholinergic neurodegeneration in the brains of wild-type mice through deficits in signaling endosome-mediated NGF trophic support.

P1-052 ALCOHOL-RELATED DEMENTIA: A COMMON DIAGNOSIS IN YOUNGER PERSONS
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Background: Young (or early) onset dementia is defined as dementia with onset before age 65. Alcohol related dementia typically has an early age of onset and often falls within this category. Little is known about the prevalence and service delivery for alcohol related dementia and disagreement often exists as to whether persons with this diagnosis should be managed within dementia services. Methods: The prevalence and diagnostic subtypes of young onset dementia were studied in the Eastern Sydney Area of Australia, which has a total population of 130,000 persons aged 30-64. A case-finding survey and hospital records search, with capture-recapture methodology, were used. In order to be included patients had to be resident within the area and alive as at 1st June 2008, have an onset of memory, behavioural and/or language symptoms before age 65 and have persistent cognitive impairment for at least 6 months. The dementia diagnosis for identified cases was verified through a medical case note review. Results: One hundred and thirty six young onset dementia patients were identified in the area. Alcohol related dementia was the most common primary diagnosis accounting for 22.1% of cases. Alcohol related dementia was a secondary diagnosis for a further 4% of cases and was usually comorbid with vascular dementia. The rate of alcohol related dementia was 18 per 100,000 population aged 30-64 at risk and the average age at onset was 52 years. This group were often isolated, had complex medical histories and had diverse health system access points. Conclusions: The rate of alcohol related dementia in this study is considerably higher than a previous 2003 UK study which reported a rate of 7 per 100,000 at risk. More research needs to be conducted to verify these