

JNeurosci

THE JOURNAL OF NEUROSCIENCE

October 31, 2018 • Volume 38 Number 44 • www.jneurosci.org



Cover legend: This image shows the spatial distribution of F-actin in a growth cone, as revealed using structured illumination microscopy (SIM), one type of superresolution microscopy. Colors indicate the height from the substrate. For more information, see the Symposium article by Igarashi et al. (pages 9459–9467).

Progressions

- 9311 **The First Annual Meeting of the Society for Neuroscience, 1971: Reflections Approaching the 50th Anniversary of the Society's Formation**
R. Douglas Fields

Viewpoints

- 9318 **Linking Nanoscale Dynamics of AMPA Receptor Organization to Plasticity of Excitatory Synapses and Learning**
Daniel Choquet

Symposium and Mini-Symposium

- 9330 **Whole-Brain Analysis of Cells and Circuits by Tissue Clearing and Light-Sheet Microscopy**
Tomoyuki Mano, Alexandre Albanese, Hans-Ulrich Dodt, Ali Erturk, Viviana Gradinaru, Jennifer B. Treweek, Atsushi Miyawaki, Kwanghun Chung, and Hiroki R. Ueda
- 9338 **The Elegance of Sonic Hedgehog: Emerging Novel Functions for a Classic Morphogen**
A. Denise R. Garcia, Young-Goo Han, Jason Triplett, William T. Farmer, Rebecca A. Ihrie, and Corey C. Harwell
- 9346 **Advances in Enteric Neurobiology: The “Brain” in the Gut in Health and Disease**
Subhash Kulkarni, Julia Ganz, James Bayrer, Laren Becker, Milena Bogunovic, and Meenakshi Rao
- 9355 **Unveiling the Extracellular Space of the Brain: From Super-resolved Microstructure to *In Vivo* Function**
Sabina Hrabetová, Laurent Cognet, Dmitri A. Rusakov, and U. Valentin Nägerl
- 9364 **The Endolysosomal System and Proteostasis: From Development to Degeneration**
Bettina Winckler, Victor Faundez, Sandra Maday, Qian Cai, Cláudia Guimas Almeida, and Huaye Zhang
- 9375 **New Frontiers in Parkinson's Disease: From Genetics to the Clinic**
Lamya S. Shihabuddin, Patrik Brundin, J. Timothy Greenamyre, Diane Stephenson, and S. Pablo Sardi
- 9383 **Algorithms for Olfactory Search across Species**
Keeley L. Baker, Michael Dickinson, Teresa M. Findley, David H. Gire, Matthieu Louis, Marie P. Suver, Justus V. Verhagen, Katherine I. Nagel, and Matthew C. Smear
- 9390 **Latent Factors and Dynamics in Motor Cortex and Their Application to Brain–Machine Interfaces**
Chethan Pandarinath, K. Cora Ames, Abigail A. Russo, Ali Farshchian, Lee E. Miller, Eva L. Dyer, and Jonathan C. Kao

- 9402 More than Just a “Motor”: Recent Surprises from the Frontal Cortex**
Christian L. Ebbesen, Michele N. Insanally, Charles D. Kopec, Masayoshi Murakami, Akiko Saiki, and Jeffrey C. Erlich
- 9414 Defining Dysbiosis in Disorders of Movement and Motivation**
Christopher T. Fields, Timothy R. Sampson, Annadora J. Bruce-Keller, Drew D. Kiraly, Elaine Y. Hsiao, and Geert J. de Vries
- 9423 Sex Differences in Risk and Resilience: Stress Effects on the Neural Substrates of Emotion and Motivation**
Cara L. Wellman, Debra A. Bangasser, Justin L. Bollinger, Laurence Coutellier, Marian L. Logrip, Kelly M. Moench, and Kimberly R. Urban
- 9433 Neurocognitive Development of Motivated Behavior: Dynamic Changes across Childhood and Adolescence**
Dylan G. Gee, Kevin G. Bath, Carolyn M. Johnson, Heidi C. Meyer, Vishnu P. Murty, Wouter van den Bos, and Catherine A. Hartley
- 9446 Specific Basal Forebrain–Cortical Cholinergic Circuits Coordinate Cognitive Operations**
Laszlo Záborszky, Peter Gombkoto, Peter Varsanyi, Gina Poe, Lorna W. Role, Mala Ananth, Prithviraj Rajebhosale, David Talmage, Michael E. Hasselmo, Holger Dannenberg, Victor H. Minces, and Andrea A. Chiba
- 9459 New observations in neuroscience using superresolution microscopy**
Michihiro Igarashi, Motohiro Nozumi, Ling-Gang Wu, Francesca Cella Zanicchi, István Katona, László Barna, Pingyong Xu, Mingshu Zhang, Fudong Xue, and Edward Boyden
- 9468 Dialogues: The Science and Power of Storytelling**
Wendy A. Suzuki, Mónica I. Feliú-Mójer, Uri Hasson, Rachel Yehuda, and Jean Mary Zarate

Research Articles

CELLULAR/MOLECULAR

- 9600 Neogenin in Amygdala for Neuronal Activity and Information Processing**
Xiang-Dong Sun, Wen-Bing Chen, Dong Sun, Jie Huang, Yuan-Quan Li, Jin-Xiu Pan, Ya-Nan Wang, Kai Zhao, Zhao-Qi Dong, Hong-Sheng Wang, Lei Xiong, Aiguo Xuan, Shen-Ting Zhao, Anilkumar Pillai, Wen-Cheng Xiong, and Lin Mei

DEVELOPMENT/PLASTICITY/REPAIR

- 9505 Molecular and Genetic Evidence for the PDGFR α -Independent Population of Oligodendrocyte Progenitor Cells in the Developing Mouse Brain**
Kang Zheng, Chunyang Wang, Junlin Yang, Hao Huang, Xiaofeng Zhao, Zunyi Zhang, and Mengsheng Qiu
- 9539 Sox14 Is Required for a Specific Subset of Cerebello–Olivary Projections**
Hong-Ting Prekop, Anna Kroiss, Victoria Rook, Laskaro Zagoraiou, Thomas M. Jessell, Cathy Fernandes, Alessio Delogu, and Richard J.T. Wingate

SYSTEMS/CIRCUITS

- 9563 Emergence of Binocular Disparity Selectivity through Hebbian Learning**
Tushar Chauhan, Timothée Masquelier, Alexandre Montlibert, and Benoit R. Cottureau

BEHAVIORAL/COGNITIVE

- 9471 Attractor-like Dynamics in Belief Updating in Schizophrenia**
Rick A. Adams, Gary Napier, Jonathan P. Roiser, Christoph Mathys, and James Gilleen
- 9486 Visuomotor Correlates of Conflict Expectation in the Context of Motor Decisions**
Gerard Derosiere, Pierre-Alexandre Klein, Sylvie Nozaradan, Alexandre Zénon, André Mouraux, and Julie Duque
- 9514 CREST in the Nucleus Accumbens Core Regulates Cocaine Conditioned Place Preference, Cocaine-Seeking Behavior, and Synaptic Plasticity**
Yasaman Alaghband, Enikő Kramár, Janine L. Kwapis, Earnest S. Kim, Thekla J. Hemstedt, Alberto J. López, André O. White, Amni Al-Kachak, Osasumwen V. Aimuwu, Kasuni K. Bodinayake, Nicole C. Oparaugo, Joseph Han, K. Matthew Lattal, and Marcelo A. Wood
- 9527 The Time Course of Target Template Activation Processes during Preparation for Visual Search**
Anna Grubert and Martin Eimer
- 9551 On the Role of Cortex-Basal Ganglia Interactions for Category Learning: A Neurocomputational Approach**
Francesc Villagrasa, Javier Baladron, Julien Vitay, Henning Schroll, Evan G. Antzoulatos, Earl K. Miller, and Fred H. Hamker

NEUROBIOLOGY OF DISEASE

- 9579 Neural Deletion of Glucose Transporter Isoform 3 Creates Distinct Postnatal and Adult Neurobehavioral Phenotypes**
Bo-Chul Shin, Carlos Cepeda, Ana María Estrada-Sánchez, Michael S. Levine, Laya Hodaie, Yun Dai, Jai Jung, Amit Ganguly, Peter Clark, and Sherin U. Devaskar

Persons interested in becoming members of the Society for Neuroscience should contact the Membership Department, Society for Neuroscience, 1121 14th St., NW, Suite 1010, Washington, DC 20005, phone 202-962-4000.

Instructions for Authors are available at <http://www.jneurosci.org/content/information-authors>. Authors should refer to these Instructions online for recent changes that are made periodically.

Submissions should be submitted online using the following url: <http://jneurosci.msubmit.net>. Please contact the Central Office, via phone, fax, or e-mail with any questions. Our contact information is as follows: phone, 202-962-4000; e-mail, jn@sfn.org.

PROGRESSIONS

The First Annual Meeting of the Society for Neuroscience, 1971: Reflections Approaching the 50th Anniversary of the Society's Formation

R. Douglas Fields

National Institutes of Health, National Institute of Child Health and Human Development, Bethesda, Maryland 20904

The formation of the Society for Neuroscience in 1969 was a scientific landmark, remarkable for the conceptual transformation it represented by uniting all fields touching on the nervous system. The scientific program of the first annual meeting of the Society for Neuroscience, held in Washington, DC in 1971, is summarized here. By reviewing the scientific program from the vantage point of the 50th anniversary of the Society for Neuroscience, the trajectory of research now and into the future can be tracked to its origins, and the impact that the founding of the Society has had on basic and biomedical science is evident. The broad foundation of the Society was firmly cast at this first meeting, which embraced the full spectrum of science related to the nervous system, emphasized the importance of public education, and attracted the most renowned scientists of the day who were drawn together by a common purpose and eagerness to share research and ideas. Some intriguing areas of investigation discussed at this first meeting blossomed into new branches of research that flourish today, but others dwindled and have been largely forgotten. Technological developments and advances in understanding of brain function have been profound since 1971, but the success of the first meeting demonstrates how uniting scientists across diversity fueled prosperity of the Society and propelled the vigorous advancement of science.

The Journal of Neuroscience, October 31, 2018 • 38(44):9311–9317

VIEWPOINTS

Linking Nanoscale Dynamics of AMPA Receptor Organization to Plasticity of Excitatory Synapses and Learning

Daniel Choquet^{1,2,3}

¹Centre National de la Recherche Scientifique, Interdisciplinary Institute for Neuroscience, Unité Mixte de Recherche 5297, F-33000 Bordeaux, France,

²University of Bordeaux, Interdisciplinary Institute for Neuroscience, Unité Mixte de Recherche 5297, F-33000 Bordeaux, France, and ³Bordeaux Imaging Center, UMS 3420 Centre National de la Recherche Scientifique, Université de Bordeaux, US4 INSERM, F-33000 Bordeaux, France

The spatiotemporal organization of neurotransmitter receptors in the postsynaptic membrane is a fundamental determinant of synaptic transmission and thus of information processing by the brain. The ionotropic AMPA subtype of glutamate receptors (AMPA receptors) mediate fast excitatory synaptic transmission in the CNS. The number of AMPARs located on face presynaptic glutamate release sites sets the efficacy of synaptic transmission. Understanding how this number is set and regulated has been the topic of intense research in the last two decades. We showed that AMPARs are not stable in the synapse as initially thought. They continuously enter and exit the postsynaptic density by lateral diffusion, and they exchange between the neuronal surface and intracellular compartments by endocytosis and exocytosis at extrasynaptic sites. Regulation of these various trafficking pathways has emerged as a key mechanism for activity-dependent plasticity of synaptic transmission, a process important for learning and memory. I here present my view of these findings. In particular, the advent of super-resolution microscopy and single-molecule tracking has helped to uncover the intricacy of AMPARs' dynamic organization at the nanoscale. In addition, AMPAR surface diffusion is highly regulated by a variety of factors, including neuronal activity, stress hormones, and neurodegeneration, suggesting that AMPAR diffusion-trapping may play a central role in synapse function. Using innovative tools to understand further the link between receptor dynamics and synapse plasticity is now unveiling new molecular mechanisms of learning. Modifying AMPAR dynamics may emerge as a new target to correct synapse dysfunction in the diseased brain.

The Journal of Neuroscience, October 31, 2018 • 38(44):9318–9329

Whole-Brain Analysis of Cells and Circuits by Tissue Clearing and Light-Sheet Microscopy

Tomoyuki Mano,^{1,2*} Alexandre Albanese,^{4*} Hans-Ulrich Dodt,^{8,9} Ali Erturk,^{10,11,12} Viviana Gradinaru,¹³ Jennifer B. Treweek,^{13,14} Atsushi Miyawaki,^{15,16} Kwanghun Chung,^{4,5,6,7,17} and Hiroki R. Ueda^{2,3,18}

¹Department of Information Physics and Computing, Graduate School of Information Science and Technology, ²International Research Center for Neurointelligence, UTIAS, ³Department of Systems Pharmacology, Graduate School of Medicine, The University of Tokyo, 113-0033 Tokyo, Japan, ⁴Institute for Medical Engineering and Science, ⁵Picower Institute for Learning and Memory, ⁶Department of Chemical Engineering, ⁷Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology (MIT), Cambridge, Massachusetts 02139, ⁸Department of Bioelectronics, Vienna University of Technology, FKE, 1040 Vienna, Austria, ⁹Center for Brain Research, Medical University of Vienna, 1090 Vienna, Austria, ¹⁰Institute for Stroke and Dementia Research, Klinikum der Universität München, Ludwig Maximilians University of Munich, 80539 Munich, Germany, ¹¹Graduate School of Systemic Neurosciences, 80539 Munich, Germany, ¹²Munich Cluster for Systems Neurology, 81377 Munich, Germany, ¹³Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, California, 91125, ¹⁴Department of Biomedical Engineering, University of Southern California, Los Angeles, California 90089, ¹⁵Laboratory for Cell Function and Dynamics, Center for Brain Science, ¹⁶Biotechnological Optics Research Team, Center for Advanced Photonics, RIKEN, Wako-City, 351-0198 Saitama, Japan, ¹⁷Broad Institute of Harvard University and MIT, Cambridge, Massachusetts 02142, and ¹⁸Laboratory for Synthetic Biology, RIKEN Center for Biosystems Dynamics Research, 565-0871 Suita, Japan

In this photo essay, we present a sampling of technologies from laboratories at the forefront of whole-brain clearing and imaging for high-resolution analysis of cell populations and neuronal circuits. The data presented here were provided for the eponymous Mini-Symposium presented at the Society for Neuroscience's 2018 annual meeting.

The Journal of Neuroscience, October 31, 2018 • 38(44):9330–9337

The Elegance of Sonic Hedgehog: Emerging Novel Functions for a Classic Morphogen

A. Denise R. Garcia,¹ Young-Goo Han,² Jason W. Triplett,³ W. Todd Farmer,⁴ Corey C. Harwell,^{6*} and Rebecca A. Ihrie^{5*}

¹Departments of Biology and Neurobiology and Anatomy, Drexel University, Philadelphia, Pennsylvania, Philadelphia, PA 19146, ²Department of Developmental Neurobiology, Neurobiology and Brain Tumor Program, St. Jude Children's Research Hospital, Memphis, Tennessee, Memphis, TN 38105, ³Center for Neuroscience Research, Children's National Medical Center, Departments of Pediatrics and Pharmacology and Physiology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, Washington, District of Columbia, 20010, ⁴Centre for Research in Neuroscience, Department of Neurology and Neurosurgery, Brain Repair and Integrative Neuroscience Program, The Research Institute of the McGill University Health Center, Montreal General Hospital, Montreal, Quebec, Canada, H3G 1A4, ⁵Departments of Cell and Developmental Biology and Neurological Surgery, Vanderbilt University School of Medicine, Nashville, Tennessee, TN, 37232-6840, and ⁶Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, MA 02115

Sonic Hedgehog (SHH) signaling has been most widely known for its role in specifying region and cell-type identity during embryonic morphogenesis. This mini-review accompanies a 2018 SFN mini-symposium that addresses an emerging body of research focused on understanding the diverse roles for Shh signaling in a wide range of contexts in neurodevelopment and, more recently, in the mature CNS. Such research shows that Shh affects the function of brain circuits, including the production and maintenance of diverse cell types and the establishment of wiring specificity. Here, we review these novel and unexpected functions and the unanswered questions regarding the role of SHH and its signaling pathway members in these cases.

The Journal of Neuroscience, October 31, 2018 • 38(44):9338–9345

Advances in Enteric Neurobiology: The “Brain” in the Gut in Health and Disease

Subhash Kulkarni,¹ Julia Ganz,² James Bayrer,³ Laren Becker,⁴ Milena Bogunovic,⁵ and Meenakshi Rao⁶

¹Department of Medicine, The John Hopkins University School of Medicine, Baltimore, Maryland 21205, ²Department of Integrative Biology, Michigan State University, East Lansing, Michigan 48824, ³Department of Pediatrics, University of California, San Francisco, San Francisco, California 94143, ⁴Department of Medicine, Stanford University, Stanford, California 94305, ⁵Department of Microbiology and Immunology, Penn State College of Medicine, Hershey, Pennsylvania 17033, and ⁶Division of Gastroenterology, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts 02115

The enteric nervous system (ENS) is a large, complex division of the peripheral nervous system that regulates many digestive, immune, hormonal, and metabolic functions. Recent advances have elucidated the dynamic nature of the mature ENS, as well as the complex, bidirectional interactions among enteric neurons, glia, and the many other cell types that are important for mediating gut behaviors. Here, we provide an overview of ENS development and maintenance, and focus on the latest insights gained from the use of novel model systems and live-imaging techniques. We discuss major advances in the understanding of enteric glia, and the functional interactions among enteric neurons, glia, and enteroendocrine cells, a large class of sensory epithelial cells. We conclude by highlighting recent work on muscularis macrophages, a group of immune cells that closely interact with the ENS in the gut wall, and the importance of neurological-immune system communication in digestive health and disease.

The Journal of Neuroscience, October 31, 2018 • 38(44):9346–9354

Unveiling the Extracellular Space of the Brain: From Super-resolved Microstructure to *In Vivo* Function

Sabina Hrabetova,¹ Laurent Cognet,^{2,3} Dmitri A. Rusakov,⁴ and U. Valentin Nägerl^{5,6}

¹Department of Cell Biology, State University of New York Downstate Medical Center, Brooklyn, New York 11203, ²Université de Bordeaux, Laboratoire Photonique Numérique et Nanosciences, F-33400 Talence, France, ³Institut d'Optique and Centre National de la Recherche Scientifique, F-33400 Talence, France, ⁴Institute of Neurology, University College London, London WC1N 3BG, United Kingdom, ⁵Institut Interdisciplinaire des Neurosciences, Université de Bordeaux, 33077 Bordeaux, France, and ⁶Institut Interdisciplinaire des Neurosciences, Centre National de la Recherche, 33077 Bordeaux, France

The extracellular space occupies approximately one-fifth of brain volume, molding a spider web of gaps filled with interstitial fluid and extracellular matrix where neurons and glial cells perform in concert. Yet, very little is known about the spatial organization and dynamics of the extracellular space, let alone its influence on brain function, owing to a lack of appropriate techniques (and a traditional bias toward the inside of cells, not the spaces in between). At the same time, it is clear that understanding fundamental brain functions, such as synaptic transmission, memory, sleep, and recovery from disease, calls for more focused research on the extracellular space of the brain. This review article highlights several key research areas, covering recent methodological and conceptual progress that illuminates this understudied, yet critically important, brain compartment, providing insights into the opportunities and challenges of this nascent field.

The Journal of Neuroscience, October 31, 2018 • 38(44):9355–9363

The Endolysosomal System and Proteostasis: From Development to Degeneration

Bettina Winckler,¹ Victor Faundez,² Sandra Maday,³ Qian Cai,⁴ Cláudia Guimas Almeida,⁵ and Huaye Zhang⁶

¹Department of Cell Biology, University of Virginia Health System, Charlottesville, Virginia 22908, ²Department of Cell Biology, Emory University, Atlanta, Georgia 30322, ³Department of Neuroscience, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104, ⁴Department of Cell Biology and Neuroscience, Rutgers, State University of New Jersey, Piscataway, New Jersey 08854, ⁵Chronic Diseases Research Center, NOVA Medical School, Universidade NOVA de Lisboa, Lisbon, Portugal 1169-056, and ⁶Department of Neuroscience and Cell Biology, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey 08854

How do neurons adapt their endolysosomal system to address the particular challenge of membrane transport across their elaborate cellular landscape and to maintain proteostasis for the lifetime of the organism? Here we review recent findings that address this central question. We discuss the cellular and molecular mechanisms of endolysosomal trafficking and the autophagy pathway in neurons, as well as their role in neuronal development and degeneration. These studies highlight the importance of understanding the basic cell biology of endolysosomal trafficking and autophagy and their roles in the maintenance of proteostasis within the context of neurons, which will be critical for developing effective therapies for various neurodevelopmental and neurodegenerative disorders.

The Journal of Neuroscience, October 31, 2018 • 38(44):9364–9374

New Frontiers in Parkinson's Disease: From Genetics to the Clinic

Lamya S. Shihabuddin,¹ Patrik Brundin,² J. Timothy Greenamyre,³ Diane Stephenson,⁴ and S. Pablo Sardi¹

¹Neuroscience Therapeutic Area, Sanofi, Framingham, MA 01701, ²Van Andel Research Institute, Grand Rapids, MI 49503, ³Pittsburgh Institute for Neurodegenerative Diseases, University of Pittsburgh, Pittsburgh, PA 15260, and ⁴Critical Path Institute, CAMD, Tucson, AZ 85718

The greatest unmet therapeutic need in Parkinson's disease (PD) is a treatment that slows the relentless progression of the symptoms and the neurodegenerative process. This review highlights the utility of genetics to understand the pathogenic mechanisms and develop novel therapeutic approaches for PD. The focus is on strategies provided by genetic studies: notably via the reduction and clearance of α -synuclein, inhibition of LRRK2 kinase activity, and modulation of glucocerebrosidase-related substrates. In addition, the critical role of precompetitive public-private partnerships in supporting trial design optimization, overall drug development, and regulatory approvals is illustrated. With these great advances, the promise of developing transformative therapies that halt or slow disease progression is a tangible goal.

The Journal of Neuroscience, October 31, 2018 • 38(44):9375–9382

Algorithms for Olfactory Search across Species

Keeley L. Baker,^{1,2} Michael Dickinson,³ Teresa M. Findley,^{4,5} David H. Gire,⁶ Matthieu Louis,^{7,8,9} Marie P. Suver,¹⁰ Justus V. Verhagen,^{1,2} Katherine I. Nagel,¹⁰ and Matthew C. Smear^{4,11}

¹Department of Neuroscience, Yale School of Medicine, New Haven 06519, Connecticut, ²John B. Pierce Laboratory, New Haven 06519, Connecticut, ³Division of Biology and Bioengineering, California Institute of Technology, Pasadena 91125, California, ⁴Institute of Neuroscience, University of Oregon, Eugene 97403, Oregon, ⁵Department of Biology, University of Oregon, Eugene 97403, Oregon, ⁶Department of Psychology, University of Washington, Seattle 98195, Washington, ⁷Neuroscience Research Institute, University of Santa Barbara, Santa Barbara 93106, California, ⁸Department of Molecular, Cellular, and Developmental Biology, University of Santa Barbara, Santa Barbara 93106, California, ⁹Department of Physics, University of Santa Barbara, Santa Barbara 93106, California, ¹⁰Neuroscience Institute, New York University Langone Medical Center, New York 10016, New York, and ¹¹Department of Psychology, University of Oregon, Eugene 97403, Oregon

Localizing the sources of stimuli is essential. Most organisms cannot eat, mate, or escape without knowing where the relevant stimuli originate. For many, if not most, animals, olfaction plays an essential role in search. While microorganismal chemotaxis is relatively well understood, in larger animals the algorithms and mechanisms of olfactory search remain mysterious. In this symposium, we will present recent advances in our understanding of olfactory search in flies and rodents. Despite their different sizes and behaviors, both species must solve similar problems, including meeting the challenges of turbulent airflow, sampling the environment to optimize olfactory information, and incorporating odor information into broader navigational systems.

The Journal of Neuroscience, October 31, 2018 • 38(44):9383–9389

Latent Factors and Dynamics in Motor Cortex and Their Application to Brain–Machine Interfaces

Chethan Pandarinath,^{1,2} K. Cora Ames,^{3,4,5,6} Abigail A. Russo,^{3,5,6} Ali Farshchian,⁷ Lee E. Miller,⁷ Eva L. Dyer,^{1,8} and Jonathan C. Kao^{9,10}

¹Wallace H. Coulter Department of Biomedical Engineering, Emory University and Georgia Institute of Technology, Atlanta, Georgia 30322, ²Department of Neurosurgery, Emory University, Atlanta, Georgia 30322, ³Department of Neuroscience, ⁴Center for Theoretical Neuroscience, ⁵Grossman Center for the Statistics of Mind, ⁶Zuckerman Institute, Columbia University, New York, New York 10027, ⁷Department of Physiology, Northwestern University, Chicago, Illinois 60611, ⁸Department of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, Georgia 30332, ⁹Department of Electrical and Computer Engineering, and ¹⁰Neurosciences Program, University of California, Los Angeles, California 90095

In the 1960s, Evarts first recorded the activity of single neurons in motor cortex of behaving monkeys (Evarts, 1968). In the 50 years since, great effort has been devoted to understanding how single neuron activity relates to movement. Yet these single neurons exist within a vast network, the nature of which has been largely inaccessible. With advances in recording technologies, algorithms, and computational power, the ability to study these networks is increasing exponentially. Recent experimental results suggest that the dynamical properties of these networks are critical to movement planning and execution. Here we discuss this dynamical systems perspective and how it is reshaping our understanding of the motor cortices. Following an overview of key studies in motor cortex, we discuss techniques to uncover the “latent factors” underlying observed neural population activity. Finally, we discuss efforts to use these factors to improve the performance of brain–machine interfaces, promising to make these findings broadly relevant to neuroengineering as well as systems neuroscience.

The Journal of Neuroscience, October 31, 2018 • 38(44):9390–9401

More than Just a “Motor”: Recent Surprises from the Frontal Cortex

Christian L. Ebbesen,^{1,2} Michele N. Insanally,^{1,2} Charles D. Kopec,³ Masayoshi Murakami,⁴ Akiko Saiki,^{5,6} and Jeffrey C. Erlich^{7,8,9}

¹Skirball Institute for Biomolecular Medicine, New York University School of Medicine, New York, New York 10016, ²Center for Neural Science, New York University, New York, New York 10003, ³Princeton Neuroscience Institute, Princeton University, Princeton, New Jersey 08544, ⁴Department of Neurophysiology, Division of Medicine, University of Yamanashi, Chuo, Yamanashi 409-3898, Japan, ⁵Institute of Biomedical and Health Sciences, Hiroshima University, Hiroshima, 734-8553, Japan, ⁶Department of Neurobiology, Northwestern University, Evanston, Illinois 60208, ⁷New York University Shanghai, Shanghai, China 200122, ⁸NYU-ECNU Institute for Brain and Cognitive Science at NYU Shanghai, Shanghai, China 200062, and ⁹Shanghai Key Laboratory of Brain Functional Genomics (Ministry of Education), East China Normal University, Shanghai, China 200062

Motor and premotor cortices are crucial for the control of movements. However, we still know little about how these areas contribute to higher-order motor control, such as deciding which movements to make and when to make them. Here we focus on rodent studies and review recent findings, which suggest that—in addition to motor control—neurons in motor cortices play a role in sensory integration, behavioral strategizing, working memory, and decision-making. We suggest that these seemingly disparate functions may subserve an evolutionarily conserved role in sensorimotor cognition and that further study of rodent motor cortices could make a major contribution to our understanding of the evolution and function of the mammalian frontal cortex.

The Journal of Neuroscience, October 31, 2018 • 38(44):9402–9413

Defining Dysbiosis in Disorders of Movement and Motivation

Christopher T. Fields,¹ Timothy R. Sampson,² Annadora J. Bruce-Keller,³ Drew D. Kiraly,⁴ Elaine Y. Hsiao,⁵ and Geert J. de Vries¹

¹Neuroscience Institute, Georgia State University, Atlanta, Georgia 30303, ²Division of Biology & Biological Engineering, California Institute of Technology, Pasadena, California 91125, ³Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, Louisiana 70808, ⁴Departments of Psychiatry & Neuroscience, Friedman Brain Institute, Icahn School of Medicine, New York, New York 10029, and ⁵Department of Integrative Biology and Physiology, University of California–Los Angeles, Los Angeles, California 90095

The gut microbiota has emerged as a critical player in shaping and modulating brain function and has been shown to influence numerous behaviors, including anxiety and depression-like behaviors, sociability, and cognition. However, the effects of the gut microbiota on specific disorders associated with thalamo-cortico-basal ganglia circuits, ranging from compulsive behavior and addiction to altered sensation and motor output, are only recently being explored. Wholesale depletion and alteration of gut microbial communities in rodent models of disorders, such as Parkinson's disease, autism, and addiction, robustly affect movement and motivated behavior. A new frontier therefore lies in identifying specific microbial alterations that affect these behaviors and understanding the underlying mechanisms of action. Comparing alterations in gut microbiota across multiple basal-ganglia associated disease states allows for identification of common mechanistic pathways that may interact with distinct environmental and genetic risk factors to produce disease-specific outcomes.

The Journal of Neuroscience, October 31, 2018 • 38(44):9414–9422

Sex Differences in Risk and Resilience: Stress Effects on the Neural Substrates of Emotion and Motivation

Cara L. Wellman,¹ Debra A. Bangasser,² Justin L. Bollinger,³ Laurence Coutellier,⁴ Marian L. Logrip,⁵ Kelly M. Moench,¹ and Kimberly R. Urban⁶

¹Department of Psychological and Brain Sciences, Program in Neuroscience, and Center for the Integrative Study of Animal Behavior, Indiana University, Bloomington, Indiana 47405, ²Psychology Department and Neuroscience Program, Temple University, Philadelphia, Pennsylvania 19122, ³Department of Pharmacology and Systems Physiology, University of Cincinnati College of Medicine, Cincinnati, Ohio 45237, ⁴Departments of Psychology and Neuroscience, Ohio State University, Columbus, Ohio 43210, ⁵Department of Psychology, Indiana University-Purdue University Indianapolis, Indianapolis, Indiana 46202, and ⁶Children's Hospital of Philadelphia, Abramson Research Center, Philadelphia, Pennsylvania 19104

Risk for stress-sensitive psychopathologies differs in men and women, yet little is known about sex-dependent effects of stress on cellular structure and function in corticolimbic regions implicated in these disorders. Determining how stress influences these regions in males and females will deepen our understanding of the mechanisms underlying sex-biased psychopathology. Here, we discuss sex differences in CRF regulation of arousal and cognition, glucocorticoid modulation of amygdalar physiology and alcohol consumption, the age-dependent impact of social stress on prefrontal pyramidal cell excitability, stress effects on the prefrontal parvalbumin system in relation to emotional behaviors, contributions of stress and gonadal hormones to stress effects on prefrontal glia, and alterations in corticolimbic structure and function after cessation of chronic stress. These studies demonstrate that, while sex differences in stress effects may be nuanced, nonuniform, and nonlinear, investigations of these differences are nonetheless critical for developing effective, sex-specific treatments for psychological disorders.

The Journal of Neuroscience, October 31, 2018 • 38(44):9423–9432

Neurocognitive Development of Motivated Behavior: Dynamic Changes across Childhood and Adolescence

Dylan G. Gee,¹ Kevin G. Bath,² Carolyn M. Johnson,³ Heidi C. Meyer,⁴ Vishnu P. Murty,⁵ Wouter van den Bos,⁶ and Catherine A. Hartley⁷

¹Department of Psychology, Yale University, New Haven, CT 06520, ²Department of Cognitive, Linguistic, and Psychological Sciences, Brown University, Providence, RI 02912, ³Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA 02138, ⁴Department of Psychiatry, Weill Cornell Medicine, New York, NY 10065, ⁵Department of Psychology, Temple University, Philadelphia, PA 19122, ⁶Department of Developmental Psychology, University of Amsterdam, Amsterdam, Netherlands, and ⁷Department of Psychology, New York University, New York, NY 10003

The ability to anticipate and respond appropriately to the challenges and opportunities present in our environments is critical for adaptive behavior. Recent methodological innovations have led to substantial advances in our understanding of the neurocircuitry supporting such motivated behavior in adulthood. However, the neural circuits and cognitive processes that enable threat- and reward-motivated behavior undergo substantive changes over the course of development, and these changes are less well understood. In this article, we highlight recent research in human and animal models demonstrating how developmental changes in prefrontal-subcortical neural circuits give rise to corresponding changes in the processing of threats and rewards from infancy to adulthood. We discuss how these developmental trajectories are altered by experiential factors, such as early-life stress, and highlight the relevance of this research for understanding the developmental onset and treatment of psychiatric disorders characterized by dysregulation of motivated behavior.

The Journal of Neuroscience, October 31, 2018 • 38(44):9433–9445

Specific Basal Forebrain–Cortical Cholinergic Circuits Coordinate Cognitive Operations

Laszlo Záborszky,¹ Peter Gombkoto,¹ Peter Varsanyi,¹ Matthew R. Gielow,¹ Gina Poe,² Lorna W. Role,³ Mala Ananth,⁴ Prithviraj Rajebhosale,⁴ David A. Talmage,⁵ Michael E. Hasselmo,⁶ Holger Dannenberg,⁶ Victor H. Minces,⁷ and Andrea A. Chiba⁷

¹Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark 07102, ²Department of Integrative Biology and Physiology, University of California, Los Angeles 90095, ³Department of Neurobiology and Center for Nervous System Disorders, Stony Brook University, Stony Brook, New York 11794, ⁴Program in Neuroscience and Center for Nervous System Disorders, Stony Brook University, Stony Brook, New York 11794, ⁵Department of Pharmacological Sciences and Center for Nervous System Disorders, Stony Brook University, Stony Brook, New York 11794, ⁶Center for Systems Neuroscience and Department of Psychological and Brain Sciences, Boston University, Boston, Massachusetts 02215, and ⁷Department of Cognitive Science, University of California, San Diego 92093

Based on recent molecular genetics, as well as functional and quantitative anatomical studies, the basal forebrain (BF) cholinergic projections, once viewed as a diffuse system, are emerging as being remarkably specific in connectivity. Acetylcholine (ACh) can rapidly and selectively modulate activity of specific circuits and ACh release can be coordinated in multiple areas that are related to particular aspects of cognitive processing. This review discusses how a combination of multiple new approaches with more established techniques are being used to finally reveal how cholinergic neurons, together with other BF neurons, provide temporal structure for behavior, contribute to local cortical state regulation, and coordinate activity between different functionally related cortical circuits. ACh selectively modulates dynamics for encoding and attention within individual cortical circuits, allows for important transitions during sleep, and shapes the fidelity of sensory processing by changing the correlation structure of neural firing. The importance of this system for integrated and fluid behavioral function is underscored by its disease-modifying role; the demise of BF cholinergic neurons has long been established in Alzheimer's disease and recent studies have revealed the involvement of the cholinergic system in modulation of anxiety-related circuits. Therefore, the BF cholinergic system plays a pivotal role in modulating the dynamics of the brain during sleep and behavior, as foretold by the intricacies of its anatomical map.

The Journal of Neuroscience, October 31, 2018 • 38(44):9446–9458

New observations in neuroscience using superresolution microscopy

Michihiro Igarashi,^{1*} Motohiro Nozumi,¹ Ling-Gang Wu,² Francesca Cella Zanacchi,³ István Katona,⁴ László Barna,⁵ Pingyong Xu,^{6,7,8} Mingshu Zhang,^{6,7} Fudong Xue,^{6,7} and Edward Boyden⁹

¹Department of Neurochemistry and Molecular Cell Biology, Niigata University Graduate School of Medicine, Niigata 951-8510, Japan, ²National Institute of Neurological Disorders and Stroke, Bethesda, Maryland 20892, ³Department of Nanophysics, Fondazione Istituto Italiano di Tecnologia, Genova 16163, Italy, ⁴Momentum Laboratory of Molecular Neurobiology, Department of Molecular and Developmental Neurobiology, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest 1083, Hungary, ⁵Nikon Center of Excellence for Neuronal Imaging, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary, ⁶Key Laboratory of Noncoding RNA, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China, ⁷Beijing Key Laboratory of Noncoding RNA, Institute of Biophysics, Chinese Academy of Sciences, Beijing, 100101, China, ⁸University of Chinese Academy of Sciences, Beijing 100049, China, and ⁹Department of Biological Engineering and Brain and Cognitive Sciences, Media Laboratory, Massachusetts Institute of Technology (MIT), Cambridge, Massachusetts 02139

Superresolution microscopy (SM) techniques are among the revolutionary methods for molecular and cellular observations in the 21st century. SM techniques overcome optical limitations, and several new observations using SM lead us to expect these techniques to have a large impact on neuroscience in the near future. Several types of SM have been developed, including structured illumination microscopy (SIM), stimulated emission depletion microscopy (STED), and photoactivated localization microscopy (PALM)/stochastic optical reconstruction microscopy (STORM), each with special features. In this Minisymposium, experts in these different types of SM discuss the new structural and functional information about specific important molecules in neuroscience that has been gained with SM. Using these techniques, we have revealed novel mechanisms of endocytosis in nerve growth, fusion pore dynamics, and described quantitative new properties of excitatory and inhibitory synapses. Additional powerful techniques, including single molecule-guided Bayesian localization SM (SIMBA) and expansion microscopy (ExM), alone or combined with super-resolution observation, are also introduced in this session.

The Journal of Neuroscience, October 31, 2018 • 38(44):9459–9467

Dialogues: The Science and Power of Storytelling

Wendy A. Suzuki,¹ Mónica I. Feliú-Mójer,^{2,3} Uri Hasson,⁴ Rachel Yehuda,⁵ and Jean Mary Zarate⁶

¹Center for Neural Science, New York University, New York, New York 10003, ²Ciencia Puerto Rico, San Juan, Puerto Rico 00919, ³iBiology, San Francisco, California 94158, ⁴Department of Psychology and the Neuroscience Institute, Princeton University, Princeton, New Jersey 08540, ⁵Department of Psychiatry and Neuroscience, Icahn School of Medicine at Mount Sinai, New York, New York 10029, and ⁶Nature Neuroscience, New York, New York 10004-1562

Skillful storytelling helps listeners understand the essence of complex concepts and ideas in meaningful and often personal ways. For this reason, storytelling is being embraced by scientists who not only want to connect more authentically with their audiences, but also want to understand how the brain processes this powerful form of communication. Here we present part of a conversation between a group of scientists actively engaged with the practice and/or the science of storytelling. We highlight the brain networks involved in the telling and hearing of stories and show how storytelling is being used well beyond the realm of public communication to add a deeper dimension to communication with our students and colleagues, as well as helping to make our profession more inclusive.

The Journal of Neuroscience, October 31, 2018 • 38(44):9468–9470

Research Articles

CELLULAR/MOLECULAR

Neogenin in Amygdala for Neuronal Activity and Information Processing

Xiang-Dong Sun,^{1,4*} Wen-Bing Chen,^{2,3,4*} Dong Sun,^{2,4*} Jie Huang,¹ Yuan-Quan Li,¹ Jin-Xiu Pan,^{2,4} Ya-Nan Wang,⁷ Kai Zhao,^{2,4} Zhao-Qi Dong,^{2,4} Hong-Sheng Wang,^{2,4} Lei Xiong,^{2,4} Aiguo Xuan,¹ Shen-Ting Zhao,¹ Anilkumar Pillai,⁵ Wen-Cheng Xiong,^{2,4,6} and Lin Mei^{2,3,4,6}

¹School of Basic Medical Sciences, Second Affiliated Hospital of Guangzhou Medical University, Guangzhou 510260, China, ²Department of Neurosciences, School of Medicine, Case Western Reserve University, Cleveland, Ohio 44106, ³Institute of Life Science, Nanchang University, Nanchang 330031, China, ⁴Department of Neuroscience and Regenerative Medicine, Medical College of Georgia, Augusta University, Augusta, Georgia 30912, ⁵Department of Psychiatry, Medical College of Georgia, Augusta University, Augusta, Georgia 30912, ⁶Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, Ohio 44106, and ⁷Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas 75390

Fear learning and memory are vital for livings to survive, dysfunctions in which have been implicated in various neuropsychiatric disorders. Appropriate neuronal activation in amygdala is critical for fear memory. However, the underlying regulatory mechanisms are not well understood. Here we report that Neogenin, a DCC (deleted in colorectal cancer) family receptor, which plays important roles in axon navigation and adult neurogenesis, is enriched in excitatory neurons in BLA (Basolateral amygdala). Fear memory is impaired in male *Neogenin* mutant mice. The number of cFos⁺ neurons in response to tone-cued fear training was reduced in mutant mice, indicating aberrant neuronal activation in the absence of Neogenin. Electrophysiological studies show that *Neogenin* mutation reduced the cortical afferent input to BLA pyramidal neurons and compromised both induction and maintenance of Long-Term Potentiation evoked by stimulating cortical afferent, suggesting a role of Neogenin in synaptic plasticity. Concomitantly, there was a reduction in spine density and in frequency of miniature excitatory postsynaptic currents (mEPSCs), but not miniature inhibitory postsynaptic currents, suggesting a role of Neogenin in forming excitatory synapses. Finally, ablating *Neogenin* in the BLA in adult male mice impaired fear memory likely by reducing mEPSC frequency in BLA excitatory neurons. These results reveal an unrecognized function of Neogenin in amygdala for information processing by promoting and maintaining neurotransmission and synaptic plasticity and provide insight into molecular mechanisms of neuronal activation in amygdala.

The Journal of Neuroscience, October 31, 2018 • 38(44):9600–9613

DEVELOPMENT/PLASTICITY/REPAIR

Molecular and Genetic Evidence for the PDGFR α -Independent Population of Oligodendrocyte Progenitor Cells in the Developing Mouse Brain

Kang Zheng,¹ Chunyang Wang,¹ Junlin Yang,¹ Hao Huang,¹ Xiaofeng Zhao,¹ Zunyi Zhang,¹ and Mengsheng Qiu^{1,2}

¹Key Laboratory of Organ Development and Regeneration of Zhejiang Province, Institute of Life Sciences, Hangzhou Normal University, Hangzhou 311121, China and ²Department of Anatomical Sciences and Neurobiology, University of Louisville, Louisville, Kentucky 40292

PDGFR α , specifically expressed by immature oligodendrocyte progenitor cells (OPCs) in the CNS, plays a critical role in OPC proliferation and migration. However, it has been uncertain whether all cells of oligodendrocyte lineage are derived from the PDGFR α -expressing OPCs. In the present study, we uncovered a PDGFR α -independent oligodendrocyte lineage in the developing cortex. This OPC subpopulation originates from the local ventricular/subventricular zone after birth and contributes to the earliest mature oligodendrocytes in the cortex. PDGFR α signaling does not regulate the generation and differentiation of cortical OPCs. Fate-mapping studies in the PDGFR α ^{CreER}; Sox10-GFP/tTom double-transgenic mice of either sex have further corroborated the PDGFR α -independent oligodendrocyte lineage. This study provides additional missing genetic evidence for PDGFR α -independent oligodendrocyte lineage in the developing hindbrain.

The Journal of Neuroscience, October 31, 2018 • 38(44):9505–9513

Sox14 Is Required for a Specific Subset of Cerebello–Olivary Projections

Hong-Ting Prekop,^{1,2} Anna Kroiss,¹ Victoria Rook,² Laskaro Zagoraiou,^{3,4} Thomas M. Jessell,⁴ Cathy Fernandes,⁵ Alessio Delogu,¹ and Richard J.T. Wingate²

¹Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 9NU, United Kingdom, ²MRC Centre for Neurodevelopmental Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE1 1UL, United Kingdom, ³Biomedical Research Foundation Academy of Athens, 11527, Athens, Greece, ⁴Department of Neuroscience, Columbia University, New York, 10027, New York, and ⁵Centre for Social, Genetic and Developmental Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 8AF, United Kingdom

We identify *Sox14* as an exclusive marker of inhibitory projection neurons in the lateral and interposed, but not the medial, cerebellar nuclei. *Sox14*⁺ neurons make up ~80% of *Gad1*⁺ neurons in these nuclei and are indistinguishable by soma size from other inhibitory neurons. All *Sox14*⁺ neurons of the lateral and interposed cerebellar nuclei are generated at approximately E10/10.5 and extend long-range, predominantly contralateral projections to the inferior olive. A small *Sox14*⁺ population in the

adjacent vestibular nucleus “Y” sends an ipsilateral projection to the oculomotor nucleus. Cerebellar *Sox14*⁺ and glutamatergic projection neurons assemble in non-overlapping populations at the nuclear transition zone, and their integration into a coherent nucleus depends on *Sox14* function. Targeted ablation of *Sox14*⁺ cells by conditional viral expression of diphtheria toxin leads to significantly impaired motor learning. Contrary to expectations, associative learning is unaffected by unilateral *Sox14*⁺ neuron elimination in the interposed and lateral nuclei.

The Journal of Neuroscience, October 31, 2018 • 38(44):9539–9550

SYSTEMS/CIRCUITS

Emergence of Binocular Disparity Selectivity through Hebbian Learning

Tushar Chauhan,^{1,2} Timothée Masquelier,^{1,2} Alexandre Montlibert,^{1,2} and Benoit R. Cottureau^{1,2}

¹Centre de Recherche Cerveau et Cognition, Université de Toulouse, 31052 Toulouse, France, and ²Centre National de la Recherche Scientifique, 31055 Toulouse, France

Neural selectivity in the early visual cortex strongly reflects the statistics of our environment (Barlow, 2001; Geisler, 2008). Although this has been described extensively in literature through various encoding hypotheses (Barlow and Földiák, 1989; Atick and Redlich, 1992; Olshausen and Field, 1996), an explanation as to how the cortex might develop the computational architecture to support these encoding schemes remains elusive. Here, using the more realistic example of binocular vision as opposed to monocular luminance-field images, we show how a simple Hebbian coincidence-detector is capable of accounting for the emergence of binocular, disparity selective, receptive fields. We propose a model based on spike timing-dependent plasticity, which not only converges to realistic single-cell and population characteristics, but also demonstrates how known biases in natural statistics may influence population encoding and downstream correlates of behavior. Furthermore, we show that the receptive fields we obtain are closer in structure to electrophysiological data reported in macaques than those predicted by normative encoding schemes (Ringach, 2002). We also demonstrate the robustness of our model to the input dataset, noise at various processing stages, and internal parameter variation. Together, our modeling results suggest that Hebbian coincidence detection is an important computational principle and could provide a biologically plausible mechanism for the emergence of selectivity to natural statistics in the early sensory cortex.

The Journal of Neuroscience, October 31, 2018 • 38(44):9563–9578

BEHAVIORAL/COGNITIVE

Attractor-like Dynamics in Belief Updating in Schizophrenia

Rick A. Adams,^{1,2*} Gary Napier,^{1*} Jonathan P. Roiser,¹ Christoph Mathys,^{3,4,5†} and James Gilleen^{6,7†}

¹Institute of Cognitive Neuroscience, University College London, London WC1N 3AZ, United Kingdom, ²Division of Psychiatry, University College London, London W1T 7NF, United Kingdom, ³Scuola Internazionale Superiore di Studi Avanzati, 34136 Trieste, Italy, ⁴Translational Neuromodeling Unit, Institute for Biomedical Engineering, University of Zurich and ETH Zurich, 8032 Zurich, Switzerland, ⁵Max Planck Centre for Computational Psychiatry and Ageing Research, University College London, London WC1B 5EH, United Kingdom, ⁶Department of Psychology, University of Roehampton, London SE15 4JD, United Kingdom, and ⁷Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, Kings College London, London SE5 8AF, United Kingdom

Subjects with a diagnosis of schizophrenia (Scz) overweight unexpected evidence in probabilistic inference: such evidence becomes “aberrantly salient.” A neurobiological explanation for this effect is that diminished synaptic gain (e.g., hypofunction of cortical NMDARs) in Scz destabilizes quasi-stable neuronal network states (or “attractors”). This attractor instability account predicts that (1) Scz would overweight unexpected evidence but underweight consistent evidence, (2) belief updating would be more vulnerable to stochastic fluctuations in neural activity, and (3) these effects would correlate. Hierarchical Bayesian belief updating models were tested in two independent datasets ($n = 80$ male and $n = 167$ female) comprising human subjects with Scz, and both clinical and nonclinical controls (some tested when unwell and on recovery) performing the “probability estimates” version of the beads task (a probabilistic inference task). Models with a standard learning rate, or including a parameter increasing updating to “disconfirmatory evidence,” or a parameter encoding belief instability were formally compared. The “belief instability” model (based on the principles of attractor dynamics) had most evidence in all groups in both datasets. Two of four parameters differed between Scz and nonclinical controls in each dataset: belief instability and response stochasticity. These parameters correlated in both datasets. Furthermore, the clinical controls showed similar parameter distributions to Scz when unwell, but were no different from controls once recovered. These findings are consistent with the hypothesis that attractor network instability contributes to belief updating abnormalities in Scz, and suggest that similar changes may exist during acute illness in other psychiatric conditions.

The Journal of Neuroscience, October 31, 2018 • 38(44):9471–9485

Visuomotor Correlates of Conflict Expectation in the Context of Motor Decisions

Gerard Derosiere,¹ Pierre-Alexandre Klein,¹ Sylvie Nozaradan,² Alexandre Zénon,³ André Mouraux,¹ and Julie Duque¹

¹Institute of Neuroscience, Université Catholique de Louvain, Brussels, 1200, Belgium, ²MARC Institute, Western Sydney University, Sydney, 2214, New South Wales, Australia, and ³INCLIA, Unité Mixte de Recherche, Centre National de la Recherche Scientifique, Bordeaux, 33076, France

Many behaviors require choosing between conflicting options competing against each other in visuomotor areas. Such choices can benefit from top-down control processes engaging frontal areas in advance of conflict when it is anticipated. Yet, very little is known about how this proactive control system shapes the visuomotor competition. Here, we used electroencephalography in human subjects (male and female) to identify the visual and motor correlates of conflict expectation in a version of the Eriksen Flanker task that required left or right responses according to the direction of a central target arrow surrounded by congruent or incongruent (conflicting) flankers. Visual conflict was either highly expected (it occurred in 80% of trials; mostly incongruent blocks) or very unlikely (20% of trials; mostly congruent blocks). We evaluated selective attention in the visual cortex by recording target- and flanker-related steady-state visual-evoked potentials (SSVEPs) and probed action selection by measuring response-locked potentials (RLPs) in the motor cortex. Conflict expectation enhanced accuracy in incongruent trials, but this improvement occurred at the cost of speed in congruent trials. Intriguingly, this behavioral adjustment occurred while visuomotor activity was less finely tuned: target-related SSVEPs were smaller while flanker-related SSVEPs were higher in mostly incongruent blocks than in mostly congruent blocks, and incongruent trials were associated with larger RLPs in the ipsilateral (nonselected) motor cortex. Hence, our data suggest that conflict expectation recruits control processes that augment the tolerance for inappropriate visuomotor activations (rather than processes that downregulate their amplitude), allowing for overflow activity to occur without having it turn into the selection of an incorrect response.

The Journal of Neuroscience, October 31, 2018 • 38(44):9486–9504

CREST in the Nucleus Accumbens Core Regulates Cocaine Conditioned Place Preference, Cocaine-Seeking Behavior, and Synaptic Plasticity

Yasaman Alaghband,^{1,2,4} Enikő Kramár,^{1,4} Janine L. Kwapis,^{1,3,4} Earnest S. Kim,⁵ Thekla J. Hemstedt,^{1,4} Alberto J. López,^{1,2,4} André O. White,^{1,2,4} Amni Al-Kachak,^{1,4} Osasumwen V. Aimuwu,^{1,4} Kasuni K. Bodinayake,^{1,4} Nicole C. Oparaugo,^{1,4} Joseph Han,^{1,4} K. Matthew Lattal,⁵ and Marcelo A. Wood^{1,2,3,4}

¹Department of Neurobiology and Behavior, Center for the Neurobiology of Learning and Memory, ²Irvine Center for Addiction Neuroscience, ³Institute for Memory Impairments and Neurological Disorders, University of California, Irvine, Irvine, California 92697, ⁴Center for the Neurobiology of Learning and Memory, Irvine, California, 92697, and ⁵Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, Oregon 97239

Epigenetic mechanisms result in persistent changes at the cellular level that can lead to long-lasting behavioral adaptations. Nucleosome remodeling is a major epigenetic mechanism that has not been well explored with regards to drug-seeking behaviors. Nucleosome remodeling is performed by multi-subunit complexes that interact with DNA or chromatin structure and possess an ATP-dependent enzyme to disrupt nucleosome-DNA contacts and ultimately regulate gene expression. Calcium responsive transactivator (CREST) is a transcriptional activator that interacts with enzymes involved in both histone acetylation and nucleosome remodeling. Here, we examined the effects of knocking down CREST in the nucleus accumbens (NAc) core on drug-seeking behavior and synaptic plasticity in male mice as well as drug-seeking in male rats. Knocking down CREST in the NAc core results in impaired cocaine-induced conditioned place preference (CPP) as well as theta-induced long-term potentiation in the NAc core. Further, similar to the CPP findings, using a self-administration procedure, we found that CREST knockdown in the NAc core of male rats had no effect on instrumental responding for cocaine itself on a first-order schedule, but did significantly attenuate responding on a second-order chain schedule, in which responding has a weaker association with cocaine. Together, these results suggest that CREST in the NAc core is required for cocaine-induced CPP, synaptic plasticity, as well as cocaine-seeking behavior.

The Journal of Neuroscience, October 31, 2018 • 38(44):9514–9526

The Time Course of Target Template Activation Processes during Preparation for Visual Search

Anna Grubert¹ and Martin Eimer²

¹Department of Psychology, Durham University, Durham, DH1 3LE, United Kingdom and ²Department of Psychology, Birkbeck College, University of London, London, WC1E 7HX, United Kingdom

Search for target objects in visual scenes is guided by mental representations of target features (attentional templates). However, it is unknown when such templates are activated during each search episode and whether this can be controlled by temporal expectations. We used electrophysiological measures to track search template activation processes in real time. In three experiments, female and male humans searched for a color-defined target object in search displays where targets were accompanied by distractors in different nontarget colors. Brief task-irrelevant color singleton probes that matched the target template were flashed rapidly (every 200 ms) throughout each block. Probes presented at times when the target template is active should capture attention, whereas probes presented at other times should not. To assess this, N2pc components were measured as markers of attentional capture, separately for probes at each successive temporal position between two search displays. Results demonstrated that search templates were active from ~1000 ms before the arrival of the next search display, and were deactivated after each search episode, even when the preceding search display did not contain a target object. Templates were activated later when the predictable interval between search displays was increased. Results demonstrate that search templates are not continuously active but are transiently activated during the preparation for each new search episode. These activation states are regulated in a top-down fashion by temporal expectations about when an attentional template will become task-relevant.

The Journal of Neuroscience, October 31, 2018 • 38(44):9527–9538

On the Role of Cortex-Basal Ganglia Interactions for Category Learning: A Neurocomputational Approach

Francesc Villagrasa,¹ Javier Baladron,¹ Julien Vitay,¹ Henning Schroll,¹ Evan G. Antzoulatos,² Earl K. Miller,³ and Fred H. Hamker¹

¹Chemnitz University of Technology, Department of Computer Science, 09107 Chemnitz, Germany, ²University of California Davis Center for Neuroscience and Department of Neurobiology, Physiology and Behavior, Davis, California 95616, and ³The Picower Institute for Learning and Memory and Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

In addition to the prefrontal cortex (PFC), the basal ganglia (BG) have been increasingly often reported to play a fundamental role in category learning, but the circuit mechanisms mediating their interaction remain to be explored. We developed a novel neurocomputational model of category learning that particularly addresses the BG–PFC interplay. We propose that the BG bias PFC activity by removing the inhibition of cortico–thalamo–cortical loop and thereby provide a teaching signal to guide the acquisition of category representations in the corticocortical associations to the PFC. Our model replicates key behavioral and physiological data of macaque monkey learning a prototype distortion task from Antzoulatos and Miller (2011). Our simulations allowed us to gain a deeper insight into the observed drop of category selectivity in striatal neurons seen in the experimental data and in the model. The simulation results and a new analysis of the experimental data based on the model's predictions show that the drop in category selectivity of the striatum emerges as the variability of responses in the striatum rises when confronting the BG with an increasingly larger number of stimuli to be classified. The neurocomputational model therefore provides new testable insights of systems-level brain circuits involved in category learning that may also be generalized to better understand other cortico–BG–cortical loops.

The Journal of Neuroscience, October 31, 2018 • 38(44):9551–9562

NEUROBIOLOGY OF DISEASE

Neural Deletion of Glucose Transporter Isoform 3 Creates Distinct Postnatal and Adult Neurobehavioral Phenotypes

Bo-Chul Shin,¹ Carlos Cepeda,² Ana María Estrada-Sánchez,² Michael S. Levine,² Laya Hodaei,¹ Yun Dai,¹ Jai Jung,¹ Amit Ganguly,¹ Peter Clark,³ and Sherin U. Devaskar¹

¹Department of Pediatrics, Division of Neonatology and Developmental Biology and Neonatal Research Center at the UCLA Children's Discovery and Innovation Institute, ²Intellectual and Developmental Disabilities Research Center and Brain Research Institute, and ³Department of Molecular and Medical Pharmacology and Crump Institute for Molecular Imaging, David Geffen School of Medicine, University of California, Los Angeles, California 90095

We created a neural-specific conditional murine *glut3* (*Slc2A3*) deletion (*glut3*^{flox/flox/nestin-Cre⁺}) to examine the effect of a lack of Glut3 on neurodevelopment. Compared with age-matched *glut3*^{flox/flox} = WT and heterozygotes (*glut3*^{flox/+ /nestin-Cre⁺}), we found that a >90% reduction in male and female brain Glut3 occurred by postnatal day 15 (PN15) in *glut3*^{flox/flox/nestin-Cre⁺}. This genetic manipulation caused a diminution in brain weight and cortical thickness at PN15, a reduced number of dendritic spines, and fewer ultrasonic vocalizations. Patch-clamp recordings of cortical pyramidal neurons revealed increased frequency of bicuculline-induced paroxysmal discharges as well as reduced latency, attesting to a functional synaptic and cortical hyperexcitability. Concomitant stunting with lower glucose concentrations despite increased milk intake shortened the lifespan, failing rescue by a ketogenic diet. This led to creating *glut3*^{flox/flox/CaMK2 α -Cre⁺} mice lacking Glut3 in the adult male limbic system. These mice had normal lifespan, displayed reduced IPSCs in cortical pyramidal neurons, less anxiety/fear, and lowered spatial memory and motor abilities but heightened exploratory and social responses. These distinct postnatal and adult phenotypes, based upon whether *glut3* gene is globally or restrictively absent, have implications for humans who carry copy number variations and present with neurodevelopmental disorders.

The Journal of Neuroscience, October 31, 2018 • 38(44):9579–9599