USC-Chen Institute Frontiers Forum on “Sensation and Motivation”

Organizers:

Dr. Li Zhang, Center for Neural Circuits & Sensory Processing Disorders;

Zilkha Neurogenetic Institute, Keck School of Medicine, USC;

& Tiaoqiao and Chrissy Chen Institute (TCCI)

Introduction

How external and internal sensory information is processed to produce proper behavioral responses has recently been actively explored. By bringing together outstanding researchers working on different sensory modalities (including visual, auditory, somatosensory, olfactory and gustatory), the forum will be focused on two general questions about sensory information processing in the brain: first, the neural circuitry mechanisms underlying the processing of behaviorally important sensory information; and second, how valence of sensory signals is assigned, encoded and transformed to produce different emotional motivations including reward seeking and avoidance. The forum will serve as a platform for exchanging the latest research progress and ideas, and aims at stimulating substantial discussions between researchers working on different sensory modalities to identify key general questions and principles as well as to foster future collaborations. The forum is co-organized by Tianqiao & Chrissy Chen Institute (TCCI) and held by the Center for Neural Circuits and Sensory Processing Disorders in Zilkha Neurogenetic Institute of USC.

The two-day meeting will be structured with a series of short talks and workshop for discussion. The forum aims at stimulating discussions between researchers working on different sensory modalities to exchange ideas, identify general questions, and foster future collaborations.

Speakers (Left to right):
Drs. Yuki Oka, Xiaoke Chen, Andrew Hires, Robert Liu, James Poulet, Huizhong Whit Tao, Jennifer Hoy, Maria Geffen, Weizhe Hong, Sachiko Yamanaka, Li I. Zhang, Lisa Stower.

 

Dr. Carolyn C Meltzer, Dean of the Keck School of Medicine of USC, and Dr. Berislav Zlokovic, Director of the Zilkha Neurogenetic Institute gave opening remarks.

Scientific Presentation

Dr. Maria Geffen, University of Pennsylvania
Cortical coding drives efficient auditory perception

Dr. Geffen’s research interests lie in how the brain processes and encodes information about the world, and how our perception is influenced by our emotional states and previous experiences. Using a blend of computational and biological methods, she explores the mechanisms that underpin dynamic auditory perception, memory, and learning. Dr. Geffen's work particularly emphasizes the concepts of plasticity and efficient coding. In her presentation, she has demonstrated that neurons can adjust their dynamic range of response to align with the dynamic range of stimuli they encounter. This means that auditory cortical neurons tend to decrease their gain in response to high-contrast stimuli. She also discusses how the detectability of a signal can be influenced by the level of noise. Specifically, high contrast is associated with low noise, and vice versa. This contrast level, in turn, impacts the threshold of detection. In addition, Dr. Geffen has illustrated the process of neurometric adaptation during contrast transitions, further deepening our understanding of the intricate workings of the auditory system.

Dr. Andrew Hires, University of Southern California

Neural correlates of tactile sensation and action across task learning

Dr. Hires's lab is committed to understanding the neural circuit mechanisms that govern sensorimotor coding, integration, and learning. He aims at leveraging this knowledge to develop more effective treatments for neurological disorders. In his presentation, Dr. Hires discussed the representation of the shape of an object through surface angles. He posed the question of how tactile input can be used to identify these surface angles. To investigate this, his lab utilized the tactile sensation of mouse whiskers as a model. After training, the mice achieved a 75% accuracy rate in detecting angled stimulation, with a resolution of 15 degrees. The team then decoded the angled stimulation into 12 distinct features. Of these, vertical bending and slide distance emerged as the two most critical features. Dr. Hires' team also performed volumetric two-photon recording in GCamp mice. They compared the responses from passive versus active touch and discovered that these two types of touch engaged distinct, non-overlapping neuronal populations. Interestingly, the neurons in the barrel cortex showed object angle tuning, and sharpened tuning curve after training. This discovery provides an intriguing insight into how our neural system adjusts and learns over time.

Dr. Whit Huizhong Tao, University of Southern California

Contextual and cross-modality modulation of cortical processing

Dr. Huizhong Tao from USC presented her recent research on how a second-order thalamic nucleus, the lateral posterior nucleus (LP), influences sensory information processing in the sensory cortex. In both primary visual and auditory cortices, her group discovered that through a direct excitatory projection from LP to layer 1 of the cortex, layer 2/3 pyramidal neuron responses to sensory stimuli are modulated in a subtractive suppression manner, resulting in enhanced selectivity to sensory features and better signal-to-noise ratios. Her research demonstrates that second-order thalamic inputs can enhance cortical processing in a context-dependent manner. In addition, LP neurons can mediate cross-modality enhancements of cortical processing by integrating visual and auditory information relayed from the superior colliculus in the midbrain.

Dr. Jennifer Hoy, University of Nevada-Reno

Adolescence: a critical time for the development of sensory-motivational integration?

Dr. Jennifer Hoy's laboratory is dedicated to identifying the neural circuit basis of prey-capture behavior in mice. This work forms part of a broader objective to understand how vision informs action in the mammalian brain. By investigating the circuits involved in this natural behavior, they hope to contribute to the long-term goal of understanding how molecular-developmental processes influence sensory system functionality and behavior throughout an organism's lifespan. The lab also employs a comparative approach, contrasting their findings with studies of visually-guided foraging behaviors and visual searches in other species. In her presentation, Dr. Hoy demonstrated that mice at different developmental stages exhibit distinct behavioral responses to crickets. Young mice tend to exhibit defensive, prey-like behavior upon their first encounter with a cricket. In contrast, adult mice display predator-like behaviors. In their experimental design, the team used a screen to digitally simulate a cricket using a moving dot. They found that mice at the P21 developmental stage showed a longer latency to approach the moving dot. Meanwhile, the P30-P45 adolescent group demonstrated more proactive approach behaviors compared to those at the adult stage. In conclusion, they hypothesized that the ventromedial hypothalamus (VMH) projection to the periaqueductal gray (PAG) might mediate these observed behaviors.

Dr. Xiaoke Chen, Stanford University

Circuitry and Molecular Mechanisms Drives Descending Pain Facilitation

Dr. Chen's laboratory at Stanford is focused on studying the brain circuits responsible for motivated behaviors, and understanding how maladaptive changes in these circuits lead to chronic pain, addiction, and depression.

In his presentation, Dr. Chen discussed the descending pathways that regulate pain sensation. He explained that this pathway descends from the brain to the spinal cord, with the periaqueductal gray (PAG) indirectly projecting to the spinal cord through the rostral ventromedial medulla (RVM). Within the RVM, ON and OFF cells differentially encode pain sensations. Dr. Chen's team utilized a chronic pain model known as the spared nerve injury (SNI) model. Using transgenic Opm1-Cre mice, they were able to specifically label the ON cells in the RVM, enabling cell type-specific functional manipulation. Silencing these neurons was found to increase the pain threshold in the SNI model. Using Ribotag-seq, they discovered increased expression of CamKv and Camk2a in the SNI model. Consequently, they tested the genetic knockdown of CamKv in Opm1-Cre ON neurons and found that this action could elevate the pain threshold. Consistent with this finding, they discovered that the overexpression of CaMKv is sufficient to drive pain sensation. Through the use of monosynaptic retrograde tracing and circuit specificity, they identified the lateral superior colliculus as the major upstream input that activates ON cells during pain sensitization.

Dr. Sachiko Yamanaka, University of California, Riverside
Imminence of predator threat detected by the accessory olfactory system in mice

Dr. Yamanaka's primary research focuses on understanding how the brain regulates behaviors by integrating external sensory signals with the internal hormonal state. She has particularly concentrated on the accessory olfactory system in mice, which detects and discriminates specific molecules such as pheromones and predator cues.
In her presentation, Dr. Yamanaka discussed the pathway of a chemical smell signal. This pathway begins with the signal being drawn into the Vomeronasal Organ (VNO), then relayed to the Accessory Olfactory Bulb (AOB), and eventually to the Ventromedial Hypothalamus (VMH), among other areas. Her experimental design employed olfactory predator cues to induce freezing behavior in mice. The specific predator cue used in these experiments was cat saliva. Dr. Yamanaka and her team discovered that the Transient Receptor Potential Cation Channel, Subfamily C, Member 2 (Trpc2) mediates the sensation of non-volatile olfactory stimuli. Interestingly, when they genetically modified the mice to remove the Trpc2 channel (a process known as 'knockout'), the animals' behavior towards non-volatile olfactory predator cues was completely abolished. This finding indicates a crucial role for the Trpc2 channel in the detection of predator threats.

Dr. Yuki Oka, California Institute of Technology
Neural regulation of body fluid balance

Dr. Oka's laboratory is dedicated to understanding the neural and molecular foundations of motivated behaviors that regulate homeostasis.
During his presentation, he highlighted his recent research concerning the neural circuits of thirst and sodium appetite. The primary role of central appetite neurons is to direct animals to consume specific nutrients that their bodies require. There is growing evidence suggesting that distinct appetite circuits for major nutrients — such as water, sodium, and food — utilize unique driving and quenching mechanisms. Dr. Oka's research mainly focuses on two aspects of appetite regulation. Firstly, he outlines the temporal relationship between the activity of appetite neurons and consumption behaviors. Secondly, he summarizes the ingestion-related satiation signals that uniquely quench individual appetite circuits. Dr. Oka further explores how distinct appetite and satiation systems for each nutrient may contribute to nutrient homeostasis, considering both functional and evolutionary perspectives.

Dr. James Poulet, Max Delbrück Center, Berlin
Neural circuits of thermal perception

Dr. Poulet's research has been primarily focused on identifying the neural mechanisms that underpin somatosensory processing and perception.
During his presentation, Dr. Poulet introduced their work on temperature sensation neurons in the cortex. Temperature, a fundamental sensory modality distinct from touch, has dedicated receptor channels and primary afferent neurons for both cool and warm sensations. However, the cortical encoding of temperature is less understood. Few cortical neurons have been reported to respond to non-painful temperature changes, and the existence of a dedicated 'thermal cortex' is still a matter of debate. Utilizing widefield and two-photon calcium imaging in the mouse forepaw system, Dr. Poulet's team identified cortical neurons that respond to cooling and/or warming with unique spatial and temporal response properties. They found a representation of cool, but not warm, in the primary somatosensory cortex. However, both cool and warm representations were identified in the posterior insular cortex (pIC). The thermal information representation in the pIC was found to be robust and somatotopically arranged, and reversible manipulations showed a significant impact on thermal perception. Interestingly, despite being situated along the same one-dimensional sensory axis, the encoding of cool and warm sensations were distinct, both in highly and broadly tuned neurons. Collectively, these results suggest that the pIC houses the primary cortical representation of skin temperature, potentially illuminating how the thermal system generates sensations of cool and warm.

Dr. Weizhe Hong, University of California, Los Angeles
Understanding the Social Brain.

Dr. Hong's lab investigates the logic for how the brain regulates social behavior. The Hong lab utilizes a multidisciplinary approach, employing a range of experimental and computational technologies at molecular, circuit, and behavioral levels. He study both how neural dynamics within a single brain regulate social behavioral decisions and how inter- brain neural properties arise from social interactions between individuals.

In his presentation, he discussed the critical role of caring and helping others in fostering social cohesion and contributing to the physical and emotional well-being of social species, including humans. Affiliative social touch, such as allogrooming (grooming behavior directed towards another individual), is a significant type of prosocial behavior that provides comfort to others. It serves to establish and reinforce social bonds and can help console distressed individuals. However, the neural circuits that facilitate prosocial affiliative touch have remained elusive. He revealed that mice exhibit affiliative allogrooming behavior towards distressed partners, providing a consoling effect. This increase in allogrooming is a response to various types of stressors and can be triggered by olfactory cues from distressed individuals. Using microendoscopic calcium imaging, they found that neural activity in the medial amygdala (MeA) responds differently to naive and distressed conspecifics and encodes allogrooming behavior. They were able to establish a direct causal role for the MeA in controlling affiliative allogrooming through intersectional functional manipulations. Furthermore, they identified a select subpopulation of MeA GABAergic (γ-aminobutyric-acid-expressing) neurons, which express tachykinin, that promote this behavior through their projections to the medial preoptic area. This study demonstrates that mice display prosocial comforting behavior and unveils a neural circuit mechanism that underlies the encoding and control of affiliative touch during prosocial interactions. Additionally, he introduced recent work on multi-animal prefrontal cortex recording using miniscope recording. They observed that neurons from two animals would exhibit synchronized activity following social interaction, and the degree of synchronization is proportional to their social relationship. Furthermore, he highlighted a recent study by OpenAI that demonstrated social cooperation performed by simulated AI agents.

Dr. Li Zhang, University of Southern California
Sensory circuits for affective and motivational valence

Research in Dr. Zhang's laboratory is focused on understanding the neural circuit mechanisms that underlie sensory processing and associated behaviors, specifically within the central auditory system. Dr. Zhang's presentation concerns the processing of valence in the sensory system. Valence processing is crucial for understanding the emotional regulation and motivational needs of animals. The initial encoding, distribution, and transformation of sensory valence within neural circuits are not yet fully understood. He described their recent study on how the mouse pontine central gray (PCG) contributes to encoding both negative and positive valences. PCG glutamatergic neurons are activated selectively by aversive, but not reward, stimuli, whereas its GABAergic neurons are preferentially activated by reward signals. The optogenetic activation of these two populations result in avoidance and preference behavior, respectively, and is sufficient to induce conditioned place aversion/preference. Suppression of them reduce sensory-induced aversive and appetitive behaviors, respectively. These two functionally opponent populations, receiving a broad range of inputs from overlapping yet distinct sources, broadcast valence-specific information to a distributed brain network with distinguishable downstream effectors. He concluded that PCG serves as a critical hub to process positive and negative valences of incoming sensory signals and drive valence-specific behaviors with distinct circuits. He has also discussed the underlying logic of sensory circuitry for valence processing and its significance in driving motivational behaviors.

Dr. Robert Liu, Emory University

Predispositions and Plasticity in Nucleus Accumbens Signaling for Pair Bonding in Prairie Voles

Dr. Liu's laboratory is dedicated to understanding the neurophysiological mechanisms that underlie natural social-sensory behaviors. They aim to answer how neural circuits convert social cues into behavioral responses, the plasticity that occurs within those circuits as the meaning of social cues is acquired, and the potential mediation of this plasticity by mechanisms driving social reward.

During his presentation, Dr. Liu introduced his research on pair bond behavior and its mechanisms. They conducted a partner preference test, revealing that animals exhibited huddling behavior towards paired partners. However, when they blocked the oxytocin receptors in the medial prefrontal cortex (mPFC) and the nucleus accumbens (NAcc), the preference towards the partner disappeared. Furthermore, they recorded neural activity from the mPFC and NAcc during bonding, which suggested that mPFC projections to NAcc play a crucial role in bond formation. Dr. Liu's team then investigated how the NAcc responds to oxytocin. They used the oxytocin receptor antagonist, TGOT, and performed slice recordings. The TGOT increased the amplitude of excitatory postsynaptic currents (EPSCs), suggesting a presynaptic effect. They used pair bonding in socially monogamous prairie voles as an example of socio-sexual experience that dramatically alters behaviors displayed towards others, to explore whether the functional role of social neuromodulators evolves with experience to shape the course of relationships. They found that an oxytocin receptor agonist decreases the amplitude of spontaneous EPSCs in sexually naive virgin voles, but not in pair-bonded ones. In contrast, it increases the amplitude of electrically evoked EPSCs in paired voles, but not in virgins. This oxytocin-induced potentiation of synaptic transmission relies on the new coupling between oxytocin receptor signaling and endocannabinoid receptor type 1 (CB1) receptor signaling in pair-bonded voles. Blocking CB1 receptors after pair-bond formation increased the occurrence of a specific form of social rejection - defensive upright response - that was displayed towards the partner, but not towards a novel individual. In conclusion, their results demonstrate that the action of oxytocin in the nucleus accumbens changes through social experience in a way that regulates the trajectory of social interactions as the relationship with the partner unfolds. This could potentially promote the maintenance of a pair bond by inhibiting aggressive responses. This provides a mechanism by which social experience and context shift oxytocinergic signaling to impact neural and behavioral responses to social cues.

Dr. Lisa Stowers, Scripps Research

Odor sensation and motivation during social behavior in the mouse

Dr. Stowers' Lab focuses on the study of innate social behaviors in animals, behaviors that are highly conserved across species. These include courtship, rage, fear, and newborn-parent interactions. In this model, the animal's mental state is easier to interpret, and the brain mechanisms and functions are more accessible for scientific testing. Furthermore, this research approach provides insight into various aspects of brain function. To trigger social behavior, the brain must undertake computations such as learning and memory, sensory coding, motivation, sexual dimorphism, and age-related changes, and integrate internal state needs such as hunger or sleepiness. The Stowers' group employs the framework of innate social behavior to comprehend these crucial features of general coding logic, aiming to elucidate how the brain functions.

During her presentation, Dr. Stowers discussed her work on odor sensation and motivation during social behavior, using mice as a model. She proposed that mouse ultrasound may not be considered language per se but can serve as innate social sounds. She further discussed the pathway from the vomeronasal organ (VNO) to the accessory olfactory bulb (AOB) and then to the hypothalamus, a pathway that plays a significant role in regulating emotions.

Workshop Report

Through a series of discussions, the workshop highlighted the complex interplay of various components within the nervous system, the role of reinforcement learning, the importance of plasticity at both subcortical and cortical levels, and the impact of sensory inputs and motivations. The workshop provided an insightful platform for discussions on the neural basis of sensation, behavior, and motivations. It underscored the need for continued research to better understand these complex systems and their influence on behavior. Despite advancements in understanding the nervous system, numerous questions remain unanswered, particularly about the neural substrates of motivation and the role of different neural motivation systems.

Sensory Motivational Integration and Needs Hierarchy

A significant part of the discussion was devoted to exploring sensory motivational integration and its various scales. The functional role of the Medial Preoptic Area (MPOA) in defining a hierarchy of needs was discussed, linking it to Maslow's pyramid. A lively debate ensued regarding the primacy of safety over physiological needs, even in the context of animal behavior.

Time Scales in Needs and Motivation

The symposium further explored the concept of time scales in needs and motivation. A connection to neuroethology was made through the reference to Tinbergen's Four Questions, which address behavior from both immediate and evolutionary time scales.

Tools and Methods in Studying Neural Circuits

The conversation transitioned to tools and methods employed in the study of neural circuits and behavior, including the potential to record from every neuron in every brain area. The group deliberated on the sufficiency of existing tools, the nature of questions being asked, and the possibility of unforeseen discoveries that might reshape the course of study.

Deciphering Motivation

The concept of motivation was extensively debated, focusing on its identification, quantification, and understanding. There was substantial discussion on what it would mean to 'solve' motivation and predict behavior based on knowledge of motivational states.

Brain States and Behavior

The correlation between brain states and behavior prompted discussions about the current understanding of how brain states change and the potential redundancy in neural activity. The participants agreed that current methods may not be capturing the full picture, highlighting the need for more advanced techniques.

Complexity of Brain Functioning and Behavioral Patterns

There was an in-depth discussion on the complexity of brain functioning, behavioral patterns, and animals' responses to different stimuli. The role of plasticity in triggering behavioral changes was emphasized, and the concept of hardwiring circuitry was introduced.

Motivation and the Nervous System

Motivation's role in the basic hierarchy of the nervous system was explored, and the idea that motivation might be an illusion created by a set of simple rules was put forward. The conversation also touched on the intriguing possibility of decoding brain activity to control physical objects.

Infant and Adult Brain Dynamics

Speakers discussed the differences in neural dynamics between infant and adult brains, focusing on the changes that occur when infants and adults are exposed to sensory stimuli. A significant portion of the discussion revolved around the debate between cell types versus fast temporal encoding.

Cortical and Subcortical Regions

The differences between cortical and subcortical regions were discussed, with an emphasis on the distinct types of computations these regions perform, given their unique structural characteristics.

Concluding Remarks

The conference provided an insightful platform for discussions on the neural basis of sensation, behavior, and motivations. It underscored the need for continued research to better understand these complex systems and their influence on behavior. Despite advancements in understanding the nervous system, numerous questions remain unanswered, particularly about the neural substrates of motivation and the role of different neural motivation systems.