released throughout life, in a similar amount to cortisol, until release decreases with age and is possibly associated with neurodegenerative diseases. The anti-inflammatory effects of DHEA make it a potential therapeutic agent for use in cytotoxic environments. The current study examines the effect of DHEA by comparing the levels of hyperphosphorylated tau in the absence and presence of DHEA. **Methods:** E18 rat hippocampal astrocytes were isolated and plated with DMEM (4.5 mg/ml D-glucose) + 10% fetal bovine serum. At 85% confluency, cells were trypsinized with 0.25% EDTA and re-plated in media which contained low concentration of D-glucose (1.35 mg/ml) to create stress. After incubation at 24 and 48 hours with DHEA (2mg/ml) and 30 minutes with 50 mM potassium chloride, an ELISA kit quantitatively measured levels of hyperphosphorylated tau via immunofluorescence. A Cell Counting Kit-8 (CCK-8) was used to determine cell viability by adding 10% volume per well of CCK-8 reagent. The plate was incubated at 37°C for one hour and absorbance read at 450nm. **Results:** CCK-8 showed high levels of glucose (4.5 mg/ml) produced greater cell viability than the stress condition (glucose at 1.35 mg/ml). ELISA immunofluorescence detected increased levels of hyperphosphorylated tau in conditions with low glucose. Exposure to DHEA decreased fluorescence readings in the tau ELISA (read at 450 nm). **Conclusions:** In the stress condition, exposure to DHEA was associated with decreased immunofluorescence due to hyperphosphorylated tau protein. In the experimental condition of increased stress induced via glucose manipulation in growth media, DHEA may have a cytoprotective role in these rat hippocampal astrocyte cells.

P3-188 UBIQUILIN-2 REGULATION OF TAU AND α-SYNUCLEIN IN NEURODEGENERATIVE DISEASE

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Background: A failure in protein homeostasis is a common factor in the most prevalent age-related neurodegenerative diseases associated with protein aggregation. The protein, ubiquilin-2 (UBQLN2), helps ensure protein homeostasis by shuttling ubiquitinated substrates to the proteasome for degradation and by modulating autophagy. UBQLN2 is implicated indirectly in various dementing disorders, including tauopathies and synucleinopathies, due to its accumulation in neuropathological deposits. More recently, UBQLN2 has been directly connected as a cause of frontotemporal dementia when mutated, and our laboratory has linked the toxicity of UBQLN2 to its aggregation. **Methods:** To evaluate whether UBQLN2 regulates tau and α-synuclein expression, aggregation or clearance, we co-expressed tau or α-synuclein with UBQLN2 in human embryonic kidney-293 cells and assessed levels of monomeric and oligomeric tau or α-synuclein. The specificity of UBQLN2 in lowering levels of tau and α-synuclein was compared to that of UBQLN1, a highly homologous protein that lacks a robust correlation to disease. The ability of these two ubiquilins to regulate other common aggregate-prone disease proteins, including TDP43 and Huntingtin, was also evaluated. To determine whether changes to UBQLN2 occur in the disease setting, brain tissue from human disease, as well as from mice overexpressing tau and α-synuclein, was analyzed for UBQLN2 levels. **Results:** Co-expressed UBQLN2 markedly lowered levels of monomeric α-synuclein and both monomeric and oligomeric tau. Conversely, siRNA knockdown of UBQLN2 significantly elevated levels of α-synuclein and tau monomer and oligomers. In contrast, UBQLN1 did not exhibit the same ability to decrease tau and α-synuclein levels. Likewise, UBQLN2 selectively had an effect on levels of TDP43 and Huntingtin. The possibility that UBQLN2 also undergoes alterations in disease was evidenced by the fact that more UBQLN2 was insoluble in human disease brain and in transgenic mouse models of synucleinopathy and tauopathy than in healthy/non-transgenic controls. **Conclusions:** Our findings highlight a new role for UBQLN2—but not UBQLN1—in managing levels of tau and α-synuclein and other important neurodegenerative disease proteins. However, lowered levels of soluble UBQLN2 in disease brain suggest that UBQLN2 may be dysfunctional in synucleinopathies and tauopathies, due to its intrinsic aggregation or accumulation in disease aggregates.

P3-189 EVALUATING TAU EXPRESSION IN THE RETINA OF TRIPLE REPEAT TAU MICE UNDERPERFORMING IN VISUAL-SPATIAL TEST

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Background: Symptoms of visual impairment usually precede cognitive symptoms in patients with dementia such as Alzheimer's disease (AD). Thinning of the retinal fiber layer along with deposits of amyloid beta and hyper-phosphorylated tau, pathological hallmarks of AD, in the retina of AD patients suggest impairment may occur at the level of the retina. However, it is unclear how either amyloid beta or tau affects retinal function. Abnormal levels of phosphorylated tau and decrease of total tau have been observed in the inner plexiform layer (IPL) in the retinas of glaucoma patients, suggesting that dysregulation of tau expression may play a role in visual impairment. **Methods:** To understand the role of tau overexpression in the visual pathway, we utilized a transgenic mouse line overexpressing three-repeat tau (3R tau) at different ages: 3 months, 6 months, 9 months and 12 months. Visual-spatial learning was measured in both 3R tau and non-transgenic littermates by performance in the visual probe trial of the Morris Water Maze. Histological analysis of the outer nuclear layer of the retina and expression of 3RTau was assessed through immunohistochemistry. **Results:** 3R tau mice at 6 months of age took longer to locate the platform in the visual probe trial of the Morris Water Maze compared to non-transgenic mice. There were no differences in outer nuclear layer (ONL) thickness between wildtype and transgenic mice, suggesting 3R tau overexpression does not induce photoreceptor degeneration. However, 3R tau expression in the retina was observed through immunohistochemical analysis as early as 3 months, mainly in the ganglion cell layer (GCL) and the IPL. **Conclusions:** Expression of 3R tau precedes visual impairment in 3R tau mice. Although no retinal thinning is observed, it is possible that early 3R tau expression may alter vision processing at the level of the IPL. The IPL is a stratified structure that houses synapses of the multiple retinal cell types responsible for processing vision. Further investigation into tau expression the IPL may provide further insight into the molecular mechanism of visual impairment and retinal pathology in tauopathies.