WHAT'S NEW IN ATLANTA NEUROSCIENCE
THURSDAY 11/03/2022
6–8PM
Hosted by ACSfN

ENJOY LIGHT BITES AND DRINKS WHILE PREVIEWING THE BEST OF ATLANTA NEUROSCIENCE!

Located at The Hatchery in Emory Point
1578 Avenue Place
Suite 200
Atlanta Georgia 30329

Free 3hr parking available across the street (validation required at check-in)

SNOWBALL, Emory University
Sensory processing and behavioral flexibility in Drosophila

Chris Rodgers, Emory University
Learning by doing: distributed neural circuitry for perception and action

Alberto Stolfi, Georgia Tech
Tunicates: our closest invertebrate relatives

Shawn Dotson, Georgia State University
Exploring mechanisms of alimentary chemosensation and modulation

Jennifer Larimore, Agnes Scott College
Characterizing the effects of SCN1A mutations on CACNA1C expression

An Zhou, Morehouse School of Medicine
Epigenetic reprogramming of cortical neurons in response to brain ischemia

& POSTER PREVIEW SESSIONS!

REGISTER AND SUBMIT ABSTRACTS WITH EVENTBRITE

For accommodations and questions please email amabb@gsu.edu
Thank you to our donors!

This event was organized by the Atlanta Chapter of SfN. Learn more about us at https://acsfn.cbn.gsu.edu/

Our volunteers included: Angela Mabb, Kristen Frenzel, Jill Ward, Jennifer Walcott, Hannah Sturgeon, Erin Lottes, Tana Pottorf, Yahia Ali, and Claudia Espinosa among others!

Individual Donors:
Jessica Bolton
Nancy Forger
Angela Mabb
Kristen Frenzel

Enjoyed this event? You can continue to donate to ACSfN using the eventbrite for this event via this QR code!

Thank you to the Hatchery for opening up their space for this event!
Location and Parking Information

What's New '22 will take place in The Hatchery at Emory Point.

Address:
1578 Avenue Place
Suite 200
Atlanta Georgia 30329

Free 3hr parking is available across the street. Please bring your parking garage ticket to check-in for validation.
6:00 pm  Welcome by ACSfN President
Kristen Frenzel, PhD (Emory)

6:05 pm  Lightning Talks
Anita Devineni, PhD (Emory)
Chris Rodgers, PhD (Emory)
Alberto Stolfi, PhD (Georgia Tech)

6:30 pm  Poster session I and faculty group I breakout sessions

7:05 pm  Lightning Talks
Shawn Dotson, PhD (GSU)
Jennifer Larimore, PhD (Agnes Scott)
An Zhou, PhD (Morehouse)

7:30 pm  Poster session II and faculty group II breakout sessions
**Poster Session I: Molecular subtopic**

**Christine Bowen, Emory University: Kv1.3 potassium channels exhibit domain specific protein interactions in activated microglia**

**Introduction:**
Alzheimer’s Disease (AD) is characterized by progressive Aβ pathology and neuroinflammation. Disease-activated microglia in the brain, with potential contributions from peripheral T cells, promote neuroinflammation in AD. The Kv1.3 potassium channel is highly expressed on proinflammatory microglia and memory T cells. Blockade of Kv1.3 reduces Aβ pathology and decreases the proinflammatory phenotype of microglia. The molecular mechanisms regulated by Kv1.3 channels remain unexamined. Identifying proteins that interact with N and C terminal cytosolic domains of Kv1.3 channels will evaluate Kv1.3-regulated mechanisms and pathways.

**Methods:**
We utilized TurboID, a biotin ligase that biotinylates proteins within a 10nm proximity, fused to Kv1.3 and validated Kv1.3-TurboID fusion constructs in HEK Cells. We created three constructs, where TurboID was fused to the N terminus, C terminus, and a truncated Kv1.3, where the PDZ-binding domain is removed. We transduced these constructs into BV2 cells, a murine microglial cell line, and Jurkat T-cells, a human T-cell line, to determine potential immune interactors with Kv1.3. BV-2 and Jurkat T-cell stable cell lines were created and confirmed via qPCR and electrophysiology. Western blot and Flow cytometry confirm TurboID biotinylates proteins. Mass spectrometry (MS) of biotinylated proteins was performed to identify proteins within proximity to Kv1.3.

**Results:**
BV2 biotinylated proteomes identified by MS revealed distinct N terminal and C terminal Kv1.3 interactors. Many Kv1.3 interactors overlap between the N and C terminus in the presence or absence of LPS inflammatory stimulation. The N terminus interacts with translation (e.g. Rpl10 and Eef1a1), plasma membrane proteins (e.g. Calr1 and Psma1), and mitochondrial tracking proteins (e.g. Tmm23), while the C terminus interacts with immune response proteins (e.g. Cd68, Tlr2, and Csf1). With the removal of the C terminal PDZ-binding domain, we observed reduced immune response and inflammatory proteins (e.g. Tmem106b, Larp1, and Gbp2) interacting with Kv1.3.

**Conclusions:**
Immune interactors with Kv1.3 likely depend on the C terminal PDZ domain while the primary function of the N terminus is protein processing and transport to the plasma membrane. Overall, this data identifies strong candidates for potential interactors with Kv1.3 and provides insight on how Kv1.3 influences microglial and leukocyte immune function in AD.

**Erin Lottes, Georgia State University: CCT and the TORC1 pathway function to shape dendritic arbors**

**Developing neurons rely on three major forms of proteostatic regulation – protein synthesis, maintenance, and degradation – to grow and maintain a dendritic arbor. In Drosophila melanogaster, larval multidendritic (md) neurons develop to form a variety of arbor shapes, ranging from simple class I (CI) to complex class IV (CIV) neurons, each dependent on carefully balanced proteostatic processes. One such process is protein maintenance, which is carried out by chaperones that ensure proper conformation of other proteins. While chaperones are particularly important to maintaining neurons, they have been understudied in dendrites. Chaperonin-containing tailless complex polyepptide-1 (CCT) is an ATP-dependent chaperonin comprised of eight subunits which together form a double-ringed complex. CCT is thought to fold anywhere from 1-15% of the cellular proteome. Two of its most notable clients are actin and tubulin – major cytoskeletal components essential to the development and maintenance of dendritic arbors. Using live confocal imaging of larval md neurons, we have found that knockdown of CCT results in significant decreases in arbor complexity in CIV neurons, appearing at approximately 72 hours after egg lay. Two-channel live imaging of CCT loss-of-function (LOF) CIV neurons has revealed an underlying significant reduction in MTs, but not in Factin. Though stability of MTs is compromised, polarity of MTs is unchanged in CCT LOF conditions.

CCT has recently been shown to fold components of the TOR (Target of Rapamycin) complex 1 (TORC1). TORC1 regulates S6 kinase, and we have found that S6K LOF and overexpression results in CIV dendritic arbor complexity reduction and enhancement, respectively. Preliminary studies of Cul1 (Cul1), a component of the SCF E3 ubiquitin ligase, reveal that Cul1 LOF results in dendritic hypertrophy and increase in phosphorylated S6K signaling, opposite to the hypotrophy and decrease in phosphorylated S6K seen in CCT LOF. Cul1 has been previously linked to negative regulation of TORC1 through inhibition of Akt. Altogether, our work suggests CCT operates as a part of a regulatory network spanning protein synthesis, maintenance, and degradation that collectively cooperate to regulate dendritic growth and elaboration.

**Ruth Nelson, Emory University: Assessing the effect of systemic inflammation on the astrocyte proteome using in vivo proximity labeling**

**Background:**
Astrocytes are critical to the CNS during homeostasis and neurodegenerative disease as they perform a myriad of functions including maintenance of the blood brain barrier and aiding microglia in mediating the inflammatory response. Emerging in-vivo proteomic labeling approaches using proximity labeling provide exciting opportunities to resolve proteomic signatures of glia using mass spectrometry (MS)-based approaches, overcoming several limitations of isolation-based and transcriptomics strategies. The objective of this study is to apply a novel method called cell type-specific in-vivo biotinylation of proteins (CIBOP) to label and characterize the proteomes of astrocytes under homeostatic states and in response to systemic inflammatory challenge.

**Methods:**
CIBOP employs a Cre-lox transgenic approach to selectively express biotin ligase TurboID in astrocytes via the Aldh111 promoter. Mice heterozygous for Aldh111-Cre-ert2 and Rosa26TurboID (astro-CIBOP), and controls (Cre-only), received Tamoxifen injections followed by 3 weeks of recombinant and biotin supplementation for additional 2 weeks. Half the cohort received daily lipopolysaccharide (LPS) injections (intra-peritoneal, 10mg/dose/animal x 5d) during the first week of biotinylation to induce a robust neuroinflammatory response. Astrocyte-derived biotinylated proteins were enriched from whole-brain homogenates by streptavidin bead affinity-capture for MS. Immunofluorescence microscopy (IF) and biochemical studies were performed to confirm astrocyte-specific proteomic biotinylation and CSF was collected for detect astrocyte-derived CSF biomarkers.

**Results:**
Western blot analysis confirmed robust biotinylation of the cellular proteome of astro-CIBOP mice under homeostatic and neuroinflammatory conditions compared to their respective controls. IF confirmed that biotin signal (using streptavidin) colocalizes with astrocytic markers (GFap and Ndrg2) with preferential labeling of astrocyte cytoskeleton. Further, to validate labeling data that the astro-CIBOP technique was exclusively biotinylating astrocytic proteins we confirmed the lack of colocalization of biotin signal with microglia (Iba1) and neurons (Map2). CSF from astro-CIBOP mice, but not control mice, also revealed biotinylated CSF proteins. MS studies of biotinylaed proteins in the brain and CSF are underway.

**Conclusions:**
We validate the CIBOP approach to label the proteome of astrocytes in their native state, under homeostatic and neuroinflammatory conditions, and demonstrate labeling of astrocyte-derived CSF proteins. Our ongoing MS studies will identify astrocyte specific proteomic changes driven by systemic LPS and lay the groundwork for application of CIBOP in neurodegenerative disease contexts.
Sydney Sunna, Emory University: Comparative proteomics of LPS-induced inflammation in different brain cell types captured by TurboID proximity labeling

Chronic neuroinflammation is central to the etiology of neurodegenerative disease, but there is currently a critical gap in our understanding of how inflammatory challenges impact distinct cellular proteomes. Proximity biotin ligase TurboID, coupled with Lipopolysaccharide (LPS) challenge and mass spectrometry, can purify distinct cellular proteomes from adult mice undergoing inflammatory challenges. Proximity biotin ligase TurboID, coupled with Lipopolysaccharide (LPS) challenge and mass spectrometry, can purify distinct cellular proteomes from adult mice undergoing inflammatory challenges. To test the hypothesis first, we generated BV2 and N2A cell lines stably expressing TurboID containing a nuclear export sequence. We treated cells with 1μg/mL LPS and 200μM biotin for 48 hours and generated whole cell lysates (inputs) and streptavidin affinity-purification (AP) fractions (n=4/group) for label free quantitative MS (LFQ-MS). In vitro, TurboID biotinylated 60-65% of the entire proteome identified by LFQ-MS, with 1,754 proteins significantly enriched in the BV2 AP proteome and 2,011 proteins in the N2A AP proteome. Principal component analysis of the AP proteomes revealed that effect of LPS was driven by differentially expressed proteins by LPS treatment (LPS DEPs) were identified in both BV2 AP (>500 proteins) and N2A AP (>100 proteins) samples. K-means clustering of BV2 AP proteomes revealed 5 clusters of proteins, with cluster 1 (C1) representing LPS-purified proteomic changes shared between AP and input proteomes, and cluster 3 (C3) representing down-regulated changes in response to LPS. Gene set enrichment analysis showed C1 proteins correlating with peroxisome, phagosome, cytokine secretion and amoebiasis, and cluster 3 proteins interacting with cell cycle, protein interaction network analysis of N2A LPS DEPs identified clusters of proteins involved with protoxosomal machinery identified by local network clustering. Next to investigate the effects of systemic LPS on neuronal proteomes, we have successfully directed TurboID to CamKIIa and PV interneurons in adult mice undergoing LPS challenge (i.p. inj. x4 days) and pharmacological ablation of microglia with PLX3397 chow (290 ppm, 5 wks.). Our quantitative imaging and immunoblotting results validate the efficacy of microglial ablation in WT mice (n=10, ~50% by ibal count), and confirm robust biotinylation of proteins in CamKIIa-Cre/TurboID+/+ mice. Our in vitro studies confirm that TurboID biotinylation of proteins can capture unique biological responses of neurons and microglia to inflammatory challenge.

Meghan Vogt, Georgia State University: Perigestational morphine exposure disrupts postnatal cell proliferation in the hippocampus of male and female rats

Every nineteen minutes, a baby is born addicted to opioids. Nationally, the rate of neonatal opioid withdrawal syndrome (NOWS) has quadrupled in the last decade. Preliminary evidence suggests that children born with NOWS have exposure to opioids for many years, often without anesthesia or analgesia. Preclinical and clinical studies have shown that neonatal pain disrupts normal CNS development in adult male and female rats. Male and female rats were exposed to a short-term inflammatory insult induced by intraplantar administration of 1% carrageenan on the day of birth (P0). In addition to the inflammatory insult, we also performed an extensive proteomic analysis of microglial cell proliferation. We found that male and female rats have different responses to this insult, with male rats showing a decrease in microglial proliferation compared to female rats. These findings highlight the need to perform the correct control experiments when using these genetic tools.

Dina Yakout, Georgia State University: Role for Arc turnover in Tauopathies

Tauopathies are a diverse group of neurodegenerative disorders characterized by the deposition of aggregates of the microtubule associated protein tau (MAPT) in the brain, which is the main component of neurofibrillary tangles (NFTs). Alzheimer’s disease (AD) is the most common tauopathy. Understanding tau’s physiological role in the cell is key to the development of effective therapeutic strategies for tauopathies. Tau’s most well-known function in neurons is stabilizing microtubules. However, recent findings suggest that tau is localized to postsynaptic sites. Here, we find that WT-Tau but not P301L-Tau causes a reduction in Arc protein. This reduction requires the proteasome and the B2 region of the Tau MTBD. Surprisingly, Tau-dependent Arc degradation was not associated with Arc ubiquitination, lysosomal degradation, phosphorylation or acetylation. However, Tau-dependent degradation did depend on the endophilin binding domain of Arc. WT-Tau degradation of Arc was also found to selectively occur in hippocampal dendrites. Importantly, overexpression of WT-Tau led to abnormal targeting of synaptic GluA-1 containing AMPARs to the soma in hippocampal neurons. Our findings highlight a unique role of WT-Tau in spatially regulating Arc removal, with hints of Tau microtubule binding and Arc endocytic targeting in regulating synaptic function.

Bhoomi Desai, Georgia State University: Effects of constitutive Cx3cr1-Cre expression on microglial density and morphology in the developing mouse brain

Cx3cr1-Cre transgenic mice express Cre recombinase under the direction of the constitutive expression of the microtubule associated tau (MAPT) in the brain, which is the main component of neurofibrillary tangles (NFTs). Alzheimer’s disease (AD) is the most common tauopathy. Understanding tau’s physiological role in the cell is key to the development of effective therapeutic strategies for tauopathies. Tau’s most well-known function in neurons is stabilizing microtubules. However, recent findings suggest that tau is localized to postsynaptic sites. Here, we find that WT-Tau but not P301L-Tau causes a reduction in Arc protein. This reduction requires the proteasome and the B2 region of the Tau MTBD. Surprisingly, Tau-dependent Arc degradation was not associated with Arc ubiquitination, lysosomal degradation, phosphorylation or acetylation. However, Tau-dependent degradation did depend on the endophilin binding domain of Arc. WT-Tau degradation of Arc was also found to selectively occur in hippocampal dendrites. Importantly, overexpression of WT-Tau led to abnormal targeting of synaptic GluA-1 containing AMPARs to the soma in hippocampal neurons. Our findings highlight a unique role of WT-Tau in spatially regulating Arc removal, with hints of Tau microtubule binding and Arc endocytic targeting in regulating synaptic function.

Morgan Gomez, Georgia State University: Early life pain alters the response to an immune challenge in adult male and female rats

Premature infants are more likely to be admitted to the Neonatal Intensive Care Unit (NICU) where they experience upwards of 10-18 painful procedures each day, often without anesthesia or analgesia. Preclinical and clinical studies have shown that neonatal pain disrupts normal CNS development in multiple ways that persist into adulthood. The present study explores the effects of neonatal pain on the response to an immune challenge in adulthood. Male and female rats were exposed to a short-term inflammatory insult caused by intraplantar administration of 1% carrageenan on the day of birth (P0). In adulthood (P60-P90), Thermocron iButtons were implanted to monitor core body temperature; 14 days later, lipopolysaccharide (LPS) was injected to elicit an immune response. Rats were sacrificed at one of 3 time points post-LPS: 24 hours, group peak time at 3 hours, and 24 hours. Brain tissue was analyzed via immunohistochemistry for VGAT, VGLUT, Fos and prostaglandin receptor 3 within the hypothalamic median preoptic area (MnPO). A whole brain scan of Fos activation patterns was also conducted. LPS administration resulted in a significantly greater febrile response in males and females exposed to early life pain compared to controls. Immunohistochemical analysis revealed sex and treatment differences in cellular activation in several brain regions, but no differences in receptor expression in the MnPO. Together, these studies are consistent with clinical studies reporting children experiencing unresolved pain during the perinatal period show an increased severity of sickness behavior and altered immune signaling following exposure to a pathogen, and will provide a foundation for future studies examining the biological underpinnings.

Hannah Harder, Georgia State University: Long-term immune consequences of perigestational opioid exposure

Neonatal opioid withdrawal syndrome (NOWS) rates have quadrupled in the last decade. Preliminary evidence suggests that children born with NOWS have an increased risk of infection in childhood; however, confounding factors, including comorbid drug use, make identification of underlying mechanisms challenging.
Although animal models of perigestational opioid exposure (POE) can help resolve these difficulties, current animal models often utilize steady-state truncated dosing paradigms that fail to recapitulate the intermittent and prolonged use typical of human opioid users. Our lab has developed a novel clinically-relevant model of POE utilizing surgically-implanted minipumps to provide intermittent morphine exposure before, during, and after pregnancy, allowing pups to be indirectly exposed to morphine throughout gestation and immediately following parturition. To assess the impact of POE on fever, adult male and female POE rats are given an immune challenge with lipopolysaccharide (LPS), and eight hours later, fever responses, sickness behavior, and cytokine release are measured. Compared to controls, morphine-exposed males and females showed an increased fever response to LPS and altered peripheral cytokine levels, suggesting immunomodulation. This novel rodent model provides an opportunity to study long-term immune deficits in a tractable way to investigate potential treatments to ameliorate immune dysregulation noted in NOWS infants.

Yumnia Wang, Emory University: Wide-field Voltage Imaging of Fast Cortical Dynamics during Locomotion and Reaching in Mice

Population imaging of wide-field activities has shed light on the cortical dynamics and functional networks of motor control. To date, the majority of wide-field imaging studies utilize calcium indicators. The relatively slow kinetics of calcium sensors has left the investigation of fast cortex-wide dynamics at the time scale of limb kinematics an uncharted area. In order to better understand cortical activities of motor control with higher temporal resolution, we performed wide-field voltage imaging at 200 Hz with a novel genetically encoded voltage sensor, JEDI-1P. First, we demonstrated that JEDI-1P reliably follows responses of air-puff stimulation of up to 60 Hz in somatosensory cortex. Given that this finding establishes fast-frequency following of JEDI-1P in vivo, we then investigated the effect of either vevo imaging with a wheel left forelimb reach. In both cases, we observed a global decrease in high-frequency power during sensory stimulation. For the wheel running task, animals showed an increase in beta band activity during reward consumption as they stopped running. During the reaching task, imaging data showed rich and fast temporal signals in the caudal forelimb area orchestrating this reaching task. Pending detailed analyses of this rich dataset on fast cortical dynamics with voltage imaging is expected to provide further insights on how sensorimotor information is processed for modulating locomotion and controlling dexterous movement.

Cognitive Subtopic

Dieter Jaeger, Emory University: Layer specific cortical processing of thalamic input in a cued left/right lick motor task in mice

Previous studies have established causally impactful participation of a thalamo-cortical loop involving anterolateral motor cortex (ALM) and ventromedial thalamus (VM) in the execution of lick decision making tasks with a delay period in mice. In our current studies we are expanding our knowledge of how this task is performed in mouse cortex through 1) retrograde anatomical tracing, 2) manipulating dendritic dynamics in ALM through optogenetic manipulations, 3) 2-photon (2p) imaging and 4) wide-field cortical voltage imaging. Retrograde tracing shows a rich and distinct connectivity for different layers in ALM, with both VM and MD thalamic input projecting to layer 1. A particular interest in understanding VM input to layer 1 (L1) in ALM depends on the relative balance between direct activation of apical tufts of pyramidal cell dendrites and L1 inhibitory interneurons. Since previous work has specifically implicated GABA-B receptors in the suppression of apical dendritic calcium spikes we used the GABA-B blocker Baclofen applied locally to the surface of ALM during lick decision task execution to study the behavioral relevance of this mechanism. We found that this GABA-B block leads to an increased error rate of the mouse licking at the wrong side, which appears in a clustered manner, indicating perseveration. Dendritic activity imaged with Gcamph showed a side-specific ramping prior to lick execution, indicating dendritic involvement in the task. Overall, a picture begins to emerge that apical dendritic processing is critical for the processing of VM input to ALM in cued lick decision making in mice. To determine cortical network integration in this task we used the novel genetically expressed voltage sensor JEDI for brain-wide imaging. We find that lick task processing is widely distributed across many cortical areas. Activity occurred in distinct spatial and temporal patterns, with sensory responses mixed with ramp components prior to lick initiation. These results indicate cortex-wide participation in task processing.

Computational Subtopic

Nathanael Cruzado, Georgia Institute of Technology: Bridging model and experiment with CLEO: a testbed for in-silico prototyping of complex neuroscience experiments

Recent advances in neuroscience methods enable exciting new kinds of experiments. One of these is closed-loop optogenetic control, which combines simultaneous photostimulation and electrode recording to precisely control mesoscale neural activity on the order of milliseconds. Experiments such as these often require significant effort and resources to implement, which can slow development, limit opportunities to optimize experimental parameters, and pose a barrier to adoption. A potential solution is simulating an experiment—creating an in-silico prototype or proof-of-concept—which can demonstrate feasibility or reveal promising experiment designs for a fraction of the cost. Moreover, a virtual experiment with inputs and outputs resembling data collected in the lab allows for the realism of a spiking neural network model to be more directly evaluated. However, a convenient tool does not exist integrating optogenetics, electrode recording, and flexible closed-loop processing with neural population simulations. Thus, we have developed and now present Closed Loop, Electrophysiology, and Optogenetics Simulator (CLEO)—a Python package built around the Brian 2 simulator enabling closed-loop processing in a virtual environment. CLEOSim includes devices for spiking neural networks and enables retrograde anatomical tracing as well as a reaching task cued for either vevo imaging with a wheel left forelimb reach. In both tasks, we observe a global decrease in high-frequency power during sensory stimulation. For the wheel running task, animals showed an increase in beta band activity during reward consumption as they stopped running. During the reaching task, imaging data showed rich and fast temporal signals in the caudal forelimb area orchestrating this reaching task. Pending detailed analyses of this rich dataset on fast cortical dynamics with voltage imaging is expected to provide further insights on how sensorimotor information is processed for modulating locomotion and controlling dexterous movement.

Mykhailo Fomenko, Georgia State University: Dynamics of a high spike-frequency bursting in a Central Pattern Generator

Life-supporting motor functions like heartbeating in invertebrates and breathing in vertebrates require an indefatigable generation of a robust rhythm by oscillatory circuits, Central Pattern Generators (CPGs). CPGs are adjusted by neuromodulation to meet environmental challenges. Leech heartbeating is controlled by a CPG based on two pairs of mutually inhibiting interneurons (HNs) forming half-center oscillators (HN-HCO).

Neuromodulation in vertebrates includes Na+/K+ pump current, IP3, neurotransmitters, and neuromodulatory factors such as glycine, GABA, and 5-HT. Neurons in the superior colliculus and inferior colliculus have both an excitatory and an inhibitory input, conveyed by the thalamus and the spinal cord, respectively. The thalamic input to the somatosensory thalamus projects via the lateral geniculate nucleus to the primary visual cortex, which then projects to the secondary visual cortex. The secondary visual cortex projects to the frontal cortex, which then projects to the parietal cortex. The parietal cortex then projects to the motor cortex, which then projects to the spinal cord. The spinal cord then projects to the muscles.
Furthermore, aerobic exercise has been shown to increase B2AR (Adrb2) expression. Sympathetic nervous system (SNS) activity. Patients with myopathies; however, how exercise improves locomotive function remains largely unknown. Research shows that exercise influences thousands of people a year and can cost millions of dollars per patient. Exercise is currently the only therapeutic that partially restores motor function in Myopathies are neuromuscular diseases that affect the muscle and result in muscle weakness from dysfunctional muscle fibers. They affect hundreds of muscle quality with exercise. Jordan Owyoung, Emory University: The role of the sympathetic nervous system in improving skeletal muscle quality with exercise. Myopathies are neuromuscular diseases that affect the muscle and result in muscle weakness from dysfunctional muscle fibers. They affect hundreds of thousands of people a year and can cost millions of dollars per patient. Exercise is currently the only therapeutic that partially restores motor function in patients with myopathies; however, how exercise improves locomotive function remains largely unknown. Research shows that exercise influences sympathetic nervous system (SNS) activity. β2-adrenergic receptors (B2ARs) are the main receptors of the SNS and play a role in muscle protein synthesis. Furthermore, aerobic exercise has been shown to increase B2AR (Adrb2) expression.
I hypothesize that aerobic exercise modulates skeletal muscle metabolic health and function via sympathetic nervous system signaling. I will test my hypothesis in two ways. First, I will evaluate whether exercise can improve skeletal muscle function in mice with an ablated sympathetic system and in mice with a tamoxifen-induced homozygous knockout of Adrb2 in skeletal muscles. For each of the treatments, I will exercise a subset of mice. I hypothesize that a functional SNS is required for exercise to improve skeletal muscle function and therefore expect that exercise will not improve skeletal muscle function in either the symptomatic Adrb2-/- mice. Next, I will evaluate whether B2ARs are required for exercise to influence skeletal muscle health. I will use my Adrb2-/- mice and exercise a subset. Because B2ARs are essential for SNS signaling in the skeletal muscle, I hypothesize that exercise will not improve skeletal muscle health in Adrb2-/- mice.

Behavioral Subtopic

Erica Cross, Georgia State University: Taste buds treated with AAV vectors encoding PYY and exendin-4 impact upon taste perception and body mass accumulation in mice.

The availability of high-calorie foods is likely a causative factor for high rates of obesity and metabolic disorders, which have been linked to food intake dysregulation. Several gut peptides have been implicated in satiety and reduce food intake. While systemic administration of such peptides has been shown to induce behavioral sensitization and shifts. Together, these data demonstrate that the cold nociceptive system is capable of experience-dependent activated caspase cell-death construct in OXTR-Cre male and female mice, using their wildtype (Cre-) littermates as controls, and assessed their social, sexual, and aggressive behaviors. In males, lesioning LS OXTR-expressing cells increased communicative behavior (urine marking) in the presence of a caged male, without altering their investigatory behavior. Additionally, males with significant deletion of LS OXTR cells increased their copulatory behavior toward females (decreased latency to mount and intromit; greater proportion of males ejaculating) but decreased their aggressive behavior towards other males, compared to control males. Removing LS OXTR-expressing neurons in females also increased their copulatory performance, as evidenced by increased mounts by males, but without increased aggressive behavior. Our results indicate that OXTR neurons in the LS may normally suppress both male and female pro-social (copulatory) behavior. This, in turn, suggests that OXT may not act in all brain regions to increase prosocial tendencies and argues, instead, for separate and circuit-specific functions of OXT/OXTR systems.

Behnoush Dadkhah, Georgia State University: Oxytocin Receptor Expressing Neurons in the Lateral Septum Regulate Social Behavior in Mice

The neuropeptide oxytocin (OXT) and the oxytocin receptor (OXTR) regulate social behaviors and communication in mammals, including humans. One brain region that contains abundant levels of OXTR is the forebrain lateral septum (LS), an area known to play an important role in social behaviors like aggression. To investigate the behavioral role of the OXTR system in the LS, we deleted OXTR – expressing neurons in the LS using viral delivery of a Cre-dependent active caspase cell-death construct in OXTR-Cre male and female mice, using their wildtype (Cre-) littermates as controls, and assessed their social, sexual, and aggressive behaviors. In males, lesioning LS OXTR-expressing cells increased communicative behavior (urine marking) in the presence of a caged male, without altering their investigatory behavior. Additionally, males with significant deletion of LS OXTR cells increased their copulatory behavior toward females (decreased latency to mount and intromit; greater proportion of males ejaculating) but decreased their aggressive behavior towards other males, compared to control males. Removing LS OXTR-expressing neurons in females also increased their copulatory performance, as evidenced by increased mounts by males, but without increased aggressive behavior. Our results indicate that OXTR neurons in the LS may normally suppress both male and female pro-social (copulatory) behavior. This, in turn, suggests that OXT may not act in all brain regions to increase prosocial tendencies and argues, instead, for separate and circuit-specific functions of OXT/OXTR systems.

Kevin Donaldson, Georgia State University: Chronic activation of primary cold nociceptors causes increased sensitivity to subsequent cold challenge

Organisms encounter constantly changing sensory stimuli requiring timescale-specific processing to ensure proper growth, development, and survival. The predictive qualities of many stimuli are encoded via inherent neuronal circuitry, but some are modified through exposure. While experience-dependent plasticity has been well documented in recent years, little is known about its role in mediating behavioral responses. In this study, we investigated the role of chronic cold exposure on subsequent cold sensitivity in larval Drosophila melanogaster. We found that larvae exposed to a chronic cold treatment exhibited increased sensitivity to subsequent cold challenge, as evidenced by a decrease in the latency to respond to cold stimuli. This response was mediated by central mechanisms, as evidenced by the absence of a response in larvae with lesions to the LS. The results suggest that chronic cold exposure can alter subsequent cold sensitivity, likely through a central mechanism that involves the LS. These findings highlight the importance of the LS in mediating the behavioral response to cold stimuli and provide insight into the mechanisms underlying cold sensitivity in a variety of contexts.

Satya Iyer, Georgia State University: Taste buds treated with AAV vectors encoding PYY and exendin-4 impact upon taste perception and body mass accumulation in mice.

The availability of high-calorie foods is likely a causative factor for high rates of obesity and metabolic disorders, which have been linked to food intake dysregulation. Several gut peptides have been implicated in satiety and reduce food intake. While systemic administration of such peptides has been shown to induce behavioral sensitization and shifts. Together, these data demonstrate that the cold nociceptive system is capable of experience-dependent activated caspase cell-death construct in OXTR-Cre male and female mice, using their wildtype (Cre-) littermates as controls, and assessed their social, sexual, and aggressive behaviors. In males, lesioning LS OXTR-expressing cells increased communicative behavior (urine marking) in the presence of a caged male, without altering their investigatory behavior. Additionally, males with significant deletion of LS OXTR cells increased their copulatory behavior toward females (decreased latency to mount and intromit; greater proportion of males ejaculating) but decreased their aggressive behavior towards other males, compared to control males. Removing LS OXTR-expressing neurons in females also increased their copulatory performance, as evidenced by increased mounts by males, but without increased aggressive behavior. Our results indicate that OXTR neurons in the LS may normally suppress both male and female pro-social (copulatory) behavior. This, in turn, suggests that OXT may not act in all brain regions to increase prosocial tendencies and argues, instead, for separate and circuit-specific functions of OXT/OXTR systems.

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The availability of high-calorie foods is likely a causative factor for high rates of obesity and metabolic disorders, which have been linked to food intake dysregulation. Several gut peptides have been implicated in satiety and reduce food intake. While systemic administration of such peptides has been shown to induce behavioral sensitization and shifts. Together, these data demonstrate that the cold nociceptive system is capable of experience-dependent activated caspase cell-death construct in OXTR-Cre male and female mice, using their wildtype (Cre-) littermates as controls, and assessed their social, sexual, and aggressive behaviors. In males, lesioning LS OXTR-expressing cells increased communicative behavior (urine marking) in the presence of a caged male, without altering their investigatory behavior. Additionally, males with significant deletion of LS OXTR cells increased their copulatory behavior toward females (decreased latency to mount and intromit; greater proportion of males ejaculating) but decreased their aggressive behavior towards other males, compared to control males. Removing LS OXTR-expressing neurons in females also increased their copulatory performance, as evidenced by increased mounts by males, but without increased aggressive behavior. Our results indicate that OXTR neurons in the LS may normally suppress both male and female pro-social (copulatory) behavior. This, in turn, suggests that OXT may not act in all brain regions to increase prosocial tendencies and argues, instead, for separate and circuit-specific functions of OXT/OXTR systems.

Behnoush Dadkhah, Georgia State University: Oxytocin Receptor Expressing Neurons in the Lateral Septum Regulate Social Behavior in Mice

The neuropeptide oxytocin (OXT) and the oxytocin receptor (OXTR) regulate social behaviors and communication in mammals, including humans. One brain region that contains abundant levels of OXTR is the forebrain lateral septum (LS), an area known to play an important role in social behaviors like aggression. To investigate the behavioral role of the OXTR system in the LS, we deleted OXTR – expressing neurons in the LS using viral delivery of a Cre-dependent active caspase cell-death construct in OXTR-Cre male and female mice, using their wildtype (Cre-) littermates as controls, and assessed their social, sexual, and aggressive behaviors. In males, lesioning LS OXTR-expressing cells increased communicative behavior (urine marking) in the presence of a caged male, without altering their investigatory behavior. Additionally, males with significant deletion of LS OXTR cells increased their copulatory behavior toward females (decreased latency to mount and intromit; greater proportion of males ejaculating) but decreased their aggressive behavior towards other males, compared to control males. Removing LS OXTR-expressing neurons in females also increased their copulatory performance, as evidenced by increased mounts by males, but without increased aggressive behavior. Our results indicate that OXTR neurons in the LS may normally suppress both male and female pro-social (copulatory) behavior. This, in turn, suggests that OXT may not act in all brain regions to increase prosocial tendencies and argues, instead, for separate and circuit-specific functions of OXT/OXTR systems.

Kevin Donaldson, Georgia State University: Chronic activation of primary cold nociceptors causes increased sensitivity to subsequent cold challenge

Organisms encounter constantly changing sensory stimuli requiring timescale-specific processing to ensure proper growth, development, and survival. The predictive qualities of many stimuli are encoded via inherent neuronal circuitry, but some are modified through exposure. While experience-dependent plasticity has been well documented in recent years, little is known about its role in mediating behavioral responses. In this study, we investigated the role of chronic cold exposure on subsequent cold sensitivity in larval Drosophila melanogaster. We found that larvae exposed to a chronic cold treatment exhibited increased sensitivity to subsequent cold challenge, as evidenced by a decrease in the latency to respond to cold stimuli. This response was mediated by central mechanisms, as evidenced by the absence of a response in larvae with lesions to the LS. The results suggest that chronic cold exposure can alter subsequent cold sensitivity, likely through a central mechanism that involves the LS. These findings highlight the importance of the LS in mediating the behavioral response to cold stimuli and provide insight into the mechanisms underlying cold sensitivity in a variety of contexts.
Lisa Meyer-Baese, Emory University: Cortical networks relating to arousal are spatiotemporally coupled to neural activity and hemodynamics

Even in the absence of specific sensory input or a behavioral task, the brain produces structured patterns of activity. This organized activity has been shown to be modulated by changes in arousal. Here, wide-field voltage imaging was used to establish the relationship between cortical network activity and arousal in spontaneously behaving head-fixed mice expressing voltage sensitive fluorescent proteins (VSFP). Video recordings were used to parse out the contribution of arousal by measuring changes in pupil diameter whilst tracking spontaneous orofacial movements. Changes in pupil diameter were strongly coupled to global voltage cortical signals but not global hemodynamics, with low frequency (<1Hz) having the highest coherence. In addition, we found bilateral correspondence between the spatiotemporal patterns of both changes in voltage and hemodynamics which was localized to medial sensory-motor and secondary sensory/auditory cortices. Correlations in these areas were found to be driven by periods of orofacial movements. These observations demonstrate a consistent contribution of both arousal and orofacial motion to changes in cortical activity in distinct spatial patterns and frequency bands.

Chris Searles, Georgia State University: Perigestational Opioid Exposure Alters Alcohol Consumption in Adolescent Male and Female Rats

Every fifteen minutes, a baby is born in the US experiencing neonatal opioid withdrawal syndrome (NOWS). NIDA reports that since 2004, the rate of NOWS has increased 7-fold. Clinical studies have established intrauterine exposure to drugs of abuse as a risk factor for adverse health outcomes in adult life, including the potential for drug-related behavior and substance use disorders. Using knowledge of common mechanisms of action in the neural circuitry that drives opioid and alcohol reward, there is little data on the risks that those born with NOWS incur with alcohol use later in life. Here, we investigate the impact of perigestational opioid exposure (POE) on the mesolimbic reward system of male and female Sprague Dawley rats at postnatal and adolescent ages. Our lab has developed a clinically relevant model for morphine exposure spanning pre-conception to the first week of life. Using this model, we found that POE increased alcohol consumption in female rats under noncontingent conditions. POE also reduced latency and impulsive actions to earn alcohol rewards during operant conditioning sessions. Increased alcohol-seeking behaviors also extend to relapse testing scenarios without differences in relapse potential, possibly indicating long-term enhanced reward task focus or memory.

Dawn Jensen, Georgia State University: Epigenetic Regulation of Adolescent Grey Matter Maturation and Cognitive Development

Introduction

Adolescence is the second most critical phase of neurodevelopment, a period of brain maturation marked by many changes including non-linear decreases in grey matter volume and cognitive development. While animal studies have shown that there are large-scale epigenomic changes happening during phases of heightened synaptogenesis, there is currently little or no information regarding what role methylation plays in the development of human brain structures past fetal development. Here we analyze the dynamic methylation networks and their modulating effect on human adolescent brain reorganization. To do this, we used longitudinal data collected during the Developmental Chronnnecto-Genomics (Dev-CoG) to expand our model of normal brain development. The Dev-CoG project recruited 200 subjects aged 9 -14 years for a multi-modal longitudinal study, collecting structural MRI (sMRI), DNA methylation (DNAm), and cognitive data at three time points.

Methods

A difference map to represent the changes over time was created for each measure (DNAm, sMRI, and cognitive scores) by subtracting time point 1 from time point 2 (deltaT1) and time point 2 from time point 3 (deltaT2). Three analyses were done on these measures, one multivariate (MANCOVA) to capture as many sub-jects as possible, one repeated measures linear mixed effects regression to capture effects over time, and one multi-level mediation analysis to explore the indirect effects of the brain between methylation and cognition.

Results

The multivariate analysis revealed that multiple CpGs had relationships with all the spatial maps of GM volume change and with several of the measures of cognition. The repeated measures analysis highlighted networks of GM changes that were related to changes in methylation of several of the CpGs. These same net-works were also related to increases in executive function as well as decreases in episodic memory. The multi-association also showed these same regions of GM volume change to be mediating the relationship between several of the CpGs and the changes in executive function.

Conclusion

These analyses give a first look into the varied relationships between the dynamic changes of DNAm and their connections to GM volume changes and cognitive development in adolescence.

Kyle Johnsen, Georgia Institute of Technology: CLOCTools: A library of tools for closed-loop neuroscience

Closed-loop control enables scientists to adapt stimulation based on measured activity to drive a system towards a target. In neuroscience, the ability of closed-loop experiments to reduce variability and decouple connected systems has proven to be valuable. However, despite the promise of enabling stronger inference from experimental measurements, it remains challenging to implement fast, real-time feedback control. To address this obstacle, we are releasing CLOCTools, an open-source software collection designed to accelerating the use of closed-loop optogenetic control (CLOC). CLOCTools is designed to assist neuroscientists in online estimation, decoding, and control by providing fast, cross-platform C++ libraries implementing core algorithms and various support tools. These libraries and tools include: ldsCtrlEst, which features linear dynamical systems; hmm, which implements system identification and decoding algorithms for Hidden Markov Models (HMMs); wrapper modules, which implement ldsCtrlEst and hmm in the Real-Time eXperimental Interface (RTXI) system in tandem with Tucker-Davis Technologies (TDT) electrophysiology data acquisition; support tools for profiling new algorithms; and tools for multi-language compatibility in the form of Python and MATLAB interfaces. CLOCTools thus provides a unified set of tools for developing and deploying powerful new closed-loop stimulation approaches for deciphering the function of complex neural circuits. CLOCTools documentation: https://cloctools.github.io

Jack Taylor, Georgia State University: Principal component and network analyses reveal relationships between sex, social status, oxytocin receptor, vasopressin V1a receptor, and serotonin 1A receptor densities across the social decision-making network

The social decision-making network (SDMN) has been a useful concept for examining the roles of interconnected nodes in the expression of social behavior. In order to understand these brain networks, it is necessary to describe the relationships between nodes and to relate connections and patterns within the network to distinct social behavioral states, such as sex or dominance status. In this study, we used graph theory network analysis (NA) and principal component analysis (PCA) to analyze oxytocin (OTR), vasopressin (V1a), and serotonin (5HT1A) receptor binding data from 34 regions across the SDMN with the purpose of elucidating novel receptor expression networks and relationships. To investigate differences based on sex and social status (dominant, subordinate, nonsocial control) we extracted PCA scores and performed 2 (sex) x 3 (social status) ANOVAs using these data as dependent variables. Three PCA components accounted for nearly 50% of the variance. Component 1 was dominated by positive loadings from OTR nodes and V1a nodes within the mesolimbic dopamine system. Component 2 was more heterogeneous, and was marked by strong loadings from V1a and 5HT1A in the AH and the MPOA. Males loaded significantly more highly than females on this component. Component 3 was dominated by V1a nodes, particularly those within the mesolimbic dopamine system. Our NA revealed similar and complementary results. OTR nodes represented 60% of the top 25% of nodes.
The three most central nodes were OTR in the paraventricular nucleus, the bed nucleus of the stria terminalis, and the medial prefrontal cortex (mPFC). Despite the high centrality of the mPFC with regard to OTR expression, the nodes representing V1a and 5HT1a in the mPFC were among the least central. The NA between males and females showed similar patterns of centrality among nodes. Notable differences include OTR in the anterior hypothalamus, which was the ninth-most central node for females, but 22nd for males, and OTR in the medial preoptic area, which was the 12th-most central node for females, but 25th for males. Node centralities were largely similar between dominants and subordinates. Notable exceptions were V1a in the central amygdala, which was the 35th-most central node for dominants, but was 21st for subordinates. These data show that, in Syrian hamsters, OTR expression in nodes in the SDMN are tightly coupled, and V1a and 5HT1a expression in these nodes differ between males and females but not between hamsters with differing dominance statuses. Supported by R01MH122622 and R01MH110212 to HEA and KLH. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or GSU.

**Nerve Repair Subtopic**

**Tina Tian, Emory University: Neuronal activity-based therapies do not enhance sympathetic axonal regeneration**

Introduction: Axonal injuries are common and lead to a loss of motor, sensory, and autonomic functions that lead to lifelong disabilities. Enhancing axon regeneration is important for the development of novel therapeutics to complement surgical repair, such as nerve transfers for hand reanimations after spinal cord injury. However, the regenerative capacity of post-ganglionic sympathetic axons and their functional recovery has rarely been studied. Sympathetic innervation plays a major role in muscle strength and thermoregulation. The objective of this study is to study the regenerative capacity of sympathetic axons in the sciatic nerve after injury following neuronal activity-based treatments.

Methods: A conditioning lesion (CL) paradigm and a bioluminescent optogenetics approach were used to stimulate the whole nerve or sympathetic axons, respectively. To study sympathetic regeneration, I performed immunohistochemistry on sciatic nerve sections and utilized retrograde tracing techniques.

Results: My results suggest that the elongation of sympathetic axons is not enhanced with a conditioning lesion or electrical stimulation. Additionally, selective activation of sympathetic axons with bioluminescence decreases the number of sympathetic axons that have reached 5 mm of growth from the injury site 2 weeks after transection and repair of the sciatic nerve. Thus, activity-based therapies neither enhance sympathetic axonal elongation nor increase the number of sympathetic neurons participating in regeneration.

Conclusions: My preliminary data indicate that neuronal activity-based therapies that have previously been shown to enhance regeneration of motor and sensory axons may be detrimental to sympathetic axon regrowth. This data will have implications for activity-based therapeutic methods, such as electrical stimulation which has reached clinical populations, that can potentially be used to complement nerve repair surgeries.

Future Directions: I will further investigate the effects of neuronal stimulation on functional sympathetic recovery. Additionally, I plan to alter the traditional electrical stimulation paradigm to stimulate sympathetic neurons more effectively.
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