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Dialogues Between Neuroscience and Society

001. Food for Thought: Tastes, Aromas, and Memories of Food

Location: Hall D

Time: Sat, Nov. 15, 2014, 11:00 AM – 1:00 PM

Speakers: B. VOLTAGGIO

Abstract: From the alluring smells and colors of a prepared dish to the deep emotions surrounding the act of sharing a meal, food unites us. The rich sensory experience that takes place every time we eat is made possible by the brain, which shapes perception of taste and smell, and seals the meal to memory. Hear noted chef, restaurateur, and Top Chef contestant Bryan Voltaggio discuss how he strives to create culinary treasures that not only satiate but entertain and transform how his guests think about food.

Disclosures: B. Voltaggio None.

Special Lecture

008. Nanoscopy With Focused Light: Principles and Applications

Location: Hall D

Time: Sat, Nov. 15, 2014, 2:00 PM - 3:10 PM

Support: Gottfried Wilhelm Leibniz Prize

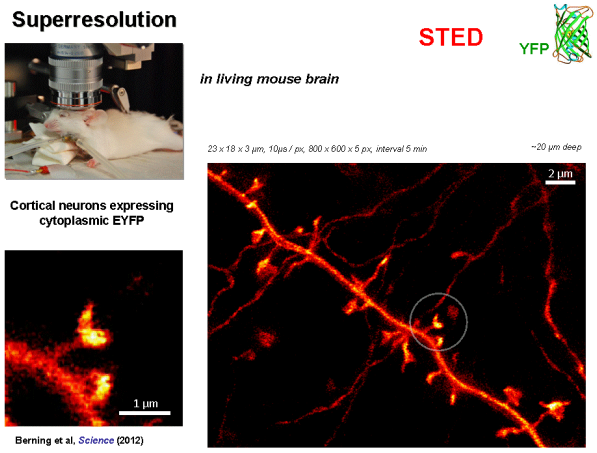
Koerber European Science Prize

Center for Nanoscale Microscopy and Molecular Physiology of the Brain, Goettingen

Speakers: S. W. HELL;
Max Planck Inst. for Biophysical Chem., Göttingen, Germany

Abstract: Throughout the 20th century it was well accepted that lens-based light microscopy cannot discern details that are finer than half the wavelength of light (>200 nm). However, in the 1990s, it was discovered that this barrier can be effectively overcome, such that fluorescent features can be resolved virtually down to molecular dimensions. Here we discuss the simple yet powerful physical principles that allowed us to overcome the diffraction limit, with special

emphasis on STED and RESOLFT microscopy. We exemplify the relevance of these 'nanoscopy' techniques to the neurosciences.



Disclosures: **S.W. Hell:** E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); Significant shares of Abberior GmbH producing fluorophores, and of Abberior Instruments GmbH, producing microscopes for superresolution.

Presidential Special Lecture

009. The Living Record of Memory: Genes, Neurons, and Synapses

Location: Hall D

Time: Sat, Nov. 15, 2014, 5:15 PM - 6:25 PM

Support: NIH Grant R01 NS045324

NIH Grant R01 MH077022

NIH Grant R21 MH101684

NARSAD Distinguished Investigator Award

Speakers: *K. C. MARTIN;
Dept Psychiat & Biochem, UCLA, Los Angeles, CA

Abstract: Memory requires stimulus-induced changes in gene expression, which in turn alters synaptic connectivity and wiring in the brain. In this way, experience combines with our genome

to determine who we are as individuals. This talk describes efforts to understand how experience regulates gene expression within neurons. How are stimulus-induced signals transported from distal synapses to the nucleus to alter gene expression, and how is gene expression spatially restricted to specific subcellular compartments?

Disclosures: K.C. Martin: None.

Special Lecture

100. What Drives Sleep - Wake Cycles: Identification of Molecules and Circuits in *Drosophila*

Location: Hall D

Time: Sun, Nov. 16, 2014, 8:30 AM - 9:40 AM

Support: HHMI

NIH

Ellison Medical Foundation

Speakers: *A. SEHGAL;
Perelman Sch. of Med. at the Univ. of Pennsylvania, Howard Hughes Med. Instiitute, Philadelphia, PA

Abstract: The lecture focuses on the cellular and molecular mechanisms that regulate sleep. The 24-hour rhythm of sleep is driven by a circadian clock, while the need to sleep comes from a homeostatic system, which ensures adequate sleep levels. The lecture shows how the use of *Drosophila* has led to the identification of mechanisms that generate a circadian clock and to some of the downstream circuitry required for circadian timing of behavior. It also highlights recent developments in identifying molecular components and cellular circuits that underlie homeostatic regulation.

Disclosures: A. Sehgal: None.

Special Lecture

107. The Glymphatic System and Its Possible Roles in CNS Diseases

Location: Hall D

Time: Sun, Nov. 16, 2014, 10:00 AM - 11:10 AM

Support: NIH Grant R01NS078304

NIH Grant R01NS078167

Speakers: *M. NEDERGAARD;
Neurosurg. Ctr. Aging & Devel Biol, Univ. of Rochester, ROCHESTER, NY

Abstract: Past work has focused on cellular recycling of proteins involved in neurodegeneration. This lecture will expand the traditional framework to include a macroscopic clearance system - the glymphatic system - by which the brain exports waste products of neural metabolism. Glymphatic clearance is driven by convective CSF influx and is especially active during sleep. Macromolecules, such as amyloid beta, are literally swept out of CNS for ultimate degradation in the liver. As such, the glymphatic system represents a novel and unexplored target for treatment of neurological diseases.

Disclosures: M. Nedergaard: None.

David Kopf Lecture on Neuroethics

108. Mind, Brain, and the Ethics of Intergroup Behavior

Location: Hall D

Time: Sun, Nov. 16, 2014, 11:30 AM - 12:40 PM

Support contributed by David Kopf Instruments

Speakers: M. BANAJI;
Harvard Univ., Boston, MA

Abstract: From the moment of birth, every human is a member of many groups. Group memberships create affiliations of “us” and “them” and sensitivity to status in social hierarchies. Human minds reflect these in a myriad attitudes and beliefs that contain deep knowledge about the hidden presence or surprising absence of group love. Unveiling them by observing brain activity and behavior allows understanding of the natural and cultivated ways in which the meanings of in-group and out-group (self and other) are represented and group love is elusively tuned up and down.

Disclosures: M. Banaji: None.

Special Lecture

189. Surprising Origins of Sex Differences in the Brain

Location: Hall D

Time: Sun, Nov. 16, 2014, 1:00 PM - 2:10 PM

Support: R01 NS050525

R01 MH091424

RO1 MH52716

Speakers: *M. M. MCCARTHY;
Univ. of Maryland Sch. of Med., Baltimore, MD

Abstract: The developing brain is permanently and differently organized in males and females as a result of variance in hormonal exposure, with perinatal males producing high levels of testicular androgens that are aromatized to estrogens in neurons. Developing females experience far less hormone exposure and feminization is considered the default pathway in the process of sexual differentiation. Endpoints impacted by steroids in the developing brain include synaptic patterning, neurogenesis, glial genesis, differential cell death, migration and phenotype differentiation. Multiple attempts to identify a neurotransmitter system subject to hormonal regulation and serving as the final common denominator of steroid-hormone induced masculinization of the brain have largely failed. We now understand this to be due to the origins of many sex differences in the brain being outside the realm of neurotransmission but instead involving inflammatory and immune mediators such as prostaglandins, microglia and mast cells, as well as another class of membrane derived signaling molecules, endocannabinoids, all of which are higher in males. Cell-to-cell communication via diffusible but short lived signaling molecules expands the impact of steroids beyond those cells expressing steroid receptors and likely contributes to regional specificity. Once sex differences are established, they must also be maintained into adulthood to assure reproductive behavior and physiology are in register. Epigenetic modifications to DNA imprint early life environment and experience onto the genome. Emerging evidence suggests the default female pattern involves epigenetic repression of the male genome which is emancipated by gonadal steroid inhibition of DNMT activity and subsequent demethylation of key genes, allowing for their expression. Understanding how male and female brains develop differently informs us of the sources of well established gender bias in risk of developmental disorders which are more prevalent in males and increased in frequency and severity by early life injury or inflammation.

Disclosures: M.M. McCarthy: None.

Peter and Patricia Gruber Lecture

195. Circuits and Strategies for Skilled Motor Behavior

Location: Hall D

Time: Sun, Nov. 16, 2014, 2:30 PM - 3:40 PM

Support contributed by The Gruber Foundation

Speakers: *T. JESSELL;
Columbia University, Howard Hughes Med. Inst., NY

Abstract: The capacity to generate movement on demand is a reflection of neural computations that integrate internal command and external feedback for the purpose of patterned motor output. Advances in deciphering the logic of motor systems have not yet resolved the strategies and mechanisms through which neural circuits direct motor behavior. This lecture will probe this issue through an analysis of motor circuits in the mammalian spinal cord, focusing on the functions of interneurons assigned to two feedback circuits, one that evaluates the fidelity of intended motor acts and a second that filters external sensory reports.

Disclosures: T. Jessell: None.

Presidential Special Lecture

196. The Integration of Interneurons Into Cortical Circuits: Both Nurture and Nature

Location: Hall D

Time: Sun, Nov. 16, 2014, 5:15 PM - 6:25 PM

Speakers: *G. J. FISHELL;
Smilow Neurosci. Program, New York Univ. Neurosci. Inst., NEW YORK, NY

Abstract: Since the seminal finding that cortical GABAergic interneurons originate within the subpallium, extraordinary mechanisms must exist to ensure they are precisely and reliably embedded into cortical circuitry. Considerable efforts indicate that genetic programs initiated within progenitors assign interneurons into specific cardinal classes. It is less clear whether their synaptic specificity also is intrinsically determined. Fishell will discuss recent evidence concerning how intrinsic genetic programs within interneurons are shaped by local activity-dependent cues. These results suggest that sensory information complements earlier established genetic programs to shape the way interneuronal subtypes integrate into nascent cortical circuits.

Disclosures: G.J. Fishell: None.

Special Lecture

273. Building a Synapse Through Nuclear Export of Large RNA Granules and Exosomes

Location: Hall D

Time: Mon, Nov. 17, 2014, 8:30 AM - 9:40 AM

Support: 2 R37 MH070000-11 MERIT

R01 NS-085993-01 EUREKA

RO1 NS063228-04

Speakers: *V. BUDNIK;
Dept. of Neurobio., Univ. of Massachusetts Med. Sch., Worcester, MA

Abstract: In recent years, genetic studies in Drosophila have led to the discovery of novel and likely fundamental mechanisms that regulate synapse development and plasticity. Particularly intriguing is a Wnt signaling pathway that conveys a message from the plasma membrane to the nucleus to promote the nuclear assembly of ultra-large ribonucleoprotein (megaRNP) granules. These megaRNP granules, which contain mRNAs that encode postsynaptic proteins, exit the nucleus through a likely ancient mechanism coopted by Herpes-type viruses to escape from the nucleus. Studies suggest that this mechanism is likely conserved from insects to mammals, and provide unexpected insight into diseases such as laminopathies and dystonia. A second development regards the discovery that exosomes, extracellular vesicles that contain proteins, lipids and RNA, function in trans-synaptic communication by allowing the transport of hydrophobic and membrane proteins from one cell to another. Until recently, the plasma membrane has been considered a major barrier for the trans-cellular transfer of certain molecules, such as trans-membrane proteins and RNAs; however, the discovery of exosomes and their function at synapses is shifting these views and providing a new dimension to our understanding of trans-synaptic signaling.

Disclosures: V. Budnik: None.

Special Lecture

280. Genes and Environment Interaction During Development: Redox Imbalance in Schizophrenia

Location: Hall D

Time: Mon, Nov. 17, 2014, 10:00 AM - 11:10 AM

Support: Swiss National Science Foundation (#31-116689 and #310030_135736/1)

SNSF National Center of Competence in Research (NCCR) “SYNAPSY"

Avina Foundation

Damm-Etienne Foundation

Loterie Romande

Alamaya Foundation

Speakers: *K. Q. DO;
Ctr. for Psychiatric Neurosci., Prilly-Lausanne, Switzerland

Abstract: Understanding how the interaction of genes and environment risk factors during neurodevelopment leads to cognitive, affective and social impairment is one central challenge in psychiatric neuroscience. Converging evidence points at redox imbalance and oxidative stress in the blood, fibroblasts, CSF and brain of patients suffering of schizophrenia. The genetic vulnerability factors involve either redox regulation genes directly affecting glutathione (GSH) metabolism, or genes which indirectly lead to oxidative stress. Environmental factors known to favor major psychiatric disorders generate ROS as well. As a consequence, two key systems, essential for cognitive, affective and social functioning, will be particularly affected: local microcircuits and long range connections. The critical role of redox imbalance has been validated in GSH deficit models (*gclm*-/-) reproducing numerous schizophrenia phenotypes including neuroinflammation, NMDA receptor hypofunction, brain Gln/Glu ratio alteration, impaired parvalbumin fast-spiking GABA interneurons, neural synchronization and behavioral anomalies. Redox dysregulated experimental models also highlight the childhood and peripuberty as critical periods of high vulnerability for environmental adverse insults. Indeed, additional oxidative challenges in juvenile and peripubertal ages, but not in adult *gclm*-/- mice, lead to severe and permanent PVI and perineuronal net (PNN) impairment. The PNN plays a critical role in PVI protection against oxidative stress. Regulation of redox state in PVI also balances plasticity and stability across cortical development, through delaying and/or keeping critical periods of plasticity open-ended. On the other hand, the long range connections may be also affected by redox dysregulation during development: *gclm*-/- mice present myelin markers deficits in prefrontal cortex at peripuberty, involving the Fyn kinase pathway dysregulation which lead to decreased oligodendrocytes proliferation. Most importantly, the antioxidant, GSH precursor N-acetyl-cysteine (NAC), can prevent the morphological, biochemical, physiological and behavioral alterations described above. In chronic schizophrenia patients, add on treatment with NAC improved their negative symptoms, NMDA-dependant mismatched negativity and local neural synchronization without side effects. Evidence, both in patients and experimental models, supports the view that the redox dysregulation in schizophrenia could be corrected by safe GSH

precursors, and, if applied early enough in the disease development, could potentially prevent its emergence.

Disclosures: K.Q. Do: None.

Special Lecture

281. The Brain Is Needed to Cure Spinal Cord Injury

Location: Hall D

Time: Mon, Nov. 17, 2014, 11:30 AM - 12:40 PM

Support: KAKENHI from MEXT, Japan

SRPBS from MEXT, Japan

CREST from JST, Japan

HFSP Group Grant from HFSPO

Speakers: *T. ISA;
Dept Integrative Physiol, Natl. Inst. for Physiological Sci., Okazaki, Japan

Abstract: After the spinal cord injury, patients experience severe paralysis but some recovery can occur through rehabilitative training, however, the underlying neuronal mechanism is still not well understood. We have been studying the neuronal mechanism of recovery after partial spinal cord injury using non-human primate models by combining multidisciplinary approaches and found that the recovery is based on the plastic change in the neural circuit operation not just in the spinal cord, but also in the large-scaled network throughout the central nervous system. It is generally accepted that evolutionally, direct connection from the motor cortex to spinal motor neurons is first established in higher primates and that the direct pathway is the basis of dexterous hand movements in these species. However, in addition to the direct pathways, there exist indirect pathways mediated by propriospinal neurons (Alstermark and Isa, 2012). Recently, we clarified that after lesion of the direct pathway, such indirect pathways can compensate for the dexterous hand movements, first by classical lesion experiments, and more recently by a newly developed genetic tool that enabled pathway-selective and reversible transmission blockade with double viral vectors in macaque monkeys (Kinoshita et al. Nature, 2012). Moreover, we showed that various cortical areas including ipsilateral M1 and ventral premotor cortex are causally involved in the functional recovery (Nishimura et al. Science, 2007). Contribution of these areas varies depending on the stages of the recovery. In addition to these motor-related structures, we found that ventral striatum (VSt) including the nucleus accumbens increases the activation during the recovery from the spinal cord injury in association with the

motor cortex (Nishimura et al. PLos One 2011), and that the VSt causally contributes to the recovery by local inactivation technique. This may underlie the mechanism of how the motivation facilitates the functional recovery. Such knowledge about the systems underlying the recovery will contribute to development of novel therapeutic strategies against the neuronal damage. References; 1.Kinoshita et al. (2012) Nature, 487: 235-238. 2.Alstermark B, Isa T. (2012) Annual Review of Neuroscience,35:559-578. 3.Nishimura et al. (2011) PLoS One 6: e24854. 4.Nishimura et al. (2007) Science, 318: 1150-1155.

Disclosures: T. Isa: None.

Albert and Ellen Grass Lecture

380. Cellular and Molecular Mechanisms of Explicit Learning in the Hippocampus

Location: Hall D

Time: Mon, Nov. 17, 2014, 3:15 PM - 4:25 PM

Support contributed by The Grass Foundation

Support: NIH Grant MH080379

NIH Grant MH070957

NIH Grant MH-38256

Speakers: *R. A. NICOLL;
Dept Cell & Mol Pharmacol, Univ. of California, San Francisco, San Francisco, CA

Abstract: One of the most remarkable features of the brain is its ability to store vast amounts of information. Changes in the strength of synaptic connections as a mechanism underlying learning and memory had been proposed by Cajal at the beginning of the last century and then formulated into a concrete synaptic model by Hebb in 1949. However, it was not until the discovery of long-term potentiation (LTP), in which brief high frequency synaptic stimulation in the hippocampus results in a long lasting increase in synaptic strength, that there was experimental evidence supporting such a proposal. LTP has remained to this day the most compelling cellular model for learning and memory. Indeed, there are no competing models in the field. Since its discovery, thousands of papers have been published on this phenomenon. With this massive amount of information, it is difficult not to be overwhelmed, especially for someone not directly involved in the field. In my talk I peel away as many layers of complexity as possible, and probe the core properties of LTP. I would argue that the many dozens of proteins that have been implicated in the phenomenon are not essential, but rather modulate, often in indirect ways, the threshold and/or magnitude of LTP. What is required is NMDA receptor

activation followed by CaMKII activation. The consequence of CaMKII activation is the rapid recruitment of AMPA receptors to the synapse. In my talk I will fill in the steps between CaMKII activation and the recruitment of AMPA receptors.

Disclosures: R.A. Nicoll: None.

Presidential Special Lecture

381. The First Steps in Vision: Computation and Repair

Location: Hall D

Time: Mon, Nov. 17, 2014, 5:15 PM - 6:25 PM

Support: ERC grant from EU,

SNSF grant from Switzerland,

Gebert-Ruf Foundation grant

SEEBETTER grant from EU,

TREATRUSH grant from EU,

OPTONEURO grant from EU

3X3D Imaging grant from EU

Speakers: B. ROSKA;
Neurobio. Program, Friedrich Miescher Inst. for Biomed. Research, Univ. of Basel, Basel, Switzerland

Abstract: At the front end of the visual system a sophisticated image processor, the retina, creates about a dozen movies about the visual scene and presents them to higher visual brain areas. How do the thalamus and the cortex interpret these movies and how does the retina create them? Furthermore, how can we use our understanding of neuronal computations at the front end of the visual system to design repair strategies for blinding diseases? I will present a “cell type” based approach to address these questions.

Disclosures: B. Roska: None.

Special Lecture

472. Learning and Relearning Movement

Location: Hall D

Time: Tue, Nov. 18, 2014, 8:30 AM - 9:40 AM

Speakers: *A. J. BASTIAN;
Kennedy Krieger Institute, Johns Hopkins Univ. Sch. of Med., Baltimore, MD

Abstract: Human motor learning depends on a suite of brain mechanisms that are driven by different signals and operate on timescales ranging from minutes to years. Understanding these processes requires identifying how new movement patterns are normally acquired, retained, and generalized, as well as the effects of distinct brain lesions. The lecture focuses on normal and abnormal motor learning and how we can use this information to improve rehabilitation for individuals with neurological damage.

Disclosures: A.J. Bastian: None.

Special Lecture

479. Persistent Cocaine-Induced Plasticity and Synaptic Targets for Its Reversal

Location: Hall D

Time: Tue, Nov. 18, 2014, 10:00 AM - 11:10 AM

Support: NIH Grant DA009621

NIH Grant DA015835

NIH Grant DA029099

Speakers: *M. E. WOLF;
Neurosci., Rosalind Franklin Univ. of Med. and Sci., NORTH CHICAGO, IL

Abstract: Addiction is a chronic relapsing disorder. Cue-induced cocaine craving, a major trigger for relapse, progressively intensifies (incubates) over the first 1-2 months of withdrawal in a rat model of addiction. Ultimately, incubated craving depends on a persistent strengthening of AMPA receptor transmission in the nucleus accumbens that is maintained by alterations in group I metabotropic glutamate receptor signaling and protein translation. Positive allosteric modulators of mGluR1 may be useful therapeutic agents because they suppress AMPA receptor plasticity and craving.

Disclosures: M.E. Wolf: None.

Special Lecture

480. How Do You Feel? The Role of Mechanically Activated Ion Channels in Touch, Pain, Hearing, and Beyond

Location: Hall D

Time: Tue, Nov. 18, 2014, 11:30 AM - 12:40 PM

Support: Howard Hughes Medical Institute

NIH Grant DE02215

NIH Grant DE022358

NIH Grant NS046303

NIH Grant NS083174

Speakers: *A. PATAPOUTIAN;
ICND 210, The Scripps Res. Institute, Howard Hughes Med. Inst., La Jolla, CA

Abstract: Mechanosensation is perhaps the last sensory modality not understood at the molecular level. Ion channels that sense mechanical force are postulated to play critical roles in sensing touch/pain (somatosensation), sound (hearing), sheer stress (cardiovascular tone), etc. However, the identity of ion channels involved in sensing mechanical force has remained elusive. This lecture focuses on the identification, using functional genomics approaches, and characterization of novel mechanically activated channels including Piezo1 and 2.

Disclosures: A. Patapoutian: None.

Special Lecture

567. Generating and Shaping Novel Action Repertoires

Location: Hall D

Time: Tue, Nov. 18, 2014, 1:00 PM - 2:10 PM

Support: HHMI IECS Grant

ERC STG 243393

FCT Project Grant

Marie Curie IRG Reintegration Grant

Speakers: R. M. COSTA;
Champalimaud Fndn., Lisboa, Portugal

Abstract: Many actions are learned anew throughout life, likely through a process of trial and selection. We investigated how novel self-paced actions are generated, and how actions that lead to particular outcomes are then selected. We found that dopamine is critical for the initiation of novel actions, and that plasticity in cortico-basal ganglia circuits is essential for action selection. With iteration, actions become organized in modules, and neural substrates of chunking emerge in these circuits.

Disclosures: R.M. Costa: None.

Presidential Special Lecture

575. Stem Cells in the Brain: Glial Identity and Niches

Location: Hall D

Time: Tue, Nov. 18, 2014, 5:15 PM - 6:25 PM

Support: NIH NINDS NS074039

NIH NIA AG042671

NIH NINDS NS053884

NIH NINDS NS075610

NYSDOH, NYSTEM CO28101

NYSDOH, NYSTEM CO28118

NYSDOH, NYSTEM C026401

Speakers: *F. DOETSCH;
Columbia Univ., New York, NY

Abstract: Glia play key roles in brain development, homeostasis, plasticity, and injury. Specialized glia are stem cells both during development and in adults, and continuously generate new neurons in restricted brain regions throughout life. Doetsch will review the current understanding of the nature of specialized glia cells in the brain and the unique features of the niche in which they reside. Illuminating the biology of endogenous neural stem cells has important implications for brain repair.

Disclosures: F. Doetsch: None.

Special Lecture

662. Exocytosis of Synaptic Vesicles — A Molecular Perspective

Location: Hall D

Time: Wed, Nov. 19, 2014, 8:30 AM - 9:40 AM

Support: Max-Planck Society

SynSys (European Commission)

German Research Foundation (SFB 803)

NIH 5GM072694-5

Speakers: *R. JAHN;
Dept Neurobiol, Max Planck Inst. for Biophysical Chem., D-37077 Gottingen, Germany

Abstract: Neurotransmitter release from presynaptic nerve endings and chromaffin cells is mediated by Ca^{2+} -dependent exocytosis of synaptic vesicles or secretory granules. Exocytotic membrane fusion is carried out by the SNARE proteins synaptobrevin/VAMP, syntaxin 1, and SNAP-25. Upon membrane contact, the vesicular SNARE synaptobrevin forms complexes with the plasma membrane-resident SNAREs SNAP-25 and syntaxin 1. Complex formation proceeds from the N-terminal end towards the C-terminal membrane anchors, thus pulling the membranes together and initiating fusion ("zipper" hypothesis of SNARE function). The steps of SNARE assembly are controlled both by members of conserved protein families such as the SM- and CATCHR-proteins and by specialist proteins responsible for calcium regulation such as the calcium sensor synaptotagmin and complexins. Membrane fusion can be conveniently reconstituted in vitro using purified SNARE proteins and artificial membranes. A variety of both single particle and bulk assays are available affording high spatial and temporal resolution of the fusion reaction. Furthermore, high-resolution structures are available of most proteins (or at least of the functionally essential domains), allowing for the development of refined models. More recently, progress has also been made in the understanding of the intermediate steps in the fusion pathway, beginning with vesicle attachment (also referred to as docking), SNARE zippering, and finally of the precise mechanism by which the two bilayers merge. While the zipper mechanism of SNARE function is supported by numerous lines of evidence, both activation of SNAREs by SM and CATCHR proteins and the mechanisms by which synaptotagmin is capable of accelerating fusion by many orders of magnitude are still unclear and controversially discussed. Synaptotagmin possesses two C2-domains each containing binding sites for several calcium ions, and one of the C2-domains has, in addition, a binding site for phosphatidylinositol (4,5)

bisphosphate that is separate but influenced by the calcium binding site. The key question that will be discussed is at which step in the pathway the molecular machinery, particularly the SNAREs, are arrested before calcium influx and how synaptotagmin is capable to overcome the arrest upon calcium activation.

Disclosures: R. Jahn: None.

Special Lecture

669. The Sensory Neurons of Touch

Location: Hall D

Time: Wed, Nov. 19, 2014, 11:30 AM - 12:40 PM

Support: NIH Grant R01NS34814

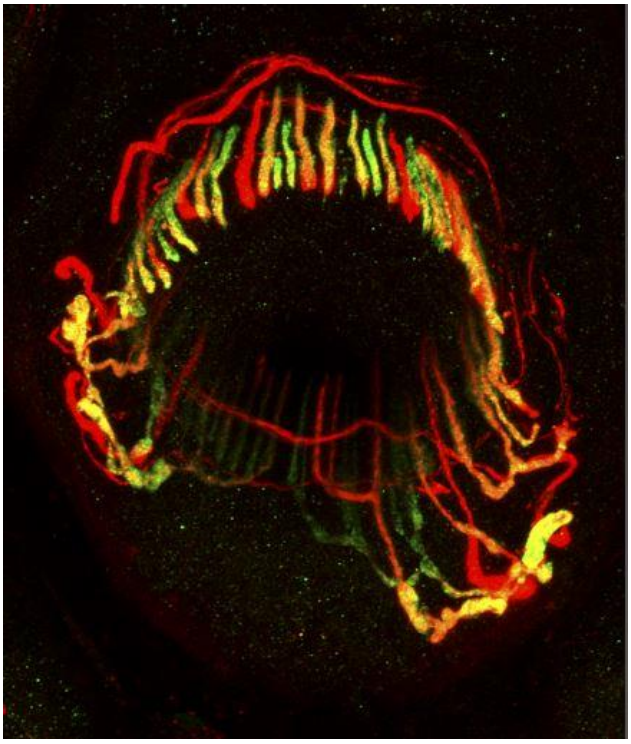
NIH Grant R01DE022750

Howard Hughes Medical Institute

Speakers: D. D. GINTY;
Harvard Med. School, Howard Hughes Med. Inst., Boston, MA

Abstract: The somatosensory system endows us with a remarkable capacity for object recognition, texture discrimination, sensory-motor feedback, and social exchange. Innocuous touch of the skin is detected by a large group of physiologically distinct low-threshold mechanosensory neurons (LTMRs) whose cell bodies are located in dorsal root ganglia and cranial ganglia. These neurons have one axonal branch that extends to the periphery and another that projects into the spinal cord thus providing the means by which touch information is conveyed from the skin to the CNS. LTMR subtypes are uniquely tuned to mechanical stimuli, including hair deflection and pulling, skin indentation, stroking, and stretching. We have generated a mouse LTMR molecular-genetic toolbox that allows for investigations into the physiology, morphology, function, and development of the major LTMR subtypes. Using these LTMR genetic tools and anatomical and physiological approaches, we have defined unique morphological and ultrastructural features of LTMR endings in both hairy and non-hairy skin and in the CNS. Interestingly, LTMR subtypes whose peripheral projections innervate the same small, overlapping region of skin exhibit central projections that terminate within narrow, three-dimensional columns of the spinal cord dorsal horn. We believe that these spinal cord LTMR columns represent units of functional organization that receive and process LTMR subtype activity ensembles emanating from the skin. We further posit that spinal cord interneurons directly receive and process LTMR inputs, whereas spinal cord projection neurons carry processed touch information from spinal cord LTMR columns to the brain. To test these ideas

and to gain insight into mechanisms of touch information processing in the spinal cord, we have amassed molecular-genetic tools that enable interrogation of the physiological properties, morphologies, synaptic connectivity patterns, and functions of spinal cord interneuron and projection neuron subtypes. The morphological and physiological properties of LTMRs and the organizational logic of their CNS projections relative to spinal cord interneurons and projection neurons will be discussed.



Disclosures: **D.D. Ginty:** A. Employment/Salary (full or part-time):; full time. F. Consulting Fees (e.g., advisory boards); NIH.

Special Lecture

761. Affective Neuroscience of Reward: Limbic Modules for Liking and Wanting

Location: Hall D

Time: Wed, Nov. 19, 2014, 1:00 PM - 2:10 PM

Support: NIH Grant DA15188

NIH Grant MH63649

Speakers: *K. C. BERRIDGE;
Psychology, Univ. of Michigan, ANN ARBOR, MI

Abstract: Reward involves several different psychological components. “Wanting” a reward is generated by robust mesolimbic circuitry, whereas “liking” the same reward is generated by hedonic-hotspot circuitry that is neuroanatomically and neurochemically more restricted. This wanting-liking difference has implications for addiction disorders. Yet surprisingly, forms of positive wanting and negative fear share some of the same brain mechanisms. New insight on the generation of these intense “liking,” “wanting,” and other emotion states are emerging in affective neuroscience.

Disclosures: K.C. Berridge: A. Employment/Salary (full or part-time):; University of Michigan. B. Contracted Research/Research Grant (principal investigator for a drug study, collaborator or consultant and pending and current grants). If you are a PI for a drug study, report that research relationship even if those funds come to an institution.; NIH only. C. Other Research Support (receipt of drugs, supplies, equipment or other in-kind support); NIH only.