Session I

Chair: Mathias Pessiglione

Monday, April 22

2:00 pm Mathias Pessiglione, *Paris Brain Institute*

The OFC as a value-making network: evidence from iEEG studies in humans

Electrophysiology studies have gathered evidence that the OFC implements a comparison between option values in binary choice tasks that animals have been conditioned to perform. Whether value comparison could be the function of OFC in humans remains debated. One issue is that value representation in the OFC has been observed in the absence of choice, when human volunteers passively view an option or just report how much they would like it. Thus, a parsimonious account of OFC function would be the transformation of option attributes into a value representation that can be read by downstream neurons. During binary choice, the OFC would simultaneously represent the values of attended and unattended options in different, distributed codes. Such a model would explain both intracerebral recordings in the OFC and choice inconsistencies following OFC lesions.

2:20 pm Camillo Padoa-Schioppa, *Washington University*

A neural circuit for economic decisions

Economic choice entails representing and comparing the subjective values of individual offers. Previous work showed that neuronal activity in OFC is causally involved in these operations. Furthermore, different groups of cells were found to represent pre-decision variables (offer values) and post-decision variables (chosen good, chosen value). These cell groups are presumably the building blocks of a decision circuit, but the structure and the mechanisms of this circuit remain unknown. To shed light on this issue, we developed a protocol for two-photon calcium imaging in mice performing a choice task. We found that the representation of decision variables in OFC is longitudinally stable. Importantly, pre- and post-decision variables are differentially represented across cortical layers.

2:40 pm Erin Rich, *Icahn School of Medicine at Mount Sinai*

Mechanisms of multi-attribute decision-making

When making a complex decision, we often consider multiple dimensions, such as costs, risks, qualities, or quantities, that vary among choice options. The orbitofrontal cortex is traditionally thought to integrate relevant features, or attributes, of an option into an overall value, then compare the values of different options to arrive at a choice. However, we have recently found evidence that choices rely, to some extent, on direct comparison of attribute values. In this talk, I will discuss behavioral and neurophysiological data that explore the role of attribute-level processing in value-based decision-making.

3:00 pm **Coffee break**

Session I

Chair: Mathias Pessiglione

Monday, April 22

3:30 pm Fabian Grabenhorst, *University of Oxford*

A view-based decision mechanism for rewards in primate amygdala neurons

Primates make decisions visually by shifting their view from one object to the next, comparing values between objects, and choosing the best reward, even before acting. I will present data to show that when monkeys make value-guided choices, amygdala neurons encode their decisions in an abstract, purely internal representation defined by the monkey's current view but not by specific object or reward properties. Across amygdala subdivisions, recorded activity patterns evolve gradually from an object-specific value code to a transient, object-independent code in which currently viewed and last-viewed objects compete to form a view-based choice. These data identify a neural mechanism that derives object choices from abstract, view-based computations, suggesting an efficient solution for decision problems with many objects.

3:50 pm Christine Constantinople, *New York University*

Role of OFC in state inference

We developed a novel temporal wagering task with hidden reward states. Inactivating the OFC impaired rats' ability to infer the hidden state of the task, and behavioral modeling suggested that rats were less effective at updating their subjective beliefs based on outcomes when OFC was inactivated. Electrophysiological recordings from expert rats and rats that were naïve to the hidden states revealed that representations of reward outcomes were worse in naïve animals, and paradoxically more sensitive to hidden states. These data suggest that veridical, context-independent outcome representations in OFC emerge with training, and may be used to update subjective beliefs about hidden states.

4:10 pm Abhishek Banerjee, *London School of Medicine, University of Oxford*

Orbitofrontal contributions to building a flexible sensory cortex

Animals adapt their behaviour in response to variable changes in reward reinforcement. The prefrontal areas of the mammalian neocortex, especially the orbitofrontal cortex (OFC), play an important role in invoking rule-based strategies to enable flexible learning. However, the neural circuit mechanisms in OFC and its interactions with different hierarchical cortical areas underlying such processes remain elusive. In my talk, I will discuss interactions between orbitofrontal and somatosensory cortices that implement flexible decision-making in a tactile reversal-learning task in mice and also briefly highlight similar circuit mechanisms in operation in humans.

4:30 pm **Discussion**

7:00 pm **Social event at the Zamansky tower**

Session II
Chair: Jay Gottfried

Tuesday, April 23

9:00 am John O'Doherty, *California Institute of Technology*

Probing the neural mechanisms by which subjective value representations are flexibly modified by changes in goal context

How can the subjective value of an item be flexibly modified depending on changes in one's overall goal? I will present evidence that value is flexibly computed and modified for objects depending on goal context by integrating over individual features or attributes of that object. The object features themselves are represented in value space in lateral and medial orbitofrontal cortex, so that when the goal context changes, the value of some of those individual features changes flexibly. Integrated value, which is computed from a context invariant weighted integration of those features, is represented more dorsally within ventral medial prefrontal cortex.

9:20 am Alicia Izquierdo, *University of California Los Angeles*

Looking for diversity in rodent frontal cortex function: Roles of OFC and ACC

Orbitofrontal cortex (OFC) and Anterior cingulate cortex (ACC) have been assigned various overlapping roles ranging from learning and responding to reward, signaling value and uncertainty, and supporting economic decisions, to name a few. Using a combination of novel behavioral paradigms, chemogenetics, and 1P calcium imaging in freely-moving rats, our lab has sought better resolution of diverse frontocortical processes. I will present data comparing subregional frontal cortex contributions in reward learning and value-based decision making. With few exceptions that I will highlight, our results suggest mostly overlapping, less specialized roles for ACC and OFC. Collectively these findings have implications for how we compare frontocortical contributions across rodent and primate species.

9:40 am Étienne Coutureau, *University of Bordeaux*

The role of orbitofrontal noradrenaline in adaptive behaviour

In a constantly changing environment, organisms must track the current relationship between actions and their specific consequences and use this information to guide choice. Such goal-directed behaviour relies on circuits involving cortical and subcortical structures. Notably, a functional heterogeneity exists within the medial prefrontal, insular, and orbitofrontal cortices (OFC) in rodents. Notably, recent data indicate that the ventral and lateral subregions of the OFC are needed to update the relationships between actions and their outcomes.

The present talk will discuss recent evidence suggesting that noradrenergic input onto the OFC is necessary for action-outcome updating. First, using fiber photometry to monitor OFC-NA during instrumental reversal learning, we found that OFC-NA specifically signals reward deliveries at the beginning of the updating process. Second, we found that chemogenetic silencing of noradrenergic inputs onto the OFC rendered rats unable to associate new outcomes with previously acquired actions. Taken together, these results suggest a pivotal role of OFC-NA in initiating adapted choice behaviour.

10:00 am **Coffee break**

Session II
Chair: Jay Gottfried

Tuesday, April 23

10:30 am Catharine Winstanley, *University of British Columbia*

Cue-induced risky choice in rats and the orbitofrontal cortex
Pairing wins with casino-inspired sound and light cues increases risky choice in both rats and humans. The neurocognitive basis of this effect remains unclear. In male rats, cue-driven risky choice is insensitive to reinforcer devaluation, indicative of habitual control of behaviour. This form of risky choice can be ameliorated by drugs which enhance cognitive flexibility, such as a serotonin receptor 2C antagonist, and the noradrenaline reuptake inhibitor atomoxetine. Both drugs similarly attenuate cue-induced risky choice in male rats when administered into the lateral orbitofrontal cortex (lOFC). Collectively, these data suggest win-paired cues may perpetuate risky choice by corrupting activity within the lOFC, leading to more automatic and less goal-directed control of option selection. Although female rats appear equally sensitive to the ability of reward-concurrent cues to drive risky choice, computational modeling suggests differences in the learning and decision-making processes in play. Furthermore, cue-induced risky choice is not insensitive to reinforcer devaluation in females, and intra-lOFC administration of atomoxetine does not reduce selection of the risky options. Collectively, these data suggest important differences in the cognitive and neurobiological mechanisms through which audiovisual cues drive risky choice in female vs male rats. This mechanistic divergence may be an important factor when considering the different trajectories of gambling disorder in men and women.

10:50 am Geoffrey Schoenbaum, *National Institute on Drug Abuse*

Effects of cocaine use on organization and dimensionality of neural representations in rat orbitofrontal cortex
*Lauren E. Mueller, Caitlin Konya, Melissa J. Sharpe, Andrew M. Wikenheiser, and Geoffrey Schoenbaum**
Maladaptive decision-making is a hallmark of substance use disorders, though how drugs of abuse alter neural representations supporting adaptive behavior remains poorly understood. Past studies show the orbitofrontal (OFC) and prelimbic (PL) cortices are important for decision making, tracking both task-relevant and latent information. However, previous studies have focused on how drugs of abuse impact the firing rates of individual units. More work at the ensemble level is necessary to accurately characterize potential drug-induced changes. Using single-unit recordings in rats during a multidimensional decision-making task and then applying population and ensemble level analyses, we show that prior use of cocaine altered the strength and structure of task-relevant and latent representations in the OFC, changes relatable to suboptimal decision making in this and perhaps other settings. These data expand our understanding of the neuropathological underpinnings of maladaptive decision-making in SUDs, potentially enabling enhanced future treatment strategies.

11:10 am Cyriel Pennartz, *University of Amsterdam*

Orbitofrontal sleep replay depends on behavioral flexibility and partially coheres with hippocampal replay
The orbitofrontal cortex (OFC) may engage in storing and consolidating information that subjects to flexibly perform cognitive tasks. Our recent results reveal an offline replay in the OFC of rats performing a place-reward association task on a hexagonal maze. Switches in place-reward coupling led to enhanced replay relative to sessions with stable contingencies. Replay correlated positively with overnight changes in behavioral performance. Orbitofrontal and hippocampal replay were largely independent, but became coordinated during a particular type of cortical state. The results are interpreted in the context of a large cortical-hippocampal-basal ganglia network for control of behavior across various time scales.

11:30 am Discussion

12:00 pm - 2:00 pm Poster session

Session III

Chair: Geoffrey Schoenbaum

Tuesday, April 23

2:00 pm Lauren Atlas, *National Institute of Mental Health*

Domain-general responses in the orbitofrontal cortex during anticipation and experience of painful heat and appetitive and aversive taste

Neurons in the orbitofrontal cortex (OFC) encode expected value across a range of outcomes, permitting direct comparisons during decision-making. In this talk, I will present results of a functional magnetic resonance imaging (fMRI) study that tested whether the brain mechanisms of learning and expectancy-based modulation differ across modalities. We presented predictive cues and compared pain with appetitive and aversive liquid tastants (i.e., sucrose and salt solutions) during fMRI scanning. Cues had robust effects on OFC activation during anticipation and stimulation, regardless of outcome modality or valence. This further supports the OFC's central role in domain-general coding of expectation and value.

2:20 pm Andrew Wikenheiser, *University of California Los Angeles*

OFC responses on a continuous spatial bandit task

Many laboratory tests of decision making involve repeated, stereotyped choices between a few discrete response options. This approach affords great experimental control but comes at the expense of ecological validity. Motivated by a desire to study decision making in a more naturalistic context, we developed a bandit problem for rats that translates a commonly-used probabilistic decision making task from the operant box to a continuous, spatial setting. Rats make value-sensitive decisions by inferring the latent spatial structure that determines reward probability. High-density neural recordings in lateral OFC reveal prominent representations of task structure that are invariant across space, as well as representations of value and reward. These results provide proof-of-concept for a novel means of studying orbitofrontal function in a naturalistic framework.

2:40 pm Laura Bradfield, *University of Technology Sydney*

The role of the lateral orbitofrontal cortex in contingency learning and retrieval

Maedeh Mahmoudi, Laura A. Bradfield.

We investigated whether the lateral OFC is involved in contingency learning, using a degradation design that did not involve extinction. In Experiment 1, we demonstrated that degradation learning/retrieval differs from extinction in the sense that it does not spontaneously recover over time. In Experiment 2, we chemogenetically inhibited the glutamatergic neurons in the lateral OFC during learning. Animals injected with the control virus (mCitrine+DCZ group) learned degradation, whereas animals for whom the lateral OFC was inhibited (hM4Di+DCZ group) did not (i.e. nondegraded = degraded), showing that the lateral OFC is necessary for degradation learning per se. Moreover, this pattern of results was retained at both immediate and delayed tests.

3:00 pm **Coffee break**

Session III

Chair: Geoffrey Schoenbaum

Tuesday, April 23

3:30 pm Patrick Kanold, *Johns Hopkins University*

OFC modulation of auditory cortex function

Listening is an active process. During the performance of an auditory task, neurons in the primary auditory cortex (A1) represent both information about the sound stimulus as well as behavioral variables. We showed in mice that the orbitofrontal cortex (OFC) provides excitatory input to A1 and that OFC shows sound-evoked responses. Thus, during task performance, changes in A1 responses are thought to be driven by excitatory top-down inputs from the OFC, which may lead to response modification on a trial-by-trial basis. We used in vivo 2-photon calcium imaging of OFC terminals to observe the activity of putative OFC terminals in A1 under passive conditions and during a tone detection task. We found that behavioral activity modulates but is not necessary to evoke OFC terminal responses in A1. OFC terminals in A1 form distinct populations that exclusively respond to either the tone, reward, or error. Moreover, OFC terminal activity was modulated by task difficulty. Thus, OFC projections in A1 are heterogeneous in their encoding of auditory task variables and likely contribute to auditory processing under various conditions.

3:50 pm Joni Wallis, *University of California Berkeley*

Where is the "where" in OFC?

Recent theories of OFC function have argued that OFC plays a critical role in the representation of a cognitive map. However, a challenge for this idea is that OFC neurons in the monkey rarely represent information about space and time. In this talk, I will present a couple of results from our lab that demonstrate how OFC might incorporate spatiotemporal contingencies via its dynamical interactions with other brain areas.

4:10 pm Mona Garvert, *University of Würzburg*

Orbitofrontal cortex modulates hippocampal cognitive maps for adaptive decision-making

The ability to adapt to novel situations by drawing upon past experiences is a fundamental aspect of flexible behavior. This cognitive flexibility involves two critical components: a representation of relevant knowledge and a context-appropriate method for accessing this information. Here, I present evidence that this is reflected in an interplay between two brain regions: the hippocampus, which forms cognitive maps of relational knowledge, and the OFC, which aligns these representations with current task demands. This illustrates that hippocampal cognitive maps are not just static archives of past experiences, but dynamically adapt based on the requirements of a given decision-making situation.

4:30 pm **Discussion**

Session IV
Chair: Mehdi Khamassi

Wednesday, April 24

9:00 am Erie Boorman, *University of California Davis*

A grid-like representation for subjective value-based decision making in entorhinal and medial orbitofrontal cortex
Recent evidence has pointed to the grid coding system as an efficient representation that affords novel inferences. To test whether this system plays a role in value-based choice, we designed a novel task where human participants are asked to make value-based risky choices between two shapes that span a 2D attribute space between reward probability and reward amount while undergoing fMRI scanning. We find that blood oxygen-level-dependent activity is associated with individuals' subjective value comparisons between the two options in ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex. Using analyses developed for spatial navigation, we also find a "grid-like" representation of decision vectors in entorhinal cortex and medial OFC/vmPFC during decisions. Activity in these areas is better described by decision vectors in a subjective value space that is distorted according to an individual's subjective preference. Strength of activation in these two systems is correlated across participants, suggesting they operate in tandem to construct and compare values.

9:20 am Vincent Costa, *Oregon Health Sciences University*

Primate orbitofrontal cortex anchors a disynaptic network that codes information relevant for managing explore–exploit tradeoffs
Motivational circuits facilitate reinforcement learning and support computations relevant for solving the explore-exploit dilemma. We recorded neural activity in the posterior orbitofrontal cortex (OFC), amygdala, and ventral striatum (vSTR) of rhesus macaques as they solved a bandit task where they balanced novelty-driven exploration with exploitation of familiar choices. We identified a dissociation in how OFC and amygdala represent the immediate value of exploitative choices and future value of exploratory choices. Using an intersectional viral tracing approach involving mutant rabies virus, we found OFC inputs to amygdala neurons innervating vSTR play a role in mediating amygdala dependent control of exploration.

9:40 am Roshan Cools, *Radboud University Nijmegen Medical Center*

Chemical neuromodulation of Pavlovian conflict control
Decisions are regulated by a delicate interplay between instrumental and Pavlovian control systems. The monoamine systems of dopamine and serotonin are good candidates for controlling behavior when Pavlovian and instrumental systems compete. I will discuss the multiple routes through which dopamine and serotonin might act to control Pavlovian biases, based on a review of results from pharmacological studies in human volunteers. I will end the talk by speculating that such Pavlovian bias control involves flexible meta-level arbitration between Pavlovian and instrumental systems by medial frontal cortical regulation of monoamine release that depends on subjective task controllability.

10:00 am **Coffee break**

Session IV
Chair: Mehdi Khamassi

Wednesday, April 24

10:30 am Matthew Rushworth, *Oxford University*

A distributed network, beyond the OFC, for reversal task performance in macaques
Reversal tasks have been regarded as probes of behavioural inhibition and linked to orbitofrontal cortex (OFC). However, the centrality of behavioural inhibition to reversal task performance and the reversal task's dependence on OFC have been questioned. Using a combination of whole brain recording, transient ultrasonic disruption, two types of reversal task, and a task model emphasizing identification of transitions between latent states, we show that reversal tasks crucially require macaques to track latent state transitions in addition to choice values. Rather than OFC, tracking of latent states and choices appears to depend most crucially on dorsomedial frontal cortex, anterior and dorsomedial thalamus, and hippocampus.

10:50 am Stephanie Borgland, *Calgary University*

The effects of caloric diet exposure on orbitofrontal cortex function and decision making about food
Our food environment interacts with decision-making processes to influence and bias choices about our feeding behaviour. The lateral orbitofrontal cortex (lOFC) receives sensory information about food and integrates these signals with expected outcomes to guide future actions, and thus may play a key role in a distributed network of neural circuits that regulate feeding behaviour. Here, I will present evidence for a role of the lOFC in the cognitive control of feeding behaviour in obesity. We will show changes in synaptic strength and output of lOFC neurons that underlie the ability to use previously learned information to update actions for food.

11:10 am Mihaela Iordanova, *Concordia University*

Orbitofrontal involvement in fear time travel
The study of the neurobiology of fear has historically focused on cues that are directly paired with an aversive event (primary fear cues). However, fear can propagate backward and forward in time to other, secondary, cues that are never directly paired with the aversive event. This propagation of fear to secondary cues occurs via the primary fear cues. Here we provide evidence for the role of the orbitofrontal cortex and it's reciprocal connections with the basolateral amygdala in the spread of fear across time.

11:30 am **Discussion**

12:00 pm - 2:00 pm **Poster session**

Session V
Chair: Betsy Murray

Wednesday, April 24

2:00 pm Christina Gremel, *University of California San Diego*

Neuromodulatory regulation of goal-directed control

The OFC modulates goal-directed behaviors through microcircuit computations and output to downstream areas including central striatum. I will discuss some of our recent findings examining potential mechanisms that contribute mechanistically to such control.

2:20 pm Angela Langdon, *National Institute of Mental Health*

Title to be announced.

Abstract to be announced.

2:40 pm Peter Rudebeck, *Icahn School of Medicine at Mount Sinai*

Preferences differentially modulate encoding in prefrontal-limbic circuits

Individual preferences for the flavor of different foods and fluids exert a strong influence on behavior. Current theories posit that preferences are integrated with other state variables in orbitofrontal cortex (OFC), which is thought to derive the relative subjective value of available options to guide choice behavior. Here I will discuss work that indicates that instead of a single integrated valuation system in OFC, another complementary one is centered in ventrolateral prefrontal cortex (vlPFC) in macaques. I will then go on to describe work looking at how different subregions of OFC and vlPFC encode distinct aspects of the valuation that is used to guide decision-making.

3:00 pm **Coffee break**

Session V
Chair: Betsy Murray

Wednesday, April 24

3:30 pm Angela Roberts, *University of Cambridge*

Regulation of reward and threat-related behaviours in a primate: insights into the functional differentiation of primate orbitofrontal cortex

Altered activity within orbitofrontal cortex is commonly reported in neuropsychiatric disorders associated with emotion dysregulation, including anxiety and depression. Two core symptoms of these disorders are heightened anxiety and anhedonia, which are variably linked to either reductions or increases in orbitofrontal activity. In a series of intervention studies in marmosets the effects of inactivation or overactivation have been studied across medial (area 14), central (areas 11 and 13) and lateral (area 12/47) regions of orbitofrontal cortex on the regulation of reward and threat-related behaviours. Together these studies are providing insight not only into the functional differentiation within orbitofrontal cortex but also the varied aetiology of anxiety and anhedonia and the variable efficacy of anxiolytics.

3:50 pm Thorsten Kahnt, *National Institute on Drug Abuse*

Lateral orbitofrontal cortex integrates predictive information across multiple cues

Individuals are often faced with multiple cues that concurrently predict the same outcome, and combining these predictions may benefit behavior. Using pattern-based fMRI, we identified neural signatures of outcome integration in the lateral orbitofrontal cortex (OFC), where concurrently presented cues evoke stronger pattern-based representations of expected outcomes. Perturbing lateral OFC network activity using TMS impairs subjects' ability to leverage predictions from multiple cues to facilitate responding. These findings highlight a causal role for the lateral OFC in utilizing outcome predictions from multiple cues to guide behavior.

4:10 pm Vincent McGinty, *Rutgers University*

Orbitofrontal high-gamma reflects spike-dissociable value and decision mechanisms

Much is known about how OFC neurons encode value- and decision-related variables, but the functional properties of OFC local field potentials (LFPs) are less clear. LFPs are important because they can reflect otherwise unobservable synaptic and subthreshold activity, and because they are potential targets for less invasive forms of brain-machine interface. In this talk, I will show that high-gamma LFPs (50-150Hz) have value- and decision-coding properties that are dissociable from concurrently measured spiking. These include monotonic encoding of value, strong encoding of value comparisons, and accentuated representation of values stored in working memory. The results have implications for both basic decision mechanisms and for potential neuroengineering applications.

4:30 pm **Discussion**