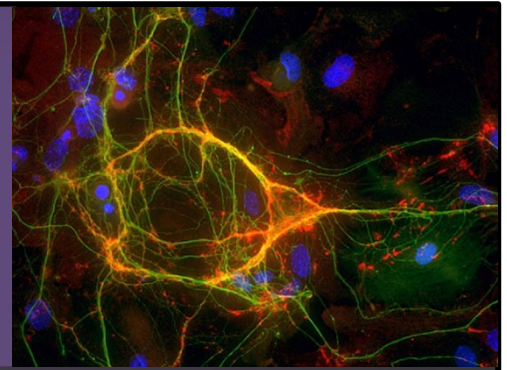


Eastern Carolina Chapter  
of the Society for Neuroscience  
Presents:



# 25<sup>th</sup> Annual Neuroscience Symposium



Featuring:

**Anne E. West, MD/PhD**

Professor of Neurobiology

Associate Director, Medical Scientist Training Program

Duke University Medical Center

*“Epigenetic Mechanisms and the  
Control of Cell-Type Specific Neuronal  
Plasticity in Addiction”*

Friday, October 27<sup>th</sup>, 2023  
East Carolina Heart Institute  
[eccsfm.ecu.edu](http://eccsfm.ecu.edu)



Funding for this event was made possible by contributions from:



Anatomy & Cell Biology  
Kinesiology  
Pathology and Laboratory Medicine  
Psychology

The Eastern Carolina Chapter of the Society for Neuroscience would like to express its sincere gratitude to the following sponsors for their generous support of this year's symposium:

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## 25th Neuroscience Symposium Schedule

Friday, October 27<sup>th</sup>, 2023  
East Carolina Heart Institute (ECHI)  
115 Heart Dr, Greenville, NC 27834  
East Carolina University, Greenville, NC



### Registration and Abstract Submission Link and QR Code

[https://ecu.az1.qualtrics.com/jfe/form/SV\\_ejTskDTKVdaltOK](https://ecu.az1.qualtrics.com/jfe/form/SV_ejTskDTKVdaltOK)

**\* It is the Friday before Halloween -  
Costumes are highly encouraged! \***

- 9:00-3:35      **Check-In / Walk-In Registration**
- 9:00-10:00     **Breakfast Available for All Registrants and Guest Speakers**
- And**
- Chat with Keynote Speaker:** Anne West, MD/PhD  
(for students, postdocs, and medical students/residents)
- 10:00-10:15    **Opening Remarks:** Chris Mizelle, PhD, ECCSfN President
- 10:15-10:45    **Lightning Talks by Graduate Students**  
(5 min each, 3 min questions)
- 10:45-11:00    **Break**
- 11:00-11:55    **Keynote Address:** Dr. Anne West, Professor of Neurobiology, Duke University  
School of Medicine  
*"Epigenetic Mechanisms and the Control of Cell-Type Specific Neuronal Plasticity in Addiction"*
- 12:00-12:30    **Lunch Available for All Registrants and Guest Speakers**
- 12:30-3:00     **Faculty Presentations**
- 12:30 – 1:15    Ozge Gunduz-Cinar, Pharm., PhD, NIH/NIAAA  
*"Endocannabinoids in the Cortico-Amygdala Neurocircuit Mediate Fear Extinction"*
- 1:20 – 2:05    Swati M. Surkar, PT, PhD, East Carolina University  
*"Remote Ischemic Conditioning as a Novel Priming Agent to Enhance Neurorehabilitation Outcomes"*
- 2:10 – 2:55    Karen Mruk, PhD, East Carolina University  
*"Developing Tools and Building Bridges: Zebrafish as a Model for Spinal cord Regeneration"*
- 3:00-4:00      **Poster Session**
- 4:00-4:15      **Closing Remarks and Awards:** Chris Mizelle, PhD, ECCSfN President

# Invited Talks

(in order of appearance)



## *Epigenetic Mechanisms and the Control of Cell-Type Specific Neuronal Plasticity in Addiction*

**Anne E. West, MD/PhD**

Professor of Neurobiology

Associate Director, Medical Scientist Training Program

Duke University Medical Center

Experience-dependent functional adaptation of nucleus accumbens (NAc) circuitry underlies the development and expression of reward-motivated behaviors. We have shown that parvalbumin-expressing GABAergic interneurons (PVINs) within the NAc are required for this process, and we have studied the chromatin mechanisms that mediate cell-type specific activation of genes in PVINs following exposure to psychostimulant drugs of abuse. Among the genes that show PVIN-specific induction upon amphetamine treatment are cell adhesion proteins and components of the extracellular matrix. Perineuronal nets

(PNNs) are extracellular matrix structures enriched around PVINs that arise during development and are proposed to mediate brain circuit stability. However, their function in adult NAc is largely unknown. I will discuss our studies of the developmental emergence and adult regulation of PNNs in mouse NAc and test the cellular and behavioral consequences of reducing the PNN component brevican in NAc PVINs. We find that regulation of brevican in NAc PVINs of the adult mouse modulates their excitatory synaptic drive and sets experience thresholds for the development of motivated behaviors driven by rewarding stimuli.



## *Endocannabinoids in the Cortico-Amygdala Neurocircuit Mediate Fear Extinction*

**Ozge Gunduz-Cinar, Pharm, PhD**

Staff Scientist

Laboratory of Behavioral and Genomic Neuroscience

National Institute on Alcohol Abuse and Alcoholism

National Institutes of Health

Ozge Gunduz-Cinar<sup>1</sup>, Laura I. Castillo<sup>1</sup>, Maya Xia<sup>1</sup>, Elise Van Leer<sup>1</sup>, Emma T. Brockway<sup>1</sup>, Gabrielle A. Pollack<sup>1</sup>, Olena Bukalo<sup>1</sup>, Aaron Limoges<sup>1</sup>, Sarvar Oreizi-Esfahani<sup>1</sup>, Veronika Kondev<sup>2</sup>, Rita Báldi<sup>3</sup>, Farhana Yasmin<sup>3</sup>, Ao Dong<sup>4</sup>, Judy Harvey-White<sup>5</sup>, Resat Cinar<sup>5,6</sup>, George Kunos<sup>5</sup>, Yulong Li<sup>4</sup>, Larry S. Zweifel<sup>7</sup>, Sachin Patel<sup>3</sup>, and Andrew Holmes<sup>1</sup>

<sup>1</sup> Laboratory of Behavioral and Genomic Neuroscience, National Institute on Alcohol Abuse and Alcoholism, NIH, Bethesda, MD, USA

<sup>2</sup> The Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN, USA

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<sup>5</sup> Laboratory of Physiologic Studies, National Institute on Alcohol Abuse and Alcoholism, NIH, Bethesda, MD, USA

<sup>6</sup> Section on Fibrotic Disorders, National Institute on Alcohol Abuse and Alcoholism, NIH, Bethesda, MD, USA

<sup>7</sup> Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington; Department of Pharmacology, University of Washington, Seattle, WA, USA

Extinction of fearful memories is impaired in anxiety and stress related disorders such as posttraumatic stress disorder. The endocannabinoid system has a key role in facilitation of extinction as evidenced by preclinical and clinical studies. Here, we extend our previous findings to investigate the neurocircuitry that underlies this effect. We focused on the basolateral amygdala (BLA) projecting medial prefrontal cortex (mPFC) neurons as this circuit is implicated in fear extinction. First, we found that optogenetic activation of these afferents during extinction CS (conditioned stimulus) presentation elevates eCBs in BLA. Next, we showed the dynamic changes of the eCBs at these afferents using the eCB biosensor. During the extinction training eCBs were increased after CS presentation when the aversive unconditioned stimulus (shock, US) is most expected. Finally, we showed that disrupting the function of the CB1Rs expressed on these afferents via CRISPR-Cas9 gene editing impairs extinction. In summary, our results reveal the temporal dynamics of endocannabinoids at prefrontal-amygdala neurons during extinction. These findings highlight targeting the eCB system as a therapeutic approach for anxiety and stress related disorders.





## ***Remote Ischemic Conditioning as a Novel Priming Agent to Enhance Neurorehabilitation Outcomes***

**Swati M. Surkar, PT, PhD**

Assistant Professor  
Department of Physical Therapy  
College of Allied Health Sciences  
East Carolina University

Ischemic conditioning is an endogenous phenomenon in which an organ exposed to a controlled, short-term, local, sublethal ischemia is protected from subsequent ischemic injury. Remote ischemic conditioning (RIC) is a clinically feasible way of performing ischemic conditioning where episodes of alternating, brief ischemia and reperfusion are delivered with cyclic inflation and deflation of a blood pressure (BP) cuff on the arm or leg. The cardioprotective effects of ischemic conditioning are well established and the recent studies have begun to explore the neuroprotective effects. Of great importance to neurorehabilitation, our foundational work suggests that when paired with task-specific training, RIC enhances motor learning in healthy young and older adults. While the neuroprotective role of RIC and mechanisms for neuroprotection are well appreciated, this talk will bridge the substantial knowledge gap in understanding whether RIC can capitalize on these neuroprotective mechanisms to facilitate motor skill learning in children with cerebral palsy.



## **Developing Tools and Building Bridges: Zebrafish as a Model for Spinal cord Regeneration**

**Karen Mruk, PhD**

Assistant Professor  
Department of Pharmacology and Toxicology  
Brody School of Medicine  
East Carolina University

Potassium channel proteins are involved in many aspects of human physiology. Small conductance calcium-activated potassium channels (SK channels) are voltage-independent and widely expressed in excitable cells. Our laboratory determined that expression of *kcnk1*, which encodes the SK1 channel, is upregulated after spinal cord injury in zebrafish. Our preliminary data using a potassium channel inhibitor, 4-aminopyridine, demonstrates that inhibition enhances swim recovery in zebrafish suggesting modulation of SK channels may be potentially useful as a therapeutic approach for SCI. However, current optochemical and chemogenetic tools often do not persist throughout development or act on the transcriptional, limiting the temporal resolution for studies, or require the use of multiple transgenic lines. We developed an RNA-based chemogenetic approach and an optogenetic transcriptional approach to turn on genes of interest in zebrafish embryos and larvae. We demonstrate that a gene of interest can be turned on in a time-dependent and concentration-dependent manner. Together these tools will clarify the role of SK channels and specifically SK1 in recovery from SCI. We expect that the developed lines will be useful to study additional neurological pathologies and facilitate drug screening to identify new therapeutics for neurodegenerative diseases.

# Lightning Talk Abstracts

(listed by presenting author in alphabetical order)

## **FRET Not, Shedding Light on Myosin Mechanical Forces**

Wesley Czika, Michelle Cobb, and Karen Litwa

Brody School of Medicine Department of Anatomy and Cell Biology, East Carolina University, Greenville, NC

Mature neurons, characterized by containing mushroom-shaped dendritic spines, play a pivotal role in learning and memory processes. Neurodevelopmental disorders, such as Autism Spectrum Disorder (ASD), are associated with alterations in dendritic spine number, size, and alterations in their morphology. Non-Muscle Myosin IIB (NMIIB), a key modulator of actin filament dynamics, has been implicated in dendritic spine formation and maintenance. While the importance of NMIIB in shaping dendritic spines is evident, research efforts addressing the mechanistic aspects of physiological alterations induced by mechanical forces generated by NMIIB remain limited. Fluorescence Resonance Energy Transfer (FRET) is a powerful molecular tool that leverages energy transfer between two fluorophores to measure mechanical forces exerted by proteins. In this context, FRET-based sensors offer a versatile approach to unravel molecular interactions, dynamics, and conformational changes. Moreover, given NMIIB's central role in cell shape and contraction, FRET sensors hold the potential to deepen our understanding of cell motility, membrane morphogenesis, embryogenesis, cell migration, and tissue formation. Our initial findings suggest a notable trend wherein younger neurons exhibit higher NMIIB mechanical forces in comparison to their more mature counterparts. This observation potentially signifies an earlier developmental stage of dendritic spines characterized by highly dynamic actin structures, aligning with the transition from filopodial to mature spine morphology. We are currently investigating how pharmacological regulation of NMIIB activity alters these mechanical forces and the resulting formation of dendritic spines. This research study is the first to examine how NMIIB-mediated mechanical forces contribute to dendritic spine formation, providing a comprehensive framework for our understanding of dendritic spine alterations in ASD.



## **The Optimization of the Combined Methodology of Golgi-Cox Staining and Immunofluorescence in Developing Mouse Brains**

Victoria Frank, Karen Litwa

Brody School of Medicine Department of Anatomy and Cell Biology, East Carolina University, Greenville, NC

Golgi staining is an old methodology which relies on the interaction between Silver Nitrate, Potassium Chromate, and Potassium Dichromate to produce a black substance which binds to a limited amount of neurons in brain tissue. It was developed in 1873 by Camillo Golgi and was modified in 1891 by W. H. Cox by adding Sodium Thiosulfate, Ammonia and Mercuric Chloride. In this new variant a metallic salt is formed and theorized to bind to the neurons to visualize them. This new technique is more consistent and provides better visualization of the dendritic spines than the original technique. The actual mechanism by how this process occurs though is unknown. In this study our purpose is to combine this methodology with immunofluorescence to correlate adhesion proteins with the different dendritic spine morphologies across development. Dendritic spines are key to forming synapses and there are adhesion proteins that are implicated in their stabilization and maturation during synaptogenesis. It is our goal to see what morphologies SynCAM, Neuroligin-1, and N-Cadherin favor in developing mice. In this current study, we are comparing we used E18 dendritic spines and associated adhesion proteins at embryonic and postnatal stages in the developing cortex (E18.5 and P17 CD-1 mice). To analyze the resulting golgi staining, we used the neuroLucida program. We are currently optimizing the combined the immunofluorescence staining to visualize adhesion proteins. These results will provide insights into when specific adhesion molecules orchestrate synapse development. This study also provides a technical foundation for future assessment of how synapse morphology and associated adhesion proteins are altered in neurodevelopmental disorders, such as autism spectrum disorders. The gender was also determined at E18.5 using a novel technique that relies on phenotypic differences in genitals to differentiate the males and females. The brain tissue was harvested from the mice and fixed with 4% Paraformaldehyde for 48 hours and 4°C. The tissue was then transferred to a Golgi-Cox solution containing 5% Potassium Chromate, 5% Potassium Dichromate, and 5% Mercuric Chloride in deionized water for 2 weeks at 4°C. After impregnation the tissue was sliced at 100µm on a cryostat then developed with 20% Ammonia and 1% Sodium Thiosulfate. For the immunofluorescence, the tissue was blocked & permeabilized overnight at 4°C with 5% Goat Serum and 0.5% TritonX100. Primary antibody incubation occurred at 4°C for 48 hours, was washed and then replaced with the secondary antibodies for 2 hours at room temperature. Gelatin coated slides were prepared and used for mounting, with the tissue being coverslipped with Fluoromount gel. An Olympus FV1000 microscope was used to image the immunofluorescence and a light microscope for the Golgi-Cox stain. The NeuroLucida program was also utilized to analyze to dendritic morphology as well as develop 3D models of the neurons. The current results were successful for the use of the Golgi-Cox stain but the immunofluorescence was not. This potentially could be due to the unknown mechanism behind the Golgi-Cox stain interfering with the antibodies ability to properly target their epitopes. Further investigation and optimization is being done to elucidate the reason behind the failure.

# Neurological Connectivity Patterns in Implicit Motor Sequence Learning: A Comparison of Right and Left Limb Dominance

Nikole B. Galman, Jennifer Painter, J.C. Mizelle

Department of Kinesiology, East Carolina University, Greenville, NC

Both limb dominance (LD) and implicit motor sequence learning (IMSL) are critical aspects of our ability to interact with the environment in a goal directed way. Current research has challenged the theory of lateralization of brain function with regard to handedness by concluding that left-handed (LH) individuals engage in bilateral neural activity compared to their right-handed (RH) counterparts who most often engage the left hemisphere of the brain during motor skill execution. This suggests that LD has a substantial influence on IMSL given that handedness may affect how motor sequences are processed in the brain. The purpose of this study is to understand the different neural mechanisms engaged between RH and LH individuals when performing IMSL tasks via creating models of brain activation. Additionally, this can improve our understanding of how complex sequential motor skills are encoded in the brain and how handedness influences this process. Thirty healthy male and female volunteers (15 RH, 15 LH) ages 18 to 35 years were recruited to participate. The participants performed all tasks with the dominant hand, and brain activity was recorded for all tasks using EEG. A fixed 10-element movement sequence was created and inserted in a longer 13-element movement sequence at random locations. Participants were not told of the repeating sequence. Four white rectangles were displayed on a screen, and when one rectangle turned black, the participant pressed the corresponding button on a keypad. Connectivity measurements of imaginary coherence and graph theory were utilized to compare EEG activation patterns across RH and LH individuals with a focus of the Theta band (4-8 Hz), on account of its association with cognitive and motor activities. RH and LH individuals were indistinguishable in terms of behavior and voltage. However, during the early phases of learning the motor sequence task, RH individuals engaged their left hemisphere, while LH individuals exhibited a more balanced activation in both hemispheres. Interestingly, in the later stages of learning, brain activation between the two groups gradually became similar. These results indicate that LH and RH individuals have very different patterns of communication across the brain during the encoding of sequences.

## Neural Entrainment Among Athlete Dyads: an EEG Hyperscanning Study

Madison Weeks, J.C. Mizelle

East Carolina University, Greenville, NC

Entrainment describes the phenomenon of synchronized, coordinating movement that can be observed between two individuals. Since the brain controls the body, one can also expect to see a neural entrainment between pairs of individuals, or dyads, that engage in collaborative movement. In the field of Neuroscience, this idea of neuronal synchronization, and its relationship to behavioral entrainment between individuals, remains vastly unexplored.

Many occupations rely on collaborative, interdependent relationships for success in high-risk environments such as military units, first responders, and surgical teams. In extreme circumstances, the success of their collaboration can mean the difference between life and death. Understanding these concepts, and determining if there is in fact a neural entrainment that occurs between individuals, is essential to furthering neuroscience research of interpersonal dynamics.

Our model for investigating neural entrainment between individuals will be athlete dyads in coed cheerleading. Stunt partners are a cheerleading dyad consisting of a female flyer and a male base who collaborate to perform a stunt. A stunt is executed when the base throws the flyer into the air, catches and holds her feet, and returns the flyer to the ground by tossing her up and catching her hips as she comes down. Stunts can be made with various positions, sequences, and elite skills for which synchronous movement is vital. The rationale behind recruiting this population is the highly interdependent nature of stunt partners, and the high stakes of performing a stunt.

Participants will be ages 18-35 and recruited from coed cheerleading squads. We will recruit 20 stunt partner dyads; 10 will be well-practiced pairs who are normally together throughout a season. The other 10 will not be regularly paired partners and will be less practiced and less familiar with each other.

Dyads will undergo EEG Hyperscanning while playing a collaborative game. Each participant will control a force transducer with their hand to move a cursor (up and down or left and right) displayed on a screen. The goal is to move the cursor in line with a moving target.

*These are preliminary ideas to be investigated soon- data collection has not yet begun.*

# Research Poster Abstracts

(listed by presenting author in alphabetical order)

## **Neuroplasticity Mechanisms of Remote Ischemic Conditioning in Children with Unilateral Cerebral Palsy**

Destiny Alling, Swati Surkar, Shailesh Gardas

Department of Physical Therapy, East Carolina University, Greenville, NC

Unilateral cerebral palsy (UCP) elicits heterogenous sensorimotor impairments in the contralesional side of the body and is a leading cause of childhood disability. Children with UCP have difficulty in bimanual coordination that restricts the child's independence. Growing evidence suggest that maladaptive plasticity largely determine the effectiveness of intervention in these children. Ischemic conditioning is an endogenous phenomenon to protect an organ from injury by exposing it to a controlled, short-term, local, sublethal ischemia. Remote ischemic conditioning (RIC) is a clinically feasible way of performing ischemic conditioning where episodes of ischemia and reperfusion are delivered with cyclic inflation and deflation of a blood pressure (BP) cuff on the arm or leg. Studies suggest the effects of RIC extend into neuroprotection and motor learning. Although the exact mechanisms of RIC for enhancing motor learning are not known, the mechanisms of RIC that offer neuroprotection also promote motor learning and neuroplasticity. The non-invasive brain stimulation technique, transcranial magnetic stimulation (TMS), is a reliable method to assess cortical excitability, inhibition and plasticity. Our hypothesis is that the multifactorial mechanisms of RIC can be harnessed as a priming agent to enhance the effects of rehabilitation and to augment neuroplasticity in children with UCP.

This study consists of 25 children with UCP, 6-16 years. Children received RIC or sham on the affected arm with conditioning protocol combined with 30 hours of Hand Arm Bimanual Intensive therapy (HABIT). Pre- and post- TMS measures to assess brain excitability/behavioral measures to assess hand function and bimanual coordination were collected. The objective is to analyze the effects of RIC plus HABIT on bimanual coordination and M1 plasticity. The secondary objective is to assess the responders and non-responders to RIC/Sham training based on brain excitability and severity of hemiplegia. We hypothesize that children who received RIC will be responders to training and will have greater M1 plasticity.

## **From Genes to Synapses: N-Cadherin's Impact on Neural Networks**

Sierra Carr, Nicholas McLamb, Otha Whitney, Gaelle Desert, Michelle Cobb, and Kara Litwa

East Carolina University

Our brains are made of intricate networks and channels that require precise communication. This is achieved by rapid electrical and chemical signals. The main communication methods are via neurons. Neurons transmit signals throughout the brain. These neurons have connections called synapses where the signals are transmitted. The presynaptic and postsynaptic make up the junction.

Neural Cadherins, N-cadherins, serve as a strong homophilic cell adhesion molecule. They contribute to the synaptic complex by providing functional and structural adhesion between the membranes. N-cadherins connect pre- and post-synapses. N-cadherins are involved in intracellular signaling pathways that utilize signaling proteins through their cytoplasmic domain to ensure proper signal reception as well as influence increased synaptic plasticity. Deregulation or loss of function of these specialized cadherins causes increased risk of schizophrenia and other numerous neurodegenerative diseases. However, little is known about whether N-Cadherin orchestrates the initial stages of synapse formation in brain development.

We hypothesize that a loss of *ncad* will reduce synapse formation in developing human neurons. To conduct these studies, we use human iPSC-derived cortical neurons at 1 week of development, when synapse formation begins. We treat these neurons with either a control scrambled siRNA or a siRNA targeting N-Cadherin to reduce its expression and analyze the resulting impact on synapses using STORM super-resolution microscopy.



## **Autoimmune Demyelination Alters Hypothalamic Transcriptome and Endocrine Function**

Jonathan J. Carver, Kristy M. Lau, Alexandra E. Puckett, Alessandro Didonna

Department of Anatomy and Cell Biology, Brody School of Medicine, Greenville, 27834 NC

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system characterized by focal inflammation, demyelination, and axonal injury. MS represent the leading cause of non-traumatic neurological disability among young adults. MS patients are more likely to report neuropsychiatric symptoms including anxiety, depression, and chronic fatigue. It is widely known from clinical and animal studies that immunogenic challenges can cause behavioral changes towards more depressive and anxious-like states via increased cytokine expression and activation of behavioral circuits. Altered hormone levels in MS patients suggest hypothalamic and endocrine dysfunction to be underlying some of these phenotypes, but the precise molecular mechanisms are still far from being fully elucidated. To fill this gap, we investigated the impact of MS animal model experimental autoimmune encephalomyelitis (EAE) on the hypothalamus transcriptome and endocrine function. RNA-seq technology was employed to capture the transcriptomic signatures of hypothalamic tissues isolated from EAE-immunized female mice and mock-injected controls at key disease stages, namely the pre-symptomatic phase (10 days post-injection, dpi), disease peak (20dpi), and the chronic phase (40dpi). Notably, differential gene expression analysis identified statistically significant changes already at 10dpi, providing evidence that altered CNS functions precede clinical symptoms. Gene ontology (GO) analysis identified “response to interferon-beta” as one of the most enriched terms at all timepoints. The transcriptomic changes in the EAE hypothalamus were independent of local lesions; we failed to detect a difference in neuronal number, no appreciable death by TUNEL stain, lack of CD3+ T-cells, and no difference in glial number or activation state. Instead, cytokine paneling of the hypothalamus detected 9 significantly upregulated cytokines, with several more trending to be higher in EAE. We next assessed the functionality of the hypothalamus by examining downstream signaling molecules and targets of the endocrine hypothalamus. We discovered hyperplasia of the adrenal in EAE mice, with enlargement of the zona fasciculata and zona glomerulosa. Next, we found decreased serum levels of gonadotropins FSH and LH, along with decreased ovarian mass and significantly less corpora lutea. Together our results show altered hypothalamus transcriptome and molecular functioning, with effects on stress-response and fertility pathways in adult mice.

## **SARS-CoV-2 Infiltration of Dopamine Neurons Suggests Potential Linkage to Parkinson's Disease**

Hannah E. Croy<sup>1</sup>, Drew Theobald<sup>2</sup>, Shaw M. Akula<sup>3</sup>, Srinivas Sriramula<sup>2</sup>, and Jeffrey B. Eells<sup>1</sup>

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<sup>3</sup>Brody School of Medicine Department of Cell Microbiology and Immunology, East Carolina University, Greenville, NC

COVID 19 has triggered a variety of neurological ailments of which the world is just beginning to deal with. COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can produce a variety of neurological symptoms such as, but not bound to, neuroinflammation, chemokine/ cytokine storms, and cognitive disorientation. These SARS-CoV-2 symptoms could exacerbate multiple neurological diseases including Parkinson's Disease (PD).

PD is caused by the progressive degradation of dopamine nerve cells located in the substantia nigra pars compacta (SNpc). The SN is the region of the brain responsible for motor control and production of dopamine, in conjunction with the ventral tegmental area (VTA). A decrease in dopamine secretion is directly correlated to tremors, muscle rigidity, and impaired coordination – all hallmark PD symptoms. A link between SARS-CoV-2 and PD has been suggested, however, data is limited. One potential mechanism for SARS-CoV-2 infection damaging dopamine neurons is direct infiltration of SARS-CoV-2 into dopamine neurons located within the SNpc. To test the vulnerability of dopamine neurons to infection in vivo, the transgenic K18-hACE2 mouse model was used. The K18-hACE2 mice were infected with SARS-CoV-2 developed severe disease and were euthanized around 6 days post infection. Immunohistochemical techniques were performed on paraffin embedded brain sections and labeled for three separate fluorescent targets: [1] neural nuclei (DAPI), [2] dopamine neurons (tyrosine hydroxylase -TH), [3] SARS-CoV-2 infection (SARS spike protein).

Following the immunofluorescence, slide imaging throughout the SNpc and VTA from rostral to caudal was obtained with a Keyence fluorescent microscope. Cell quantification was performed manually by transitioning between the overlay view and either the TH+ or SARS+ view of each section.

Cell counts resulted in an overall SARS+TH+ infection rate of 73.3%. Interestingly, the infection rate was lower in the SN averaging 66.5% than in the VTA, averaging 79.1%. These data demonstrate that dopamine neurons are vulnerable to SARS-CoV-2 infection. Currently, the mechanism of SARS-CoV-2 infection of dopamine neurons is not known. Additionally, whether SARS-CoV-2 infects dopamine neurons in mild disease has not been determined. Future studies are underway to address this question and determine the virus's persistence in dopamine neurons along with the relevance of these potentially destructive capabilities for PD patients.

## The Dopamine D3 Agonist Pramipexole Decreases the Withdrawal Potential of Morphine

Alissa L. Davis<sup>1</sup>, Dylan Marshall<sup>2</sup>, Martina De Cristofaro<sup>2</sup>, Stefan Clemens, Ph.D.<sup>2</sup>, Kori L. Brewer, Ph.D.<sup>1,2</sup>

<sup>1</sup>Brody School of Medicine, East Carolina University

<sup>2</sup>Department of Emergency Medicine and Physiology, Greenville, NC 27834

**Background or Problem Statement:** Despite dangerous labeled side effects that include physical dependence on the drugs, opioids remain the standard of care for moderate to severe pain because they are highly effective analgesics with few alternatives.<sup>1</sup> The use of an adjuvant may decrease opioid doses needed to achieve analgesia which in turn may decrease their adverse effects of tolerance, dependence, and withdrawal.

**Objective/Hypothesis/Aim Statement:** The objective of this study was to determine if using the dopamine receptor agonist pramipexole (PPX) as an adjuvant can attenuate opioid withdrawal in animals that are opioid tolerant.

**Methods:** We induced morphine tolerance in 18 male Long-Evans rats over seven days with a twice daily 10 mg/kg subcutaneous injection. At 7 days, drug administration was either stopped (control group, n=6), or animals were assigned one of two drug conditions for the seven following days: a 5 mg/kg dose of morphine (n=6) or a 5 mg/kg dose of morphine with the addition of 0.5 mg/kg pramipexole (n=6). Withdrawal symptoms were measured and compared across groups at the start of treatment and after all drug administration was stopped.

**Results:** There was no significant difference in total withdrawal scores across groups during the treatment period or after removal of drug. However, the behavioral profile of withdrawal symptoms during the treatment period was different, with the pramipexole group displaying significantly more rearing than the control or morphine reduction groups. When controlling for rearing behaviors (known to be associated with the use of dopaminergic drugs), there was a significant reduction in withdrawal symptoms in the PPX-treatment group when compared to control at both 48 (p=0.014) and 72 hours (p=0.004).

**Conclusion:** We were able to reduce the dose of morphine given to a tolerant animal without inducing withdrawal which serves as preclinical evidence for developing pramipexole as a potential opioid replacement therapy. Future research should investigate if a stepwise decrease in doses of the morphine/pramipexole combination over time can also reduce withdrawal after complete removal of drug in morphine tolerant animals. 1 NIDA. 2021, June 1. Prescription Opioids DrugFacts. Retrieved from <https://nida.nih.gov/publications/drugfacts/prescription-opioids> on 2023, July 18

## Effects of NCAM on Synapse Development in Mouse Neurons

Kara DuBois<sup>1</sup>, Rosario Lilley<sup>2</sup>, Kendall Wilkerson<sup>2</sup>, Michelle Cobb<sup>3</sup>, Gaelle Desert<sup>1</sup>, Dr. Karen Litwa<sup>3</sup>

<sup>1</sup>Department of Neuroscience, East Carolina University, Greenville, NC

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<sup>3</sup>Department of Anatomy & Cell Biology; East Carolina Diabetes and Obesity Institute, East Carolina University, Greenville, NC

Synapse development begins in utero and disruptions to synapse formation result in neurodevelopmental disorders. Adhesion molecules mediate adherence of pre- and post-synaptic compartments and are involved in synapse development. However, we lack information about which adhesion molecules initiate synapse formation. The adhesion molecule NCAM is present in early brain development and influences the formation and fasciculation of neurons as well as neurite extension. In developed neural circuits, knockdown of NCAM results in increased basal synaptic transmission and decreased synaptic plasticity. However, its role in synapse initiation is unknown. It is hypothesized that synapse development will be reduced by the knockout of NCAM in immature mouse neurons.

In our present study, hippocampal and cortical neurons have been used to assess the development of synapses in mouse neurons with the RNAi knockdown of NCAM compared to a control group, in which neurons were treated with non-targeting siRNA. The techniques used to conduct this experiment include the use of a Zeiss Airy Scan microscope and immunofluorescence staining to detect pre- and post- synaptic compartments (synapsin and DAP4) and NCAM. ImageJ analysis is being used to assess NCAM expression and effects on synapse formation.

## **The Efficacy of Blue Light in Decreasing Physiological Fear Responses**

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Mental health issues involving the psychological concept of fear conditioning are rapidly increasing in prevalence among today's society. Fear conditioning commonly affects individuals in the form of PTSD, generalized anxiety disorder, and specific phobias. Specific phobias elicit irrational fear in individuals when there is no apparent threat present. Specific phobias can decrease an individual's quality of life by preventing them from engaging in activities and occupying certain environments. Blue light has been found to increase serotonin levels, which are relatively low in individuals exhibiting anxiety. The purpose of this study is to determine if blue light therapy decreases physiological fear responses in individuals experiencing specific phobias. Using EEG, fNIRS, ECG, and EMG, an individual's physiological fear response will be measured upon exposure to a fear-inducing stimulus. Blue light therapy will then be administered for 30 minutes, and physiological readings will be collected a second time. Final analysis will be executed by calculating asymmetry relation ratio of the frontal brain area and utilizing t-test methods.

## Exploring the Relationship between Migraines, Blood Flow, and Oculomotor Dysfunction

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**BACKGROUND:** Migraines are a neurovascular disorder that causes extreme headaches, autonomic nervous system dysfunction, and sometimes aura. The purpose of this study is to assess how migraines, with and without visual aura, affect blood flow in the brain as well as oculomotor controls. **METHODS:** Participants who were healthy (H, N=13), and had migraines without aura (MO, n=14), and migraines with auras (MA, n=13) ( completed two trials of oculomotor tests while simultaneously recording oxyhemoglobin and deoxyhemoglobin levels through an fNIRS system. The fNIRS data was filtered with a lowpass filter of 0.1 and obtained through Oxysoft. Visual motor control, including horizontal, vertical, and circular smooth pursuit, was assessed with a RightEye system. An univariate analysis ( $p < .05$ ) was conducted to examine differences between groups for both fNIR and eye data. **RESULTS:** There were no significant findings in the frontal lobes between groups. However, the right and left temporal lobes showed a significant difference in total hemoglobin (mg/dL) between the H and the MA group ( $p = .0045$ ). There was no difference between the MO and MA groups in the temporal lobes. Significant difference in efficiency error ( $\geq 7$  mm off from the target location) in both the vertical and circular smooth pursuit between the H and MA groups ( $p = 0.034$ ;  $p = 0.012$ , respectively). **CONCLUSIONS:** People who suffer from migraines with aura presented decreased efficiency in 2 out of the 5 oculomotor tasks when compared to a healthy group as well, and a group of migraine suffers with no aura. Additionally, the MA group presented decreased blood flow in the temporal regions of the brain when compared to the other groups.



## **ADAP1/Centaurin- $\alpha$ 1-Bid Signaling in Alzheimer's Disease**

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**ADAP1/Centaurin- $\alpha$ 1 (CentA1)** is a brain-enriched and highly conserved, Arf6 GTPase-activating and Ras-anchoring protein. ADAP1 is involved in dendritic outgrowth and arborization, synaptogenesis and axonal polarization via regulating the dynamics of actin cytoskeleton. Increased level of ADAP1 and its association with amyloid plaques in the human Alzheimer's disease (AD) brain, suggest a role for this protein in AD progression. To further dissect the role of ADAP1/CentA1 in neurodegeneration, we crossed CentA1 KO mice with the hAPP-J20 mouse model of AD, followed by evaluation of behavioral and neuropathological hallmarks of the disease and gene expression profiling. Spatial memory evaluated by the Morris Water Maze test showed significant impairment in J20 mice, that was rescued by lack of CentA1. Neuropathological hallmarks of AD such as dendritic spine elimination, deposit of amyloid plaques and neuroinflammation were all significantly reduced in AD model mice on CentA1 KO background. To identify molecular mechanisms involved in AD phenotype rescue, we performed transcriptome profiling using Nanostring nCounter Neuropathology and Neuroinflammation panels (880 genes). We found significant upregulation of genes associated with apoptosis and gliosis in the brain of hAPP-J20 mice. CentA1 KO rescued this phenotype by reducing the level of the pro-apoptotic protein, Bid. In summary, our data indicates that CentA1 is required for progression of AD phenotypes and that targeting CentA1 signaling might have therapeutic potential for AD prevention or treatment.

## Rab10 in Neuro-Immune Crosstalk Associated with Alzheimer's Disease

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As the life expectancy of human population increases globally, the prevalence of neurodegenerative disorders such as Alzheimer's disease (AD), Parkinson disease (PD), and Huntington disease (HD) is expected to soar. A recent focus in the field of drug discovery has been the identification of factors that mediate molecular neuroresilience against neurodegeneration. One such resilience factor is the small GTPase, Rab10, involved in the pathogenesis of AD and PD. A rare variant of Rab10, that reduces Rab10 activity was shown to provide resilience even in individuals at high-risk for AD. The aim of this project was to identify the molecular mechanisms of Rab10-dependent neuroresilience, using heterozygous conditional knockout Rab10 (Rab10<sup>+/-</sup>) mice. Here we show that in the brain of Rab10<sup>+/-</sup> mice, the baseline activation status of the microglia (Iba1-immunoreactivity) in the hippocampus is significantly reduced, while no significant difference was observed for astrocytes (as indicated by GFAP immunoreactivity). To gain mechanistic insights, we treated organotypic hippocampal slices with oligomeric amyloid (oA $\beta$ 42) and measured the release of pro-inflammatory cytokines into the culture medium. We found significant decrease in the release of IL1- $\beta$ , TNF $\alpha$  and IFN $\gamma$  from Rab10<sup>+/-</sup> hippocampal slices compared to littermate Rab10<sup>+/+</sup> slices. Next, we evaluated the baseline activation of the peripheral immune system in Rab10<sup>+/-</sup> mice using flow cytometry analysis of mononuclear cells isolated from the spleen. In these experiments, single cell spleen suspensions were stained with antibodies specific to mononuclear cell markers. We found a significant difference in Natural Killer cells, lymphocytes (upregulated in Rab10<sup>+/-</sup> mice), and naïve CD4<sup>+</sup> cells (downregulated in Rab10<sup>+/-</sup> mice). Our data suggest a role for Rab10 in innate immunity that has been shown to contribute to the progression of AD neurodegeneration. By attenuating neuroinflammation and modulating immune cell phenotypes, Rab10 reduction offers a promising therapeutic avenue for prevention or treatment of AD.

# Clinical Poster Abstracts

(listed by presenting author in alphabetical order)

## **Cerebral Hemorrhage in Setting of Cerebral Arteriovenous Malformation with Concurrent Metastatic Renal Cell Carcinoma Not Previously Recognized Clinically: A Novel Cooccurrence**

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**Background:** Renal cell carcinoma (RCC) predominantly metastasizes to the lung, bone, and liver, while occurrences of brain metastases are less frequent, constituting 8.1% of all metastatic neoplasms. Progression of RCC can be attributed in part to its extensive vascularity and pronounced angiogenic profile. Likewise, RCC often exhibits a vascular-like appearance on imaging modalities due to its capacity to secrete angiogenic growth factors. In previous reports, RCC has been initially misidentified as arteriovenous malformations in various regions of the body. Herein, we present a case of metastatic RCC to the brain in association with an arteriovenous malformation (AVM).

**Methods and Materials:** Electronic medical records and imaging studies were reviewed. A PubMed.gov literature search was conducted using appropriate keywords.

**Results:** A 69-year-old woman presented with sudden-onset headaches. Brain imaging revealed a right parietal intracranial hemorrhage. Further evaluation via a 6-vessel cerebral angiogram uncovered a 4.5 cm right parietal arteriovenous malformation, fed predominantly by branches of the middle cerebral artery. Subsequent CT scans of the chest, abdomen, and pelvis identified a 5.7 cm mass in the left upper pole and a 4.2 cm mass in the left lower pole of the kidney. Histological examination revealed an abnormal collection of blood vessels within the subarachnoid space, gliotic neuroparenchyma, and neoplasm. Arterial-type vessels displayed size variation with thickened media and internal elastic lamina, while vein-type vessels exhibited fibrosis and obliteration within admixed neuroparenchyma, consistent with an arteriovenous malformation. Approximately 20% of the specimen was composed of clear cells with a nested architecture, surrounded by a rich vascular network demonstrating expression of CK8/18, CD10, PAX-8, and RCC, consistent with metastatic renal cell carcinoma. Whether the hemorrhage arose from a rupture in the AVM or hemorrhage within the neoplasm is uncertain. Several reports of metastasis of lung carcinomas to a brain AVM have been reported. To our knowledge this is the first report of metastasis of RCC to an arteriovenous malformation.

**Discussion:** Metastatic RCC often appears as a highly vascular entity on imaging, occasionally resembling a vascular malformation. In cases of suspected arteriovenous malformations, clinicians should also consider the possibility of metastasis from an angiogenic primary neoplasm.

# Neurosarcoidosis Presenting with Non-Pulmonary Symptoms: Hydrocephalus and Vasculitis-Related Stroke as an Uncommon Presentation of a Common Disease

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**Background:** Sarcoidosis is a multisystem, granulomatous disease of unknown etiology. While pulmonary symptoms (most commonly shortness of breath) are present and predominate in most patients with sarcoidosis, some patients may have non-pulmonary symptoms as the primary presentation. Central nervous system involvement by sarcoidosis constitutes a minority of the cases and commonly manifests with cranial nerve (CN) symptoms, often CN III. We report a patient who presented with hydrocephalus-related symptoms along with stroke-like manifestations due to ischemic central nervous system changes in the context of vasculitis.

**Methods and Materials:** Clinical features were summarized from the patient's medical record. Radiologic and histopathologic features were reviewed. Literature searches were undertaken using relevant key words.

**Case Report:** The patient is a 27-year-old man who presented with intermittent headaches with progressive dizziness, ataxia, and blurred vision. Communicating hydrocephalus was diagnosed and a ventricular-peritoneal shunt was placed. Imaging of his brain also identified (1) inferior cerebellar cortical infarctions, subacute, bilateral, in the PICA territories, (2) old infarctions involving basal ganglia and occipital lobes, and (3) leukoencephalopathy. Toxic-metabolic, global hypoxic-ischemic, infectious, and inflammatory etiologies were considered less likely. Thoracic CT scans identified enlarged mediastinal and axillary lymph nodes. Serum calcium was elevated. Serum and cerebrospinal fluid angiotensin converting enzyme (ACE) levels were normal. CSF evaluation was negative for (1) meningitis/encephalitis and (2) paraneoplastic encephalopathy by a screening panel. A weakly positive elevation in myelin basic protein level was noted but no oligoclonal bands were identified. Biopsy identified granulomatous inflammatory infiltrates, non-caseating, multifocal, with subarachnoid and parenchymal blood vessel wall damage consistent with vasculitis. Special stains for acid fast bacilli and fungi were negative. Combined findings consistent with an inflammatory granulomatous disease process and consistent with sarcoidosis.

**Discussion:** While pulmonary symptoms predominant in sarcoidosis, sarcoidosis can affect nearly every organ system and presentation with non-pulmonary symptoms is occasionally seen. Diagnosis is made in the context of a thorough workup including CT scan of the chest, abdomen, and pelvis. Symptoms related to parenchymal vasculitis is an uncommon presentation and brain biopsy is often necessary given the low sensitivity of tests including ACE levels.

## Large Occipital Encephalocele: Case Report and Review of the Literature

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**Background:** Encephaloceles (also known as meningoencephaloceles), along with anencephaly, rachischisis, and myelomeningocele, fall within the spectrum of neural tube defects, affecting approximately 0.8-4 out of every 10,000 live births worldwide. They manifest as cystic congenital deformities marked by the protrusion of central nervous system structures through a cranial defect with associated arachnoid and cerebrospinal fluid. Herein, we report a case of a male infant with a prenatally diagnosed large occipital encephalocele.

**Methods and Materials:** Clinical features were summarized from the patient's medical record. Key macroscopic and histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Report:** A large occipital encephalocele was identified in utero in a male fetus in the context of elevated maternal alpha-fetoprotein levels. The encephalocele progressively increased in size during the pregnancy while the head circumference was less than the first percentile with fetal growth restriction noted. He was delivered via Caesarean section at 38 weeks gestation. A CT scan and subsequent MRI evaluation of the head revealed an occipital encephalocele associated with a midline defect in the posterior calvarium. The patient underwent surgery for repair of the encephalocele. A vascular pericranial flap was reflected over the dural defect. The cranial defect was closed using autologous bone harvested from the right parietal skull region. Macroscopic examination of the meningoencephalocele, measuring 10.5 x 9.4 x 4.5 cm, revealed nodules of malformed cerebrum, 2.5 x 2.5 x 4.5 cm, enclosed by cystically dilated meninges associated with skin and subcutis filled with clear fluid intermingled with areas of clotted blood. Microscopic analysis identified dystrophic lamination and calcifications. The meninges were well-developed. No evidence of cerebellar parenchyma or other hindbrain elements was identified.

**Discussion:** Encephaloceles are a developmental malformation characterized by herniation of brain into a meningotheelial-lined sac, occurring as an isolated finding or alongside syndromes and multiple malformations. The prognosis for occipital and parietal encephaloceles is related to the size and location of the encephalocele, the presence or absence of cerebellum or other hindbrain contents within the herniated tissue, the occurrence of hydrocephalus, and the presence or absence of concurrent cerebral malformations.



# Intracranial Cerebral Fungal Infection in the Context of Immunosuppression Due to Diabetes Mellitus and Treatment of Chronic Lymphocytic Leukemia: Comparison of Ischemic vs. Hemorrhage Complications

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**Background:** Fungal infection of the central nervous system (CNS) is rare and most commonly affects immunocompromised patients. We report two cases, presenting variably with hemorrhage and infarct.

**Methods and Materials:** Clinical features were summarized from the patients' medical record. Key histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Reports:** Case A: A 23-year-old man with a history of diabetes mellitus type 1 presented with diabetic ketoacidosis. During his hospitalization, chest CT scans identified a right sphenoid sinus opacification and multiple areas of consolidation in his lungs. Initial CT scan of his brain was negative but after being found unresponsive repeat CT scan identified a right frontal lobe parenchymal hematoma. Patient B: A 75-year-old man with a history of chronic lymphocytic leukemia, undergoing therapy with Imbruvica, presented with headache, decline in cognitive ability, generalized weakness, and blurry peripheral vision in the right eye. CT and MRI scans identified abnormal left parieto-occipital region changes raising the differential of a subacute infarct and a high-grade neoplasm and resection was undertaken. He had right maxillary sinus air-fluid levels. In both cases histologic findings identified vascular-invasive hyphal fungi most consistent with Mucorales species. While ischemic injury is most commonly identified in the setting of mycotic vasculitis, occasional cases manifesting with hemorrhage have been identified.

**Discussion:** This report documents a comparison of two patient cases of central nervous system fungal infections that resulted in different cerebrovascular complications in order to compare precipitating factors and suggest why some patients may be predisposed to aneurysm or intracerebral hemorrhage resulting in progressive disease and poor prognosis.

## **Focal Cortical Dysplasia in Proximity to Arteriovenous Malformation: Report of Four Cases and Review of the Literature**

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**Background:** Central nervous system arteriovenous malformations (AVMs) and focal cortical dysplasia (FCD) are congenital lesions which arise during fetal development. We present three case in which FCD was identified in proximity to an AVM on surgical resection specimens.

**Methods and Materials:** Clinical features were summarized from the patients' medical record. Key histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Reports:** Four patients underwent resection of an AVM. The patient's ranged in age from 25-39 years; two were men and two were women. Three of the patients had a history of seizures, one with onset approximately three years prior to resection and a family history of seizures, the other two with onset at the time of presentation. Resection was undertaken and FCD was identified in intact cortex in proximity to the resected AVM. In each case there were persistent, radial columns or laminae of neurons (lamination) in proximity to arteriovenous malformations with neurons showing evidence of granular cell and pyramidal cell maturation but lacking horizontal migration in the cortex, consistent with designation as International League against Epilepsy (ILAE) FCD type Ia. In addition, in one case, the patient with a family history of seizures, dysmorphic neurons and balloon cells were identified, consistent with designation as FCD type IIb. Given the presence of FCD in proximity to an AVM, each of these cases can be classified as FCD IIIC. While the presence of a cortical AVM might be predicted to lead to altered, dysplastic cortical development, only rare reports have identified this finding, the frequency of FCD in proximity to AVM is not well characterized in the literature.

**Discussion:** Clinical correlation is critical to appropriate interpretation. Both AVMs and FCD can provide a potential anatomic substrate for seizures and it is impossible to designate which abnormality was seizuregenic. However, in the patient with FCD Type IIb and a family history of seizures, the FCD is more likely to have been clinically relevant to her seizures.

## **Atretic Meningoencephalocele: Case Report and Review of the Literature**

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**Background:** Neural tube defects include anencephaly, meningoencephalocele, and myelomeningocele. Lesions range from large and extensive to subtle and occult. We report a case of a 7-year-old girl with an encephalocele.

**Methods and Materials:** Clinical features were summarized from the patient's medical record. Key macroscopic and histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Report:** The patient is a 7-year-old girl who presented with a midline posterior parietal scalp mass-at birth. As a child, the lesion would increase in size when she was crying and was noted to be pulsatile. It has been slowly increasing in size and is now painful and now non-pulsatile. Examination revealed a palpable, midline parietal region scalp mass, in an area of scalp lacking hair growth, with no leakage of fluid, exudate, or other material; and no skin color changes. At an outside institution, previous imaging of the brain revealed normal intra-axial structures including ventricular system; a persistent falcine sinus (a connecting vein between the vein of Galen to the superior sagittal sinus), and emissary veins extending to an extracranial venous malformation in the parasagittal parietal scalp. Radiologic diagnosis was sinus pericranii. Treatment was deferred. On recent imaging at our institution, the lesion was 1.7 X 2.2 X 1.7 cm with features suggesting atretic encephalocele. Intraoperative evaluation identified a stalk at the base of the lesion; clear fluid was present on resection; a focal skull defect was present and closed. No trans-osseous venous structures were noted. Histologic evaluation revealed a meningoencephalocele.

**Discussion:** Encephaloceles are a developmental malformation characterized by herniation of brain into a meningotheelial-lined sac, occurring as an isolated finding or in syndromes. In contrast, sinus pericranii is an abnormal transosseous venous connection between intracranial and extracranial venous structures, not thought to be related to a neural tube defect. The prognosis for occipital and parietal encephaloceles is related to the size and location of the encephalocele, the presence or absence of cerebellum or other hindbrain contents within the herniated tissue, the occurrence of hydrocephalus, and the presence or absence of concurrent cerebral malformations.

# Primary Central Nervous System Lymphoma as a Manifestation of Post-Transplant Lymphoproliferative Disease in Solid Organ Transplant Patients: Report of Four Cases

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**Background:** Individuals who receive solid organ transplants need to be maintained on immunosuppressive medications to prevent transplant rejection. This immunosuppressed state can predispose to infection-associated neoplastic complications. We present four cases of central nervous system Epstein-Barr virus (EBV)-related posttransplant lymphoproliferative disorder (PTLD) in individuals with solid organ transplants.

**Methods and Materials:** Clinical features were summarized from the patients' medical record. Key histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Reports:** Patient A was a 62-year-old woman who received a kidney transplant 15 years previously. Magnetic resonance imaging (MRI) of her brain identified a left frontal lobe lesion. Patient B was a 71-year-old woman who is 15 years status-post renal transplant. MRI of her brain revealed a left temporal lobe mass and a left frontal lobe mass. Patient C was a 72-year-old man who is 16 years status-post renal transplant. An MRI study of his brain identified a medial left frontal lobe lesion. Patient D was a 70-year-old man who is 3 years status-post liver transplant. Imaging of his brain revealed a left frontal lobe lesion. In each case, biopsy of the patient's brain lesion revealed an EBV-positive diffuse large B-cell lymphoma with no evidence of lymphoma elsewhere in their body, consistent with primary central nervous system lymphoma. Combined findings are also consistent with designation of the lymphoma as an EBV-associated PTLD.

**Discussion:** In solid organ transplant recipients, PTLD is the most commonly associated malignancy. The patient's degree of T-cell immunosuppression in the context of an underlying, dormant EBV infection in the recipient or in the organ donor appears to be a critical risk factor for developing PTLD. Primary central nervous system PTLD most commonly is associated with kidney transplants, often occurs years after transplantation, usually follows an aggressive course, and most commonly shows EBV expression in neoplastic cells.

## **Endovascular Mechanical Thrombectomy as Treatment of Acute Ischemic Stroke: Histologic Assessment of Specimens and Clinical-Pathologic Correlation**

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**Background:** Treatment of ischemic stroke has most commonly relied on therapeutic administration of tissue plasminogen activator (TPA) with the goal of preserving salvageable, ischemically compromised brain parenchyma. However, TPA administration can be initiated only within 4.5 hours of the onset of symptoms of stroke. Endovascular mechanical thrombectomy provides a new tool for treatment of ischemic stroke and can be performed up to 24 hours after onset in select patients resulting in a reduced rate of death and disability.

**Methods and Materials:** Following their removal, thrombectomy specimens were evaluated histologically on three levels using hematoxylin and eosin stain and by trichrome stain. Histologic features relevant to the age of the clot were assessed including evidence of white blood cell changes (neutrophil nuclear loss, macrophage activation, and hemophagocytosis) and evidence of organization (endothelial cell or fibroblast invasion of the clotted blood) with reviewers blinded to clinical history. A review of the patients' electronic medical record was undertaken and correlation of histologic findings with clinical history was undertaken. A literature search was conducted using key words including thrombectomy, endovascular, and mechanical thrombectomy.

**Results:** Thrombectomy specimens from 5 men and 6 women, 43- to 91-years-old, who presented with clinical and radiologic features of ischemic stroke were evaluated. Early organization including endothelial cell invasion was noted in 5 specimens consistent with days-old thrombus while minimal organization was noted in the other specimens, consistent with hours- to days-old thrombus. The two specimens with the most advanced organization were seen in a patient with a previous myocardial infarct and an apical left ventricle lesion being treated with warfarin and the left atrium in a patient with atrial fibrillation subtherapeutic on warfarin, respectively. The exact origin of the other emboli was not known clinically. At least some of the thrombi originated from complex atherosclerotic plaques, but no evidence of atherosclerotic debris was identified.

**Conclusions:** Histologic evaluation of thrombectomy specimens can provide important data with the goal of helping to identify the source of the embolus and providing data to prevent recurrent emboli. In addition, this evaluation provides an important documentation in the clinical chart regarding the thrombectomy procedure.

## Recurrent Langerhans Histiocytosis of the Skull: Case Report and Review of the Literature

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**Background:** Langerhans cell histiocytosis (LCH) is a hematologic disease process where Langerhans cells proliferate as a localized or disseminated disease process, most commonly occurring in children under 15 years of age with an incidence rate of 4.5 per million children. One variant of LCH, eosinophilic granuloma, is most commonly identified in lesions within the skull as a single or multiple osteolytic lesions which may be painful. We present a case of a child with a history of disseminated LCH with recurrence in the skull.

**Methods and Materials:** A review of the patient's electronic medical record was undertaken and radiologic and histologic findings were reviewed. A literature search was conducted using appropriate key words.

**Case Report:** The patient is a 5-year-old boy. He presented initially at age 2 with left eye swelling. Imaging of his head revealed (1) a lesion in the right orbit, 2.6 cm, with mass effect on the left globe, and (2) a 2.8 cm left superior occipital skull lesion, lytic. An excisional biopsy of skull lesion revealed LCH with a BRAF V600E mutation. Right iliac crest bone marrow biopsy revealed involvement. He was treated with chemotherapy and scans showed no clear evidence of recurrent or persistent disease, although there was a subtle asymmetric T2 hyperintensity within the left orbit. He subsequently developed frequent headaches along with a new, palpable bump on his head. CT and MRI imaging of his head revealed (1) a new left parietal skull lesion, lytic, avidly contrast-enhancing lesion, 2.1 cm. The lesion was resected and histologic and immunohistochemical evaluation revealed recurrent LCH.

**Conclusions:** LCH can present in the skull as a localized lesion or as part of a disseminated disease process. The recurrence rate after treatment varies from 5.7% recurrence in unifocal bone disease, 12.5% reactivation in single system bone disease, and 23.8% recurrence in multifocal bone disease. When disseminated, with involvement of bone marrow, liver, or spleen, treatment is more challenging and survival is reduced. This case illustrates the challenges of effective treatment of LCH, particularly when disseminated, and the need for vigilant followup.

## **Schwannoma Mimics: Neurofibroma and Myopericytoma Presenting as Painful Soft Tissue Extremity Lesions**

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**Background:** Painful lesions in the soft tissue of the extremities evoke a differential diagnosis including peripheral nerve sheath tumor and, specifically, most commonly, Schwannoma. Diagnostic evaluation often includes ultrasound or/and magnetic resonance imaging (MRI) studies with in some cases resection with the goal of relieving the patient's pain. We present three cases in which the clinical diagnosis of a painful extremity soft tissue tumor errantly favored Schwannoma.

**Methods and Materials:** Clinical features of the three cases were summarized from the patients' electronic medical records. Histopathologic evaluation was undertaken.

### **Case Reports:**

Case A: A 72-year-old woman presented with pain and numbness in the dorsum of her left lower extremity. Ultrasound identified a 3.8 cm mass associated with the common fibular nerve. Resection was undertaken. Histopathologic and molecular evaluation revealed a neurofibroma. The patient's pain resolved following resection of the lesion.

Case B: A 55-year-old man presented with right arm pain. MRI identified a 1.0 cm mass adjacent to the lateral epicondyle. Resection was undertaken. Histopathologic evaluation revealed a proliferation of spindle-shaped cells consistent a myopericytoma. The patient's pain resolved following resection of the lesion.

Case C: A 46-year-old woman presented with left lower extremity pain and paresthesias. Ultrasound revealed a 0.25 cm nodule in the upper calf; the lesion could not be identified by MRI. Histopathology revealed a blood vessel partially obliterated by a proliferation of spindle-shaped cells consistent with diagnosis as a myopericytoma. The patient's pain resolved following resection of the lesion.

**Discussion:** Definitive diagnosis of soft tissue lesions requires histopathologic evaluation. Clinical pitfalls in accurate diagnosis include ascribing too much certainty to radiologic modalities including ultrasound studies and lack of generation of a thorough differential diagnosis. Given the benign nature of each of the patients' neoplasms, misdiagnosis favoring Schwannoma did not lead to any adverse outcome.

## Neurosarcoidosis Presenting with Non-Pulmonary Symptoms: Hydrocephalus as an Uncommon Presentation of a Common Disease

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**Background:** Sarcoidosis is a multisystem, granulomatous disease of unknown etiology. Respiratory deficits are the most common presenting symptom in most patients due to pulmonary interstitial injury and hilar and mediastinal lymph node involvement. However, sarcoidosis can affect nearly every organ system and presentation with non-pulmonary symptoms is occasionally seen. We report a case of neurosarcoidosis presenting with symptoms related to obstructive hydrocephalus.

**Methods and Materials:** Clinical features were summarized from the patient's medical record. Key histopathologic features were reviewed. A literature search was undertaken using relevant key words.

**Case Report:** A 29-year-old woman presented to the emergency department with a persistent headache associated with nausea, vomiting, and visual disturbances. Lumbar puncture to rule out meningitis identified an elevated opening pressure; culture was negative. Brain imaging identified non-communicating hydrocephalus with periependymal enhancement, including around the aqueduct of Sylvius and at the massa intermedia and anterior commissure. A broad differential diagnosis was considered (inflammatory, infectious, and neoplastic). CT scan of her chest identified bulky mediastinal and hilar lymphadenopathy. Emergent endoscopic third ventriculostomy with biopsy of the ependymal lesion was performed. Pathological examination revealed non-caseating granulomatous inflammation. Acid fast bacillus and fungal stains were negative. Laboratory tests were significant for an elevated serum calcium level; angiotensin-converting enzyme level was normal. Aggregate findings were most consistent with sarcoidosis with central nervous system (CNS) involvement.

**Discussion:** Sarcoidosis with CNS involvement poses diagnostic challenges due to non-specific clinical and radiological findings. Approximately 5% of patients with systematic sarcoidosis have CNS involvement, most commonly manifesting with cranial nerve (CN) symptoms. Hydrocephalus is an uncommon finding in neurosarcoidosis, observed in 6-9% of cases. Clinical awareness, CT screening for other potentially affected organs and timely biopsy are crucial for the diagnosis. Neurosarcoidosis has an overall good prognosis, with 90% of cases improved over time. However, cases presenting with hydrocephalus have a worse long-term prognosis with a mortality rate of up to 75%.



## Seizures in a 3-Year-Old Boy with a Left Frontal Lobe Lesion on Magnetic Resonance Imaging: Differential Diagnosis and Review of Focal Cortical Dysplasia

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**Background:** Epilepsy is the most common neurologic disorder in children with an incidence of 33-82 cases per 100,000 per year. We describe a case of focal cortical dysplasia type IIb as the etiology of a child's seizures. The target audience for this presentation is all neuroscience-associated health care providers.

**Case Report:** A 3-year-old boy presented to ECU Health Pediatric Neurology in August 2022 with an approximately 1-month history of seizures. The seizures included a sudden stop in his behavior / activity, right arm jerking with progression to right head version (change in normal position) and eye upgaze and on occasion generalized, tonic flexion of upper extremities with mild, clonic component, with one episode of loss of consciousness with shaking movement of his arms and legs. Electroencephalogram evaluation identified phase reversals and sharp wave discharges localized over the left central temporal region. Magnetic resonance imaging of his brain identified a left anterior-superior frontal lobe lesion. Resection was undertaken and histologic and immunohistochemical evaluation identified features consistent with the diagnosis of focal cortical dysplasia Type IIb. On followup three months after his operation he was no longer having obvious seizures and treatment with Trileptal was maintained.

**Summary of Literature Review:** Cortical dysplasias are developmental abnormalities that arise during fetal development when precursor cells from the germinal matrix fail to migrate to the cerebral cortex and differentiate resulting in aberrant neural connections. They represent a common cause of seizures. Approximately 50% of patients with seizures have an identifiable etiology for the seizures using a combination of magnetic resonance imaging, electroencephalogram, and laboratory studies to rule out metabolic or autoimmune causes. Many of the 50% of cases without an identifiable etiology have underlying cortical dysplasia. Resection of the malformation often results in significant amelioration of the patient's seizures.

**Conclusions:** Focal cortical dysplasia is a common cause of childhood epilepsy with many cases not visualized on imaging studies. When imaging abnormalities are identified, the differential diagnosis includes a neoplasm and cortical dysplasia, with resection necessary for definitive diagnosis and guidance of further treatment if necessary and with the goal of amelioration of seizures.

## **Papillary Tumor of the Pineal Region Lacking Papillary Features in a 29-Year-Old Man: A Rare Neoplasm with Risk of Recurrence and Leptomeningeal Dissemination**

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**Background:** Primary pineal region neoplasms are uncommon. We describe a case of a rare neoplasm, the papillary tumor of the pineal region (PTPR), and summarize the literature on this neoplasm.

**Methods and Materials:** Clinical, imaging, and pathology findings from the patient were summarized. A literature search using key words including primary pineal neoplasm and papillary tumor of the pineal region.

**Case Description:** The patient was a 29-year-old man who presented with intermittent headaches and dizziness. Magnetic resonance imaging (MRI) of his head identified (1) a pineal region mass, 1.8 X 1.3 X 1.4 cm, T2/FLAIR hyperintense, with contrast enhancement, with mild mass effect on tectum and minimal narrowing of the cerebral aqueduct which remained patent, (2) mild to moderate ventriculomegaly without transepidermal edema, and (3) a retrocerebellar cyst with imaging features consistent with an arachnoid cyst with mild hypoplasia of the vermis. Laboratory evaluation revealed normal serum alpha-fetoprotein, beta-hCG, and placental alkaline phosphatase levels. Resection was undertaken and combined histologic, immunohistochemical, chromosomal microarray evaluation, and methylation analysis revealed findings diagnostic of PTPR subclass A, World Health Organization grade 2, although papillary architecture was not recognized.

**Literature Review:** PTPRs are rare, neuroepithelial lesions probably originating from the subcommissural organ. They were first described in 2003 and have been included as an entity in the World Health Organization Tumors of the Central Nervous System since the 2007 edition and constitute fewer than 1% of all central nervous system neoplasms with fewer than 200 described in the literature to date. While histologically resembling ependymomas, papillary architecture is typically identified. Immunohistochemistry mirrors findings in this case with expression of cytokeratin, S100, and CD56 by neoplastic cells and typically lack of expression of antigens characteristic of ependymoma, glial fibrillary acidic protein and epithelial membrane antigen. Methylation analysis is critical to diagnosis.

**Conclusions:** PTPRs are a rare neoplasm and should be in the differential diagnosis of a pineal region lesion. The lack of papillary architectural features in this case with immunohistochemistry and molecular evaluation findings diagnostic of PTPR could represent limitations of sampling or reflect one morphologic phenotype of the neoplasm.