cytosolic calcium and activates the calcium/calmodulin-dependent phosphatase, calcineurin (CaN). A ctivated CaN relieves inhibition of protein phosphatase 1 (PP1), which in turn activates GSK3β; thus, we investigated whether CaN mediates A β O-induced transport disruption independently of tau. **Methods:** We treated hippocampal neurons from wild-type and tau knockout mice with A βOs and subsequently inhibited CaN with FK506. DCV transport was assessed by live cell imaging of fluorescently-tagged brain-derived neurotrophic factor (BDNF-mRFP). Microtubule stability was verified by semi-quantitative immunocytochemistry. To detect changes in CaN activity and assess their impact on PP1 signaling, we employed an in vitro phosphatase assay and immunoblot analyses of CaN fragmentation and inhibitor-1 (I1), a CaN substrate that enables PP1 activation when dephosphorylated. **Results:** Inhibition of CaN activity reversed A β O-induced transport defects in wild-type and tau knockout neurons. Induction and rescue of transport defects were unaccompanied by changes in post-translational tubulin modifications that confer or indicate stability. CaN activity and I1 dephosphorylation were elevated by A β Os, reduced by FK506 alone, and normalized in the presence of both agents. No changes in calpain-mediated truncation of CaN were detected, indicating that CaN is activated primarily through non-excitotoxic calcium signaling in our studies. **Conclusions:** A β Os impair BDNF transport independently of tau by activating CaN. Our findings suggest a novel role for calcium signaling in transport regulation and challenge a requirement for tau in AβO-induced transport disruption and toxicity.

P4-291 STRUCTURAL STUDIES OF ALZHEIMER'S DISEASE AMYLOID PRECURSOR PROTEIN

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Background: Alzheimer's disease (AD) has been closely linked to the plaque-forming, neurotoxic peptide β-amyloid (Aβ). Aβ is derived from amyloid precursor protein (APP) through regulated-intramembrane proteolysis. APP is not only implicated in AD pathogenesis but also in important cellular processes. The Type-I transmembrane protein has a large soluble extracelluar fragment known as sAPP, which is responsible for many of the proposed functions of APP. Understanding the structure and function of sAPP would provide a leap forward in understanding the function of full-length APP. Information inferred from the structure will also assist the development of novel therapeutic strategies to target AD. **Methods:** Recombinant expression constructs of sAPP have been cloned and successfully expressed. Purified sAPP has been put into extensive crystallisation trials. Several promising crystallisation conditions have been identified. Preliminary biophysical characterisation has been undertaken using a variety of approaches including size-exclusion chromatography, dynamic light scattering, small-angle X-ray scattering and mass spectrometry. **Results:** Results demonstrate that sAPP is elongated in shape. The majority of the protein forms a dimer in solution at pH 8.0, which breaks down to monomer at pH 6.5 or below. Dimerisation of sAPP at low pH can also be induced by adding divalent metal ions such as Zn(II) and Cu(II). APP dimerisation has been linked to Aβ overproduction. **Conclusions:** Our results and subsequent experiments to determine the structures of sAPP in its dimeric and monomeric forms will contribute to understanding the mechanism of dimerisation and APP signalling. This information may help guide rational inhibitor design of A β overproduction which in turn may slow down or halt AD progression.

P4-292 CARDIOVASCULAR RISK FACTORS AND FRONTOTEMPORAL DEMENTIA (FTD)

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Background: Cardiovascular risk factors (CRF) were widely described as related to dementia. Previous reports examined this issue in patients with vascular cognitive impairment, Alzheimer's disease and Lewy body dementia. There are lacking studies regarding this association in FTD.AIMS Compare the frequency of CRF in our population with FTD and controls. **Methods:** 100 consecutive subjects with FTD diagnosis according to Lund-Manchester clinical criteria and 200 controls matched by age and sex were included between January 2003 to February 2007 at the Cognitive and Behavior Center of Hospital Italiano de Buenos Aires.Clinical evaluation, laboratory tests, brain images (CT / MRI) and neuropsychological -neuropsychiatric assessment were performed. Multiple regression analysis was performed to analyze the differences in CRF between FTD patients and controls. **Results:** Mean age in FTD was 69.7 $\pm$ 0.9 vs. 70.1 $\pm$ 0.8 in controls (p 0.12). No difference in gender was observed between cases and controls. No differences were identified between patients and controls regarding hypertension (HTA) (65% vs 67,3% p 0,44); dyslipidemia (57% vs 54.7% p 0.74); obesity (39% vs 27,6% p 0,14) and hypothyroidism (26% vs 17,1% p 0.1). A significant difference was observed for Diabetes Mellitus (39% vs 22,6% p 0,001). **Conclusions:** In our FTD population, Diabetes Mellitus was associated as an independent risk factor compared with controls. To our knowledge this is the first study in which CRF were evaluated in FTD patients, prospective studies are needed to evaluate this association in larger populations.

P4-293 CARE: CAREGIVER LATIN AMERICAN STUDY

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Background: Caregivers play a key role in health care for individuals with Alzheimer's disease (AD). Managing medications contibutes to the workload associated with caring for AD patient. Transdermal patches offer advantages over conventional oral formulations. There is current no information about preferences of caregivers of AD people in relation to the mode of administration of medications in Latin America. **Methods:** This is a prospective, non interventional, multicenter, multinational, observational 16-week study. The primary objective was to compare AD patient's caregiver preference in relation to transdermic therapy versus oral therapy. Secondary objectives were to compare the experience, satisfaction and expectation of caregivers with the two therapies. An adapted version of the Alzheimer's Disease Caregiver Preference Questionnaires (ADCPQ) was used. Data were collected using an electronic Case Report Form. Statistical analysys was done using the SAS® software version. **Results:** The study included 653 caregivers from 7 countries from Latin America. At visit 2, 502 caregivers answered the ADCPQ. The percentage of caregivers who preferred the transdermic therapy in terms of ease of use is 94.4%; ease of adherence to treatment plan, 96.2% and in general 95.0%. Regarding to the three questions, caregiver preference for transdermic therapy is significantly greater than for the oral therapy at $p<0.001$. Oral and transdermic therapies are significantly different with respect to: a) caregiver experience on ease of use, in general or doing the AD patient to use the transdermic therapy (transdermic easier than oral $p<0.001$) b) the caregiver satisfaction with the therapy in general (greater satisfaction with transdermic $p<0.001$). The percentages of caregivers who evaluated as better than expected in terms of the ease of trandermic therapy use and the ease of adherence to transdermic therapy plan were 74.3% and 75.1% respectively. **Conclusions:** Over 90% of caregivers of AD patients in the study preferred the patch to capsules/tablets as a method of drug delivery for reasons including helping them follow the treatment schedule, overall ease of use and less interference with daily life. Understanding treatment-related preferences of caregivers and the reasons for those preferences may help to maximise intervention effectiveness.