Encoding and Decoding Behavior: Computer Vision for Genetic and Neural Analysis

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Behavior is a window into the latent, unobservable states of an organism and our ability to infer meaning from behavior experiments relies on the richness of the latent information encoded in the behaviors we quantify. By practical necessity this latent information has been restricted by behavioral data with limited complexity, diversity, duration, and context, constraining the insight that can be derived from these experiments. Computer vision, the application of machine learning principles to quantify visual information, is undergoing a revolution in sophistication and accessibility that is empowering behavioral research to transcend these historic limitations. This symposium will highlight how computer vision approaches accelerate and heighten insights in genetics and neuroscience, with emphasis placed on open-source tools and methodologies for 2D and 3D pose estimation, supervised and unsupervised behavioral segmentation, and the interpretation of these sophisticated behavioral datasets.The four speakers will demonstrate how these technologies can access rich behavioral indices, reveal temporal relationships between behaviors, and enable the study of complex social interactions. Collectively, their work illustrates how computer vision enhances our understanding of genetic and neural mechanisms underlying behavior. Attendees will gain practical insights into available tools, strategies for integrating these approaches into their own research, and opportunities to engage with these experts in the field:Co-chair Greg Corder will present his lab's work integrating computer vision-derived behavioral transitions with longitudinal neural recordings in mice. This approach has uncovered a persistent shift in cortical activity following nerve injury, reflecting an affective chronic pain state. By building a gene therapy that targets opioid-sensitive neurons in the cingulate his lab recapitulates the analgesic effects of morphine during chronic neuropathic pain, offering a new strategy for precision pain management. Co-chair Jacob Beierle will discuss his research using supervised and unsupervised learning to extract large behavioral indices to describe the genetic structure of opioid withdrawal across genetically diverse mouse populations. By comparing the heritability and genetic correlation of single traits versus composite behavioral indices, this work underscores the limitations of single outcome measures and highlights the value of multidimensional behavioral analysis in complex disease research. Ugne Klibaite will share her work applying 3D pose estimation and multi-scale behavioral analysis techniques to investigate social differences across genetic models of autism spectrum disorder in rats. Her suite of tools capture and quantify individual behaviors, interaction motifs, and patterns of social touch. Her research demonstrates how computer vision and quantitative phenotyping can reveal subtle social deficits and more broadly aims to capture the principles that underlie social behavior and social disruption.Catherine Schretter will discuss work using a modular and adaptable behavioral analysis pipeline to uncover neural circuits regulating aggressive engagement and disengagement across sexes in Drosophila melanogaster. Regulating aggression is critical for survival and, in humans, dysregulation of aggression is associated with neuropsychiatric disorders, including PTSD. Her work leveraging this analysis pipeline alongside the fly's powerful genetic toolkit and connectomic datasets generates key insights into how neural circuits integrate sensory cues and internal state to regulate complex social decisions.All speakers have confirmed their participation.

Dissecting the Development of Opioid Use Disorder Using Cross-Species Systems Genetics Approaches

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All four talks in this symposium investigate opioid use disorder (OUD) as a complex trait influenced by genetic variation, neurobiological adaptations, and environmental influence. The speakers use both human studies and rodent models, providing a cross-species perspective to examine facets of OUD risk, integrating approaches such as behavioral genetics, molecular profiling, and system genetics approaches. Collectively, their work highlights how heritability of drug self-administration shapes downstream vulnerability to tolerance and OUD, how neuroplasticity and genetic mapping reveal loci associated with behavioral phenotypes, and how transcriptomic investigations bridge acute and protracted withdrawal across species. Professor Hao Chen utilizes the escalation of oral oxycodone use to map intake behavior across 49 female and 45 male rat strains from the Hybrid Rat Diversity Panel (HRDP). GWAS and QTL mapping using GEMMA with LOCO revealed a significant region on chromosome 1 containing Cyp2r1 and Pde3b, implicated in vitamin D metabolism. These findings implicate a new pathway for future study. Graduate student Tolulope (Johnson) Ajanaku will present a summary of results from an ongoing study also using the HRDP to identify genes and pathways associated with opioid-related behaviors. Mr. Ajanaku's recent analysis of 20 strains has shown that chronic intravenous self-administration of oxycodone in these strains leads to three distinct outcomes: most strains develop robust opioid tolerance, but others display analgesic sensitization or resistance. Sex-specific opioid-induced hyperalgesia was also observed, where males exhibit greater increases in thermal sensitivity compared to females following oxycodone self-administration. Assistant Professor Brittany Kuhn leverages a multidimensional preclinical model using heterogeneous stock rats to dissect behavioral and genetic correlates of OUD vulnerability and resiliency. Dr. Kuhn's work combines comprehensive GWAS (n = 874) and neurobiological profiling, identifying heritable phenotypes and genetic loci for nociception, opioid motivation, and resilience. Critically, she has found that neuroplastic changes such as alterations in the extracellular matrix, microglia, and dendritic spine morphology in brain regions regulating reward and motivation are crucial determinants of addiction risk and resilience. Associate Professor Marianne Seney's research demonstrates that opioid addiction leads to major changes in gene expression in the human brain, with clear differences seen based on both sex and stage of opioid use or withdrawal. In women with OUD, patterns of gene activity in the nucleus accumbens closely matched those seen in female rodents across all stages of opioid exposure. For men, the gene expression changes were most similar to those observed in male rodents specifically during withdrawal. Dr. Seney also found that these shifts involve changes in gene regulation and how the brain's DNA is packaged and modified, highlighting that acute opioid exposure and long-term use leave distinct molecular signatures depending on sex and history of drug use. Collectively, these studies characterize the importance of drug use trajectory on OUD, including initial pain sensitivity, initial acute response to opioids, escalation of use, motivation, tolerance, and resilience in the context of a genetic model, providing evidence that different genetic factors may contribute to unique stages.

Bridging the rodent to human translational gap: Marmosets as model systems for the study of Alzheimer's disease

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Neurodegenerative diseases including Alzheimer's disease (AD), are characterized by key pathological hallmarks, progressive loss of neuronal structure and function, and synaptic loss. Mild behavioral changes including subjective cognitive decline and neuropsychiatric symptoms often precede the diagnosis and may be a harbinger of disease inception and progression. Despite the success of model systems to enable progress of new treatments that attenuate pathological burden, the ability to translate clinical benefit for cognitive impairment and dementia-related behavioral syndromes remain challenging. While model systems continue to be essential, it is imperative that the appropriate model is carefully chosen for the specific research question to be addressed, with complimentary model systems necessary to capture multiple aspects of disease including detecting the earliest changes of disease inception and progression in order to stop and prevent AD.Four speakers representing diverse professional levels, disciplines, and gender identities will share recent advances in the field including novel approaches in marmosets to understand pathophysiological, genetic, and environmental mechanisms underlying AD. The first presentation, "Generation of genetically engineered marmosets with AD risk mutations" by Dr. Gregg Homanics, PhD, Professor, Department of Anesthesiology, University of Pittsburgh will discuss the successes and challenges of genetic engineering approaches in marmosets, highlighting the successful generation of genetically engineered marmosets carrying knock-in point mutations in the PSEN1 gene, that in humans confers early onset AD. The second talk entitled “Behavioral characterization of marmosets with genetic risk for AD” will feature Dr. Lauren Bailey, PhD, a postdoctoral fellow at The Aging Institute, University of Pittsburgh who will describe the comprehensive phenotypic characterization including the longitudinal behavioral and cognitive testing battery of marmosets with genetic risk for AD in comparison to genetically diverse outbred populations of aging marmosets. The third talk, entitled “Investigating primate specific cellular and molecular events that precede the onset of AD pathogenesis” by Dr. Amantha Thathiah, PhD, an Associate Professor of Neurobiology, University of Pittsburgh, will describe the comprehensive cellular modeling approaches including both iPSC-derived and directly converted iNSCs from fibroblasts to understand the earliest primate specific molecular and cellular signatures that precede behavioral changes in marmosets with genetic risk for AD. The final talk entitled “Comparative genetics of Alzheimer’s Disease: from mice to marmosets to humans” by Dr. Gregory Carter, PhD, Professor at The Jackson Laboratory, will highlight how complementary model systems are being used in the AD field to improve translation and identify novel targets for drug discovery to prevent and treat AD. This interdisciplinary symposium will emphasize the use of sophisticated translational approaches and collaborative efforts required to tackle the complex genetic and environmental factors leading to pathophysiological changes and cognitive decline in AD. The speakers have agreed to participate in this symposium co-chaired by trainee Dr. Lauren Bailey along with Dr. Stacey Sukoff Rizzo, PhD, Associate Professor of Neurobiology and Medicine, University of Pittsburgh.

From Sequence to Structure: Decoding the Gene Regulatory Grammar of Addiction

Francesca Telese

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This symposium will showcase cutting-edge research at the intersection of genetics, epigenomics, and neurobiology, offering novel insights into the molecular mechanisms that shape vulnerability and adaptation to substance use disorders (SUDs). Using diverse model systems, innovative genomic tools, and genetically informed approaches, the speakers will explore how gene regulatory processes contribute to addiction-relevant neuroplasticity, including chromatin topology, transposable element activation, R-loop formation, and genetically encoded transcriptional variability. Dr. Brad Balderson will present an integrative genetic and single-cell multiomic analysis in a large cohort of genetically heterogeneous outbred rats. Using latent factor modeling and genetic association frameworks, this work identifies naturally occurring genetic variation that influences transcriptional and epigenetic programs in dopamine D3 receptor-expressing neurons of the nucleus accumbens. These genetically driven transcriptional signatures correlate with individual differences in oxycodone intake, revealing mechanistic links between neuronal gene regulation and addiction vulnerability. Dr. Peter Hamilton will present recent data on cell-type–specific manipulation of transcriptional programs using synthetic transcription factors in medium spiny neurons of the nucleus accumbens. His team demonstrates that targeted transcriptional control of transposable element-associated regulatory regions alters gene expression networks that mediate cocaine-induced behavioral plasticity, including cocaine taking behaviors. These results implicate transposable element-linked sequences as functionally active components of the neuronal regulatory landscape that can modulate transcriptional and behavioral responses to drug exposure.Dr. Ana Pombo will present work employing Genome Architecture Mapping (GAM) combined with single-nucleus transcriptomics and chromatin accessibility to profile 3D genome reorganization in dopamine neurons following acute cocaine exposure. Her findings reveal long-lasting alterations in higher-order chromatin structure and transcriptional networks that persist for at least two weeks, well beyond the exposure period, suggesting that dynamic remodeling of chromatin architecture contributes to enduring vulnerability to relapse. Dr. Makoto Taniguchi will discuss emerging evidence that long noncoding RNAs (lncRNAs) and their DNA:RNA hybrid structures, known as R-loops, play key roles in the transcriptional control of neuronal activity-regulated genes. His group demonstrates that R-loop formation at the Npas4 enhancer is essential for establishing enhancer–promoter chromatin loops and for the subsequent induction of Npas4 mRNA during neuronal activation. Disruption of this mechanism impairs cocaine-conditioned place preference, revealing a novel molecular link between R-loop-mediated chromatin architecture and SUD-related behaviors. Together, these presentations illuminate converging mechanisms by which the genome's regulatory landscape encodes, integrates, and maintains addiction-related adaptations. The session will appeal to neuroscientists, geneticists, and molecular biologists interested in the interplay between genetic diversity, chromatin topology, and neuronal transcriptional plasticity, and will stimulate new conceptual and technical directions for understanding and treating substance use disorders.

Functional Implications of co-transmission in regulating neuroplasticity and behavior

Lewis Sherer

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Background: A fundamental and widely used mechanism for transmitting information within neural circuits is co-transmission, or the release of more than one neurotransmitter, neuromodulator, or neuropeptide from a single neuron. Co-transmission is thought to generate complementary and separable responses in circuits to produce context-appropriate responses. However, the mechanisms used by co-transmitting neurons to direct and regulate behavior remain poorly understood. Understanding how co-transmitting neurons impact neuroplasticity and circuit output is crucial for understanding how behavior is regulated. Our goal is to provide four distinct but related perspectives that showcase multiple levels of analysis, ranging from genes to circuits to brains to behavioral output, to provide unique insights into the mechanisms of co-transmitting neurons and their role in regulating neuroplasticity and behavior. These insights can lead to the development of personalized therapeutic strategies in treating neurological disorders involving co-transmitting neurons and generally contribute to a broader understanding of neurological processes. Speakers:Chair is Lewis Sherer and will introduce and give a talk. Other speakers include Andrea Cuentas-Condori, Zachary Freyberg and David Root. Speakers represent diverse professional levels (from postdoc to PI). Speaker 1: Lewis Sherer will talk about the layered inhibition that exists between an octopamine/glutamate co-transmitting neuron and its downstream target, and will describe the pre- and postsynaptic mechanisms that regulate information transfer via individual transmitter release from this neuron. Speaker 2: Andrea Cuentas-Condori will talk about a discovery platform of mechanisms of synaptic plasticity and organization of co-transmitter neurons in vivo, using the nervous system of Caenorhabditis elegans. Using this platform, she will highlight a case-study of co-transmission of glutamate and acetylcholine that is modulated by sensory experience to regulate flexible animal behavior.Speaker 3: Zachary Freyberg will talk about species-conserved sex differences associated with dopamine/glutamate co-transmission in dopamine neuron survival and behavior in the contexts of aging and models of Parkinson’s disease-related neurodegeneration. Speaker 4: David Root will discuss fundamental differences in circuits, dopamine release, and signaling of motivation-related stimuli between mouse ventral tegmental area dopamine neurons that co-transmit glutamate (glutamate-dopamine neurons) and ventral tegmental area neurons that release dopamine without glutamate (nonglutamate-dopamine neurons). We will also present data suggesting that while glutamate-dopamine co-transmitting neurons may signal salience at the neuronal level, their co-transmitters may promote valence. Relevance to IBANGS Genes, Brains & Behavior meeting:This symposium brings together a group of scientists representing a diversity of career stages and will provide the audience with new insights obtained from a breadth of organisms (C. elegans, fruit fly, rodent) and experimental approaches (behavior, circuit analysis, genetics). Taken together, the presentations will bring together different perspectives and levels of analysis regarding the important but poorly understood issue of co-transmission and its role in regulating neuroplasticity and behavior.