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The Striatum

**Sainsbury Wellcome Centre
&
Gatsby Computational Neuroscience Unit**

**Thursday 24th May 2012
Kennedy Lecture Theatre
Institute of Child Health**

Programme

9:00 Registration and Coffee

Session 1: Tim Behrens

9:30 **Ann Graybiel**

“Learning, Motivation and the Basal Ganglia”

10:30 Break (Coffee/Tea)

11:00 **Michael Frank**

“Striatal contributions to learning and action selection in humans, rodents and computational models”

12:00 **Rui Costa**

“Generating and shaping novel action repertoires”

13:00 Lunch

Session 2: Peter Dayan

14:00 **Kent Berridge**

“Striatum in reward: from prediction error to incentive salience”

15:00 **Satoshi Ikemoto**

“Ventral striatal dopamine and motivation: A systems perspective”

16:00 Break (Tea/Coffee)

16:30 **Larry Swanson**

“Connections of an "hedonic hotspot" in the nucleus accumbens”

17:30 End

Note: Eduroam Guest Wi-Fi log on code: Striatum

Instructions for setting up are available at the registration desk

Speakers

Professor Ann Graybiel



Ann M. Graybiel is an Institute Professor at MIT. Her research is focused on how the regions of the forebrain that influence movement, mood and motivation – the basal ganglia and neural pathways interconnecting the basal ganglia with the cerebral cortex – operate in normal and abnormal conditions. Central to many of these studies is work on brain mechanisms underlying learning and expression of the action plans, habit formation and repetitive behaviors. The research of her laboratory has advanced significantly the understanding of how such mechanisms can become dysfunctional in neurologic and neuropsychiatric disorders such as Parkinson's disease. Dr. Graybiel and her group use methods ranging from multi-electrode recordings in awake, behaving animals to genetic engineering to approach these issues.

Professor Michael Frank



Michael J. Frank is Associate Professor of Cognitive, Linguistic & Psychological Sciences and Psychiatry in the Brown Institute for Brain Science at Brown University. He directs the Laboratory for Neural Computation. He received an undergraduate degree in Electrical Engineering at Queen's University (Canada), followed by a Master's degree in biomedicine Engineering at the University of Colorado at Boulder, where he went on to receive a PhD in Neuroscience and Psychology in 2004. Dr. Frank's work focuses primarily

on theoretical models of basal ganglia, frontal cortex and their modulation by dopamine, especially in terms of their cognitive functions and implications for neurological and psychiatric disorders. The models are tested and refined by empirical studies using a variety of methods.

Dr Rui Costa



Dr. Costa received his D.V.M. from the Technical University of Lisbon in 1996. He entered the GABBA graduate program from University of Porto in 1997, and performed his Ph.D. studies with Dr. Alcino Silva at UCLA from 1998 to 2002 in the field of learning and memory, investigating the molecular and cellular mechanisms underlying the learning disabilities

associated with NF1. For this work, Dr. Costa received the Young Investigator Award from the National Neurofibromatosis Foundation in 2001. He then joined Dr. Miguel Nicolelis at Duke University for his postdoctoral training, where he established multi-site neuronal recordings in awake behaving mice. Dr. Costa became a Section Chief at the National Institutes of Health in 2006. In 2009 he became an Investigator of the Champalimaud Neuroscience Program at Institute Gulbenkian de Ciências, and received a European Research Council Starting Grant. In 2010 he received the Seeds of Science Prize for Life Sciences, and in 2012 he became an International Early Career Scientist of the Howard Hughes Medical Institute. He is currently President of the American-Portuguese Biomedical Research Fund and Vice-President of the Portuguese Society for Neuroscience. His laboratory studies the neurobiology of action in health and disease.

Professor Kent Berridge



Kent Berridge is the James Olds Collegiate professor of Psychology and Neuroscience at the University of Michigan. Berridge's research focuses on answering questions such as: How are reward learning, 'wanting' and 'liking' generated in the brain? What functions do brain meso-cortico-striato-pallidal circuits contribute? And what causes addiction? Berridge serves on editorial boards for several scientific journals and post-publication peer review sites. Among other honors, he has been a Guggenheim fellow and a Fulbright senior scholar.

Dr Satoshi Ikemoto



Dr. Ikemoto was born and raised in Japan. He went to the US to study psychology and received his PhD in experimental psychology from Bowling Green State University for studying neuropharmacological mechanisms of reward. He received postdoctoral training in animal models of drug self-administration at Indiana University and Louisiana State University. He then joined the Intramural Research Program of NIDA/NIH in 1998 and became Senior Investigator and Chief, Neurocircuitry of Motivation Section in 2010.

Professor Larry Swanson



Dr. Swanson has studied the structure-function organization of neural systems controlling the expression of motivated and emotional behaviors throughout his career, using primarily structural and behavioral approaches. He is University Professor at the University of Southern California, a Member of the National Academy of Sciences, and President-Elect of the Society for Neuroscience. He is currently on Sabbatical at Columbia University in the laboratory of Thomas Jessell.

Abstracts

Professor Ann Graybiel

“Learning, Motivation and the Basal Ganglia”

The same brain that can construct language, music and mathematics also lets us develop habits of thought and action. These semi-automatic routines free us to think and attend to the world. This lecture will focus on the habit system of the brain and on our remarkable ability to switch from conscious activity to nearly non-conscious behavior. The lecture will highlight research directed towards understanding how we make and break habits and how the neurobiology of the habit system is helping to advance understanding of human problems ranging from Parkinson's disease to obsessive-compulsive spectrum disorders and addiction. This research supports the view that basal ganglia-based circuits can build representations of habits, and that the laying down of such representations involves genes expressed in basal ganglia-related networks. Disorders of such basal ganglia plasticity could contribute to behavioral fixity and difficulty of initiation of behavior, as in Parkinson's disease, or to the excessive release of behaviors, as in Huntington's disease, or to the repetitive behaviors and thoughts characteristic of many neuropsychiatric disorders. The basal ganglia thus may influence not only motor pattern generators, but also cognitive pattern generators.

Professor Michael Frank

“Striatal contributions to learning and action selection in humans, rodents and computational models”

Abstract: The striatum and dopaminergic systems have long been implicated in reward-based behavior, with debates focusing on the relative roles of this system in learning, motor performance, and reward-based decision making. I will present computational models (neural network and a new algorithmic description thereof) that implicate the corticostriatal system at the intersection of all of these functions, not independently but interactively. Striatal dopaminergic modulations affect the extent to which both learning and action selection is guided preferentially by positive or negative outcomes. Tonic modulations lead to changes in activity levels that directly influence gain and behavioral performance, but also influence learning. Reciprocally, phasic dopamine signals involved in learning progressively modulate synaptic weights and hence activity levels, which in turn not only influence action selection, but also the eligibility for further learning. I will present evidence for these interactive effects from human and rodent reinforcement and motor learning studies.

Dr Rui Costa

“Generating and shaping novel action repertoires”

Actions are organized as sequences of particular movements. The organization of learned actions as sequences of movements typically encompasses precise timing and/or ordering of movements within a sequence to increase precision or accuracy, and appropriate initiation and termination of the sequence. We used a self-paced operant task in which mice were trained to perform a particular sequence of lever presses to obtain an outcome, and recorded the neural activity in nigrostriatal circuits during action sequence learning. We uncovered neural activity specifically signaling the initiation and termination of sequences of actions in putative striatal medium spiny neurons, and nigral dopaminergic and GABAergic neurons. This start/stop selective activity emerged during sequence learning, was specific for particular actions, and did not seem to reflect interval timing or differences in expected action value at the beginning and end of a sequence. We verified that a striatal-specific genetic deletion of NMDA receptors selectively impairs the development of this start/stop activity and sequence learning. Next, we developed a task where mice need to perform a specific action sequence very rapidly, close to the timescale of human speech and birdsong (a limited-time fixed-ratio differential reinforcement schedule). We recorded the activity in striatum and downstream target regions of direct pathway neurons (Substantia nigra pars reticulata -SNr) and indirect pathway neurons (Globus pallidus external GPe). We found that besides start/stop activity, activity related to the execution of the whole sequence developed during learning, and that

this activity developed differentially in SNr and GPe. we used optogenetic tools to indentify and manipulate the activity of direct and indirect pathway striatal neurons during different moments of ultrafast sequence execution. These data have important implications for understanding the learning and execution of action sequences, and the impairments observed in basal ganglia disorders like Parkinson's and Huntington's disease.

Professor Kent Berridge

“Striatum in reward: from prediction error to incentive salience”

Abstract: Reward contains separable psychological components of learning, incentive motivation and pleasure. Most computational models of striatum in reward have focused only on the learning component of reward, but the motivation component is equally important to meso-cortico-striatum-pallidum circuitry. I will discuss some considerations suggesting that the contribution of striatal-related circuits to reward may best be described as generating motivation at a current moment, in a computation that draws both on learned information and non-learning neurobiological state factors.

Dr Satoshi Ikemoto

“Ventral striatal dopamine and motivation: A systems perspective”

Abstract: The ventral striatum, consisting of the nucleus accumbens and olfactory tubercle, is considered to be a medial extension of the caudate-putamen complex. Dopamine transmission in the ventral striatum has been implicated in motivational functions: in particular, incentive motivation and affect. Increased dopamine transmission appears to facilitate ongoing approach responding toward salient distal stimuli (i.e., incentive motivation). In addition, increased and decreased dopaminergic activities in the ventral striatum appear to elicit positive and negative affective states, respectively. My group has investigated such roles of dopamine using the intracranial microinjection procedure, in which rats receive small injections of neurochemicals into discrete brain regions. We found that rats voluntarily make responses to obtain (i.e., self-administer) dopaminergic agents including cocaine, amphetamine, and D1 and D2 receptor agonists into the ventral striatum. In addition, subregions of the ventral striatum have differential sensitivity to rewarding effects of these drugs. The medial portions of the olfactory tubercle and accumbens shell appear to be important in mediating rewarding effects of dopaminergic agents as indicated by intracranial self-administration. In addition, dopaminergic tone in the same subregions plays an important role in ongoing approach responding toward salient distal stimuli. However, these motivational functions are not uniquely associated with ventral striatal dopamine. Most notably, we found that modulations of GABAergic and glutamatergic transmissions in other structures in the hypothalamus or midbrain have similar rewarding and incentive motivational effects. Thus, motivational functions associated with dopaminergic activity of the medial ventral striatum may arise from concerted activity of many brain structures.

Professor Larry Swanson

“Connections of an "hedonic hotspot" in the nucleus accumbens”

Abstract: Berridge and colleagues have identified a roughly one cubic millimeter zone of the dorsomedial nucleus accumbens in the rat as an "hedonic hotspot," based on enhanced sucrose ingestion following mu-opoid agonist delivery to this site. The results presented here were stimulated by the hypothesis that the dorsomedial tip of the nucleus accumbens has different axonal inputs and outputs than the rest of the nucleus accumbens. To test this hypothesis a new strategy for tracing neural circuits was developed, and called the double coinjection method (DCI). The results indicate that the dorsomedial nucleus accumbens has unique connections with other parts of the brain, and is embedded in circuitry with a basically network organization as opposed to a hierarchical organization. The DCI strategy developed here can be applied systematically to any starting point of interest in the nervous system, and if carried out to the extreme can define the entire wiring diagram of the nervous system.