kinases can be involved in producing AD-type neurofibrillary pathology. **Methods:** Abnormally hyperphosphorylated tau was isolated from AD brain cytosol (AD P-tau), and its ability to inhibit microtubule assembly and self-assembly into filaments was studied before and after dephosphorylation with protein phosphatase-2A (PP-2A), and after rephosphorylation by several combinations of tau kinases. **Results:** We found that dephosphorylation of AD P-tau by PP-2A converts it into a normal-like protein and on rephosphorylation by PKA, cdk5 and GSK-3β or cdk5 or cdk5 plus GSK-3β, converts it back into an AD-type pathological protein. Investigation of site-specific phosphorylation revealed that phosphorylation of tau at Thr231 and Ser262 plays a pivotal role in its conversion into AD-like pathological protein. **Conclusions:** More than one etiopathogenic mechanism might be involved in AD-type neurofibrillary degeneration, and inhibition of more than one tau kinase might be required to inhibit neurofibrillary degeneration.

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O2-01-07 INFLUENCE OF DOPAMINERGIC NEUROTRANSMISSION IN AD PATHOPHYSIOLOGY

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Background: Oxidative stress is a common pathophysiological feature in all neurodegenerative disorders. Elimination of specific causes of oxidative stress may contribute to preventing various forms of neurodegeneration. Dopamine exacerbates the formation of reactive oxygen species (ROS), rendering certain neurons vulnerable to oxidative stress. Although dopaminergic neurotransmission is clearly associated with pathophysiological mechanisms of Parkinson's disease, it has received scant attention with regard to AD. Interestingly, Parkinson's disease and AD patients often show common neuropathological features. This study examines whether dopaminergic neurotransmission is associated with specific pathophysiological features of AD. **Objectives:** This study addresses the following specific questions: 1. Is dopaminergic innervation prominent in entorhinal and limbic cortices (primary targets in AD) versus sensory neocortical areas (less vulnerable areas)? 2. Do ROS and/or dopamine promote the formation of oligomeric beta-amyloid? 3. Does elevated dopaminergic neurotransmission contribute to neuropathology in AD-transgenic mice? **Methods:** 1. Density of tyrosine hydroxylase (TH) innervation was compared throughout the forebrain of control and triple-AD transgenic mice by immunostaining. 2. Spontaneous oligomerization of synthetic beta-amyloid in the presence of hydroxyl radical with and without dopamine was examined by immunoblotting. 3. Neuropathology was assessed in control and triple-AD transgenic mice administered dopaminergic agonists and antagonists. **Results:** 1. Dopaminergic fiber density is significantly greater in entorhinal and amygdalar versus primary sensory cortices. In triple-AD mice, the earliest neuropathological markers colocalize with regions of highest TH-fiber density. 2. Hydroxyl radicals enhance oligomerization of beta-amyloid in vitro, and this effect is potentiated by dopamine. 3. Sinemet intensifies immunohistochemical labeling of neuropathological markers in triple-AD mice. **Conclusions:** Oligomeric beta-amyloid is a potent synaptotoxin that impairs normal mechanisms of synaptic plasticity: enhanced production in the limbic cortices may precipitate pathophysiological processes in these regions. Dopaminergic neurotransmission, an important modulator of synaptic plasticity in limbic and neocortical circuitry, may contribute to the formation of oligomeric beta-amyloid in vivo. These data suggest that specific forms of ROS-generation may be a primary trigger in AD-pathophysiology that act via effects on beta-amyloid oligomerization.

O2-01-08 COMPARING THE IMPACT OF A CONDENSED VS EXTENDED PROTOCOL FOR DISCLOSURE OF APOE TO RELATIVES OF PATIENTS WITH AD: THE REVEAL STUDY

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Background: We previously demonstrated that genetic susceptibility testing for AD can be safely carried out using an "Extended" protocol involving 3 in-person visits to a genetic counselor for education, personal counseling and risk assessment with APOE disclosure. **Objective:** In this study, we examined the feasibility and impact of disclosing genetic risk information with a shorter 2-visit "Condensed" protocol more suited to clinical application. **Methods:** Participants in the REVEAL Study were randomized into one of two study arms: Extended or Condensed. APOE genotype and risk estimates were disclosed in both arms, and outcome variables were measured at 6 weeks, 6 months and 1 year after disclosure. After receiving genetic risk information, scores were compared on validated measures of anxiety, depression, and distress, adjusting for demographic variables, APOE genotype and baseline scores on the outcome measures. **Results:** 272 participants (mean age = 58.0 years; 70% female; 19% African American), were randomized as above. At 6 weeks post-disclosure, mean test-related distress as measured by the Impact of Event Scale (IES) was significantly higher in the Condensed arm than the Extended arm (6.5 vs 2.8, $p = 0.005$). However, at 6 months and 12 months post-disclosure, no significant differences were observed between the Condensed and Extended arms in mean IES scores; and at all time points, no significant differences between the arms were observed on the Center for Epidemiological Studies Depression Scale or Beck Anxiety Inventory. **Conclusions:** Participants in the Condensed arm experienced higher scores on the Impact of Event scales shortly after risk disclosure, but these differences resolved by 6 months after disclosure. No significant difference was found in mood or anxiety scores between study arms at 6 weeks, 6 months or 12 months after disclosure.

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EARLY DETECTION AND DIAGNOSIS 3

O2-02-01 PATTERNS OF ATROPHY ON VOXEL BASED MORPHOMETRY DIFFER BETWEEN AMNESTIC MCI CONVERTERS AND NONCONVERTERS

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Background: Amnestic mild cognitive impairment (aMCI) represents the clinically evident prodromal phase of Alzheimer's disease (AD). While the majority of aMCI subjects progress to AD, a proportion remains relatively stable. Identifying characteristics that distinguish aMCI subjects who convert more vs. less rapidly is useful for clinical and disease characterization purposes. **Objective(s):** To compare patterns of grey matter loss in subjects with aMCI who convert to AD within a fixed time interval vs. those who do not convert. **Methods:** Thirty-seven aMCI subjects were identified that