lateralsclerosis (ALS) and from totemporal lobar degeneration (FTLD) with ubiquitin-positive inclusion bodies. Besides aggregation of TDP-43, ubiquitination, hyperphosphorylation, fragmentation and loss of nuclear localization was observed in diseases. However, it remains to be clarified whether TDP-43 aggregates are toxic or not, and how abnormality of TDP-43 mediates neuronal degeneration. **Methods:** We show here that the cells with TDP-43 inclusions suppressed cell-growth, using BrdU up-take analysis. And morphological relationship between TDP-43 inclusion and several transcription factors were detected in immunocytochemical analysis. **Results:** We report here that cell-growth is strongly suppressed in the cells with TDP-43 inclusions compared to the cells without inclusions. In these cells, RNA polymerase II and several transcription factors are co-localized with TDP-43 aggregates. Furthermore, accumulation of RNA polymerase II with phosphorylated TDP-43 inclusions was detected in FTLD brains. These results suggested that abnormal TDP-43 inclusions cause growth arrest in SH-SY5Y cells by recruiting general transcription factors and leading to toxicity or cellular dysfunction. **Conclusions:** In TDP-43 proteinopathy, transcriptional dysregulation may also contribute to neuronal degeneration.

P1-025 WHAT CAN HOMING PIGEONS TELL US ABOUT NAVIGATIONAL IMPAIRMENTS IN ALZHEIMER'S PATIENTS?

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Background: In humans, deficits in olfactory discrimination are generally associated with several forms of dementia and are among the first clinical signs of Alzheimer disease (AD). The link between olfactory dysfunction and AD is interesting in the present context because roughly half of patients in the earliest stages of AD and patients at risk for AD, exhibit a specific navigational impairment associated with loss of ability to discriminate radial optic flow cues, which in turn are necessary for precise determination of heading direction and therefore for correct integration of the path. In pigeons, large body of experiments has shown that olfactory deprivation causes decreases in the accuracy of homing orientation and/or homing success **Methods:** Here, we addressed the effect of olfactory deprivation on the correct integration of the displaced path in young homing pigeons. Young homing pigeons are known to preferentially use a path integration strategy to find their way home. During the outward journey to the release site, a control group was exposed to natural odors, a no odor group was exposed to synthetic bottled air (that contain no odors), and a novel odors group was exposed to synthetic bottled air with a fixed sequence of artificial odors. **Results:** Consistent with findings from other researchers, our young birds, deprived of olfactory information during displacement were disoriented. In contrast, birds exposed to natural odors, or to artificial/novel odors that contained no spatial information, were homeward oriented. **Conclusions:** These findings show that olfactory input activates non-olfactory path integration systems and, in the absence of olfactory stimulation, cues normally used by young pigeons for path integration, failed to produce homeward orientation. Similarly we suggest that loss of olfactory activation of path integrations systems could explain the navigational impairment in the early stages of Alzheimer disease patients. The striking parallel between the failure of young pigeons to utilize non-olfactory path integration cues when deprived of olfactory stimulation, and the occurrence of deficits in olfactory discrimination, radial optic flow discrimination, and navigational ability in early AD, suggests the diminished navigational ability in AD patients may be a direct result of the loss of olfactory activation.

P1-026 EFFECT OF VARIOUS COGNITIVE ENHANCERS IN ACQUISITION TASK OF RADIAL MAZE

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Background: Cholinesterase inhibitors like donepezil along with NMDA antagonist memantine are the current approved therapies for Alzheimer's disease. It has been reported that not all of them are efficacious in all the rodent models of learning and memory. In the current study we investigated the effects of above mentioned drugs in rodent model of learning using the radial arm maze. **Methods:** Rats of 180-230g were habituated for 2 days in the radial arm maze. The rats, which were placed on restricted diet had to learn to solve the radial maze. The food cup in each arm was baited only once prior to the start of the experiment. Re-entry into an arm or entry followed by exit of the arm without eating the food pellet was considered as an error. The experiment was carried out over a period of 4 days. All the rats were challenged with scopolamine. The choice accuracy as well as total error was calculated. **Results:** It was observed that donepezil did not have any significant effect on choice accuracy and total error, while tacrine and rivastigmine was found to significantly improve acquisition in the radial arm maze by a significant increase in the choice accuracy and decrease in the total error. Memantine was found to be devoid of activity and was unable to reverse deficit induce by a scopolamine challenge. **Conclusions:** From the current study it can be concluded that not all the currently approved drugs for Alzheimer's disease is useful in acquisition or learning in rodent models. While donepezil, which is, currently prescribed for mild to moderate AD did not show any effect in acquisition, tacrine and rivastigmine did show an effect. Memantine is likely to improve cognition in pathological condition involving glutaminergic dysregulation. However cholinesterase inhibitors are likely to show an effect in retention, which is likely to be evident in a clinical set up.

P1-027 ANALYSIS OF IPS CELL MODELS OF ALZHEIMER'S DISEASE

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Background: Our goal is to generate accurate neuronal models of Alzheimer's and Parkinson's disease for the analysis of disease mechanism and for therapeutic development. No available gene-modified animal models fully recapitulate disease pathology. Furthermore, neuronal models of sporadic disease are limited by the difficulties in obtaining patient neurons. Our goal is to generate accurate neuronal models of Alzheimer's and Parkinson's disease for the analysis of disease mechanism and for therapeutic development. No available gene-modified animal models fully recapitulate disease pathology. Furthermore, neuronal models of 'sporadic' disease are limited by the difficulties in obtaining patient neurons. **Methods:** We are developing iPS cell-based models of Alzheimer's and Parkinson's. Briefly, patient-derived skin cells are transduced with a cocktail of reprogramming factor genes using lentiviral vectors, as developed by Yamanakaand colleagues. Additional lines are derived from healthy age-matched controls. **Results:** We have succeeded in generating iPS cell models of familial and sporadic forms of Alzheimer's disease. These lines have been validated using a number of standard criteria, and neurons can be generated by differentiation protocols. **Conclusions:** The generation of patient-derived iPS cells, and their differentiation into neurons, may allow for the analysis of cellular and molecular phenotypes relevant to the disease. Furthermore, the method may allow for the investigation of questions such as the role of genetic and epigenetic factors in 'sporadic' disease.

P1-028 GAMMA—SECRETASE MODULATORS DO NOT SHOW A POTENCY SHIFT IN HIGH EXPRESSING MODEL SYSTEMS

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Background: Modulation of gamma secretase activity is a promising therapeutic approach for the treatment of Alzheimer's disease. Modulation of the enzyme reduces the production of the amyloidogenic Aß42peptide while sparing the production of other Aß species. Recent progress in the identification of small molecule modulators of gamma secretase (GSMs) provides tools for comparing the pharmacology of gamma modulation in both cellular and animal model systems. **Methods:** Data presented here compare the potency and pharmacology of diverse structural classes of GSMs when dosed to cells overexpressing human amyloid precursor protein (APP), a human neuroglioma cell line (H4), transgenic mice overexpressing human APP (Tg2576) and wild type mice. Effects on Aß38,40 and 42 were assayed