levels of myoinositol (mIns/tCr, P=0.0241), glutathione (GSH/H2O, P=0.0231) and lactate (Lac/tCr, P=0.0442) in CNP vs. saline treated 3xTg-AD mice. Dendritic integrity was increased in dentate gyrus (DG) (P=0.0312) and synaptogenesis was significantly higher in the CA1 (P=0.0141), CA3 (P=0.0152) and DG (P=0.0073) in CNP vs. saline treated mice. Hippocampal-based memory acquisition (P=0.029) and novel object recognition (P=0.0073) significantly improved in CNP vs. saline treated 3xTg-AD mice.

Conclusions: CNPs delivered BDNF to the hippocampus, reversed glial hyperactivity and oxidative stress, enhanced synaptogenesis and dendritic integrity and improved memory in 3xTg-AD mice. Hence, clathrin provides a highly efficient nanoplatform for delivery of BDNF to the brain. This nanotechnology may be able to enhance neuronal regeneration/plasticity and restore brain functions better than existing treatments for neurodegenerative disorders.

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Keywords: BDNF-Clathrin Nanoparticles, Alzheimer's Disease Therapy, Magnetic Resonance Spectroscopy

Co-Morbid Asthma and Depression as Risk Factors for Neurodegeneration

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Background: Asthma is an inflammatory disease of the airways that is frequently co-morbid with mood disorders. Both peripheral inflammation and depression are associated with neuroinflammation and when chronic, neuroinflammation can lead to neurodegeneration. Diffusion weighted imaging (DWI) provides a non-invasive method to investigate white matter microstructure, and its utility as a biomarker of neurodegeneration has been validated in animal models. Using DWI, we examined whether subjects with asthma display changes in white matter microstructure and whether these changes covary with depressive symptoms.

Methods: DWI data were acquired in 111 participants with asthma and 135 age-matched controls. Multiple DWI modalities were analyzed using Permutation Analysis of Linear Models (PALM), controlling for age, sex, and motion. A composite asthma severity score was created using Principal Component Analysis and the Beck Depression Inventory assessed depressive symptoms.

Results: Asthma subjects reported greater depressive symptoms than the non-asthma sample ($p < .0001$). Depressive symptoms correlated with poor asthma control ($p < .01$). Widespread deterioration in white matter microstructure was found in those with asthma compared to controls. Specifically, both asthma severity and depressive symptoms were associated with altered white matter in several tracts, including the anterior thalamic radiation and long association fibers (all p's$< .05$ corrected).

Conclusions: Our data suggest that neurodegeneration, independent of normal aging, occurs in asthma and is more pronounced with greater asthma severity and symptoms of depression. Although the mechanisms linking asthma, depression, and white matter deterioration remain unknown, our data suggest that efforts to achieve asthma and depression control may be neuroprotective.

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Keywords: Depression, Asthma, Diffusion-Weighted Imaging, Neurodegeneration

Cocaine Receptor Identified as BASP1

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Background: Cocaine exerts its behavioral actions mainly through inhibition of dopamine reuptake. However, cocaine is a weak and non-selective inhibitor of the monoamine transporters. In addition, many dopamine reuptake inhibitors do not produce psychotropic effects in drug-experienced volunteers. On the other hand, previous evidence indicates more potent effects of cocaine. For example, low nanomolar cocaine regulates dopamine D2 receptor signaling. In planarians, low nanomolar levels of cocaine produces environmental place conditioning. These signaling and behavioral actions of cocaine could not be mediated through the inhibition of monoamine transporters. Furthermore, previous a study describes 16 nM cocaine binding in rat striatal synaptosomes suggesting the existence of a high-affinity receptor for cocaine. However, the identity of such receptor is unknown.

Methods: Using affinity pull-down, mass spectrometry, subcellular fractionation, ligand binding assays, stereotaxic brain surgery, genetic, and behavioral approaches, we identify a putative high-affinity receptor for cocaine.

Results: Using anti-cocaine immunoprecipitation followed by mass spectrometry, we identified the nerve terminal enriched brain acid soluble protein 1 (BASP1) as a cocaine-binding protein. Our ligand binding assays indicate that BASP1 binds potently to cocaine (Kd: 7 nM). Depletion of striatal BASP1 by 50% results in 50% reduction in [3H]cocaine binding to striatal synaptosomes. Using 11 mice/group and One-Way-ANOVA analysis, injecting a retrograde transduction capable AAV in mice nucleus accumbens (NAc) to deplete BASP1 inhibits the locomotor stimulant effect of cocaine.

Conclusions: Our findings suggest that BASP1 is a high-affinity receptor for cocaine. BASP1 may be a fruitful target for designing agents to modify the behavioral effects of cocaine.

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Keywords: Cocaine, Locomotor Activity, Receptor Binding

Cognitive Ability and MRI-Predicted Age Gap in Healthy Individuals From a Large Epidemiological Sample

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