dsRed-synaptobrevin fusion protein with NMUR2 on synaptic inputs into the medial prefrontal cortex. Following quantification of pre- and post- treatment events using the InScopix data acquisition software, total events during the pre- and post-treatment time periods were calculated. In these studies, both animals demonstrated a clear increase in calcium transient activity between pre- and post- treatment evaluations, suggesting that NMU administration increases the neuronal activity of neurons in the prefrontal cortex. DISCUSSION/SIGNIFICANCE: This research provides a new site of action for the known therapeutic effects of NMU. We demonstrate the presence of presynaptic NMUR2 in the mPFC and show that systemic administration of NMU increases mPFC neuronal activity. This illustrates NMU may act as a top-down mediator for substance use disorders and binge eating behaviors.

409

Diffusion MRI to investigate atypical corticospinal tract microstructure and motor impairments in hemiplegic cerebral palsy

Alexandra Hruby[1], Divya Joshi[1], Julius PA Dewald[1] and Carson Ingo[1]
[1]Northwestern University

OBJECTIVES/GOALS: Hemiplegic cerebral palsy (HCP) limits the functional ability of one side of the body, but motor impairments are very heterogeneous among children with this diagnosis. The purpose of this study was to evaluate the CST using DTI and tractography analyses as it relates to quantitative measures of the severity of weakness and mirror movements in HCP. METHODS/STUDY POPULATION: Preliminary results include five participants with HCP (2M, 16Â±7.8 years) and six controls (2M, 12Â±3.5 years). DTI data were collected using a spin-echo echo-planar imaging sequence with diffusion weighting of b=1000 s/mm2 in 60 different directions and 8 scans without diffusion weighting (b=0 s/mm2). Images were processed with steps of brain extraction, denoising, motion and eddy current correction, and fit with tensors to generate maps of diffusivity metrics. Anatomical landmarks were used to guide probabilistic tractography of the CST for analyses in both the lesioned and non-lesioned hemispheres. To quantify grasp weakness and mirroring severity, participants completed a bilateral assessment of grip strength using handheld force measurement devices and custom MATLAB data acquisition software. RESULTS/ANTICIPATED RESULTS: DTI is a feasible method to evaluate CST microstructure in HCP and typically developing pediatric participants. Spearman correlation analyses, using age and sex as covariates, revealed that for the lesioned hemisphere CST, there were significant positive correlations between grasp weakness severity and mean diffusivity (MD) (Ï =0.66, p=0.038) and between grasp weakness severity and axial diffusivity (AD) (Ï =0.68, p=0.030). There was not a significant correlation between grasp weakness severity and fractional anisotropy (FA) (Ï =-0.47, p=0.166). For the non-lesioned hemisphere CST, there was a significant positive correlation between mirroring severity and radial diffusivity (RD) (Ï =0.70, p=0.023). There was not a significant correlation between mirror movement severity and FA (Ï =-0.41, p=0.2361). DISCUSSION/SIGNIFICANCE: The correlations demonstrated here show a potential relationship between CST microstructure and the severity of hand impairments in HCP. While these relationships between CST diffusivity properties and hand function are preliminary, they provide the first steps to better understand underlying neural mechanisms for motor impairments in HCP.

410

Mild Maternal Undernutrition Results in a Premature Neonatal Leptin Surge and Resistance in Male Offspring to a High Fat Diet†

Tiffany K. Miles[1], Melody L. Allensworth[1], Ana Rita Silva Moreira[1], Angela K. Odle[1], Anessa Haney[1], Alexandra Lagasse[1], Angus M. MacNicol[1] and Gwen V. Childs[1]
[1]University of Arkansas for Medical Sciences

OBJECTIVES/GOALS: Maternal undernutrition, a form of malnutrition, can alter neonatal leptin signaling and result in metabolic dysfunction in adulthood. We developed a mild undernutrition model to relate more to societys nutritional challenges and to test the hypothesis that a shift in the neonatal leptin surge would result in sex-specific metabolic changes. METHODS/STUDY POPULATION: We studied pups from undernourished dams which were calorically restricted by 20% (CR20) from embryonic day 15 until postnatal day (PND) 21. We tested 216 offspring from 11 Fed dams and 13 undernourished dams (CR20), detecting a leptin surge in control fed progeny at PND11. At 3 months of age, offspring from 3 dams per maternal nutrient status were either exposed to a 45% high fat diet (HFD) or control diet (10% fat) for 16 weeks. Anterior pituitary hormones were analyzed in the pituitary and serum of neonates and adults. To determine the mechanism of the phenotype observed in male adult offspring on the HFD, single cell RNA sequencing was used to analyze the pituitary, fat and liver. RESULTS/ANTICIPATED RESULTS: Offspring of CR20 dams had an early leptin surge peaking at PND8 and GH levels at PND1 were higher in CR20 progeny. Weights of both male and female CR20 offspring were lower and body lengths were shorter than controls. As adults, Fed mice from both sexes had increased weight gain with HFD. However, although CR20 females gained weight on the HFD, male progeny from CR20 dams did not gain weight on the HFD and appeared protected from impact. We found sex-specific changes in pituitary Gh, Ghrhr, and Ghsr mRNA levels. Single cell RNA sequencing of pituitary, fat and liver of male offspring showed significant regulation of transcripts in fat of male offspring from Fed dams that was not found in CR20 males when compared to control fed mice. DISCUSSION/SIGNIFICANCE: Mild undernutrition causes a prematurely high leptin surge and sex-specific growth responses to a HFD, including resistance to a HFD in underfed males. Transcript analysis in fat of males resistant to HFD induced obesity may reveal mechanisms that provide protection against HFD induced weight gain.

411

Essential role for the neurodevelopmental disorder-linked gene, MEF2C, in inhibitory neuron function and neurotypical behaviors*

Yongjoo (Jennifer) Cho[1], Ahlem Assali[2], Evgeny Tsvetkov[2] and Christopher W. Cowan[2]
[1]Medical University of South Carolina, [2]Medical University of South Carolina Department of Neuroscience, Charleston, SC

OBJECTIVES/GOALS: The MEF2 family of transcription factors regulate gene expression controlling cell differentiation and synapse development. Mutations or deletions in the MEF2C gene cause a neurodevelopmental disorder that includes symptoms of autism spectrum disorder. In this study, we aim to study the role of MEF2C in GABAergic populations using an animal model. METHODS/

https://doi.org/10.1017/cts.2022.236 Published online by Cambridge University Press