Fourth Quadrennial Meeting on Orbitofrontal Cortex Function

OFC 2019

Paris, France

November 13-15

PARTNERS AND FUNDERS

National Institutes of Health (NIH)

Institut du Cerveau et de la Moelle épinière (ICM)

Institut des Systèmes Intelligents et de Robotique (ISIR)

Sorbonne Université (SU)

Institut National de la Santé et de la Recherche Médicale (INSERM)

Centre National de la Recherche Scientifique (CNRS)

Team *Motivation, Brain, and Behavior* (MBB)

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PART 1 – GENERAL INFORMATION

INTRODUCTION

The Fourth Quadrennial Meeting on Orbitofrontal Cortex Function will be held November 13-15, 2019, at the **Institut du Cerveau et de la Moelle épinière** (ICM) in the Pitié Salpêtrière Hospital at 47, Boulevard de l'Hôpital, 75013 Paris, France.

Similar to past years, the meeting will feature 2 ½ days of talks and poster sessions, with half of the second day free for sightseeing. In addition, an evening reception will take place at Sorbonne Université, at the top of the Tour Zamansky, overlooking the old city. Talks will be 20 minutes long. Discussion periods will be interspersed among the talks, with a goal of encouraging interactions among panelists and attendees.

We dedicate this meeting to Dr Howard Eichenbaum, in recognition of his magnificent spirit, unstinting generosity to the field, and landmark contributions to our understanding of how the brain organizes information and guides behavior.

To this end, we welcome 30 speakers, grouped into five sessions.

We are also delighted to welcome 35 poster presenters to be held during Thursday lunch.

On Wednesday evening, a social event will take place at the top floor of the Tour Zamansky on the Jussieu Campus of the Sorbonne University; during this event, a cocktail dînatoire will be served. Wednesday and Friday will have extended lunch breaks. These, as well as the free afternoon on Thursday, will allow you to enjoy a bit of Parisian life.

ORGANIZERS

The **scientific committee** hosting the speakers consists of:

Jay Gottfried
(University of Pennsylvania, Philadelphia, PA, USA)

Mehdi Khamassi
(CNRS – ISIR, Sorbonne Université, Paris, France)

Betsy Murray
(NIMH - NIH, Bethesda, MD, USA)

Mathias Pessiglione
(INSERM – ICM, Sorbonne Université, Paris, France)

Geoffrey Schoenbaum
(NIDA - NIH, Baltimore, MD, USA)

The **local organizers** responsible for the event are:

Mehdi Khamassi
(CNRS – ISIR, Sorbonne Université, Paris, France)

Mathias Pessiglione, Roeland Heerema, Elodie Lévy, Thelma Landron
(INSERM - ICM, Sorbonne Université, Paris, France)

DAILY PROGRAMS

WEDNESDAY, 13 NOVEMBER

09:10 Geoffrey Schoenbaum: Welcome and opening remarks

09:30	**12:30**	**Session I Chair: Mathias Pessiglione**
09:30	**09:50**	Camillo Padoa-Schioppa *Causal links between OFC activity and economic decisions*
09:50	**10:10**	Peter Rudebeck *Reward identity and probability encoding in prefrontal-striatal-amygdala circuits*
10:10	**10:30**	Susanne Ahmari *Characterization of OFC activity patterns associated with distinct OCD-relevant behaviors*
10:30	**11:00**	**Coffee break (poster room)**
11:00	**11:20**	Lesley Fellows *OFC contributions to discovering value*
11:20	**11:40**	Stephanie Groman *Orbitofrontal circuits control multiple reinforcement-learning and addiction-relevant processes*
11:40	**12:00**	Mathias Pessiglione *Bridging the gap between electrical and hemodynamic OFC value signals*
12:00	**12:30**	Discussion

12:30 15:00 Lunch out in Paris

15:00	**18:00**	**Session II Chair: Elisabeth Murray**
15:00	**15:20**	Erin Rich *Stable and dynamic representations of value in orbitofrontal cortex*
15:20	**15:40**	Christina Gremel *Thalamic mechanisms supporting OFC-based value updating*
15:40	**16:00**	Vincent McGinty *A population approach to choice prediction in the OFC*
16:00	**16:30**	**Coffee break (poster room)**
16:30	**16:50**	Thorsten Kahnt *Inference-based behavior depends on outcome-specific expectations in orbitofrontal cortex*
16:50	**17:10**	Erie Boorman *Map Making: Constructing, Combining, and Navigating Abstract Cognitive Maps in the OFC*
17:10	**17:30**	Tianming Yang *Orbitofrontal Cortex Plays A Limited Role in Value Computation During Decision Making*
17:30	**18:00**	Discussion

19:00 22:00 Social event – Tour Zamansky (Jussieu Campus, Sorbonne University)

THURSDAY, 14 NOVEMBER

08:30	**11:30**	**Session III Chair: Jay Gottfried**
08:30	**08:50**	John P. O'Doherty *The construction of value: attribute-based value integration in orbital and medial prefrontal cortices.*
08:50	**09:10**	Alicia Izquierdo *Orbitofrontal cortex in adjusting to changes in reward delay and probability*
09:10	**09:30**	Shauna Parkes *OFC tracks changes in action-outcome contingencies in rats*
09:30	**10:00**	**Coffee break (poster room)**
10:00	**10:20**	Kate Wassum *Corticolimbic circuitry in reward learning and pursuit*
10:20	**10:40**	Catharine Winstanley *Cue-biased risky choice and the orbitofrontal cortex*
10:40	**11:00**	Miriam Klein-Flügge *Multiple neural mechanisms of knowledge acquisition*
11:00	**11:30**	Discussion
11:30	**14:00**	**Poster session & Lunch (poster room)**

14:00	**19:00**	**Free afternoon in Paris**

FRIDAY, 15 NOVEMBER

09:30	**12:30**	**Session IV Chair: Mehdi Khamassi**
09:30	**09:50**	Steve Kennerley *Dynamic computations supporting information search and choice in prefrontal cortex*
09:50	**10:10**	Lauren Atlas *Orbitofrontal contributions to expectancy, learning, and pain*
10:10	**10:30**	Jay Gottfried *What Tim Hath Wrought: Following Your Nose to Find Your Way*
10:30	**11:00**	**Coffee break (poster room)**
11:00	**11:20**	Daniela Schiller *A cognitive map of social space*
11:20	**11:40**	Masayuki Matsumoto *Value-to-choice signal transformation in midbrain dopamine neurons and orbitofrontal neurons during economic decision-making in monkeys*
11:40	**12:00**	Mehdi Khamassi *Hippocampal replay and preplay through the lenses of model-based reinforcement learning*
12:00	**12:30**	Discussion
12:30	**15:00**	**Lunch out in Paris**
15:00	**18:00**	**Session V Chair: Matthew Shapiro**
15:00	**15:20**	Matthew Shapiro *Visualizing goal-modulated neuronal coalitions in distributed circuits.*
15:20	**15:40**	Elisabeth Murray *Macaque orbitofrontal cortex is necessary for developing and sustaining autonomic arousal in anticipation of positive emotional events*
15:40	**16:00**	Joni Wallis *Orbitofrontal-hippocampal interactions during reward-guided learning*
16:00	**16:30**	**Coffee break(poster room)**
16:30	**16:50**	Alison Preston *Hippocampal—prefrontal cortex interactions support formation of cognitive maps of space, time, and concepts*
16:50	**17:10**	Tim Behrens *The Tolman-Eichenbaum Machine*
17:10	**17:30**	Yael Niv *Hippocampus-OFC interactions in building a cognitive map of task space*
17:30	**18:00**	Discussion
18:00	**18:05**	**Geoffrey Schoenbaum: Closing remarks**

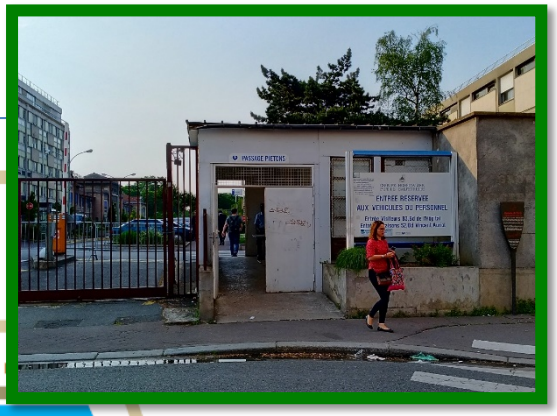
VENUES

INSTITUT DU CERVEAU ET DE LA MOELLE EPINIERE (ICM)

The speakers' talks and poster sessions will take place in the auditorium of the ICM, a research institute located within the Pitié-Salpêtrière Hospital. You can access it through one of two entries:

- From **83 Boulevard de l'Hôpital** (main entry): next to the metro station **Saint-Marcel** (**metro line 5**). Alternatively, walk 10 minutes from Gare d'Austerlitz (metro line 5, RER C) or take bus 57 or 91 .

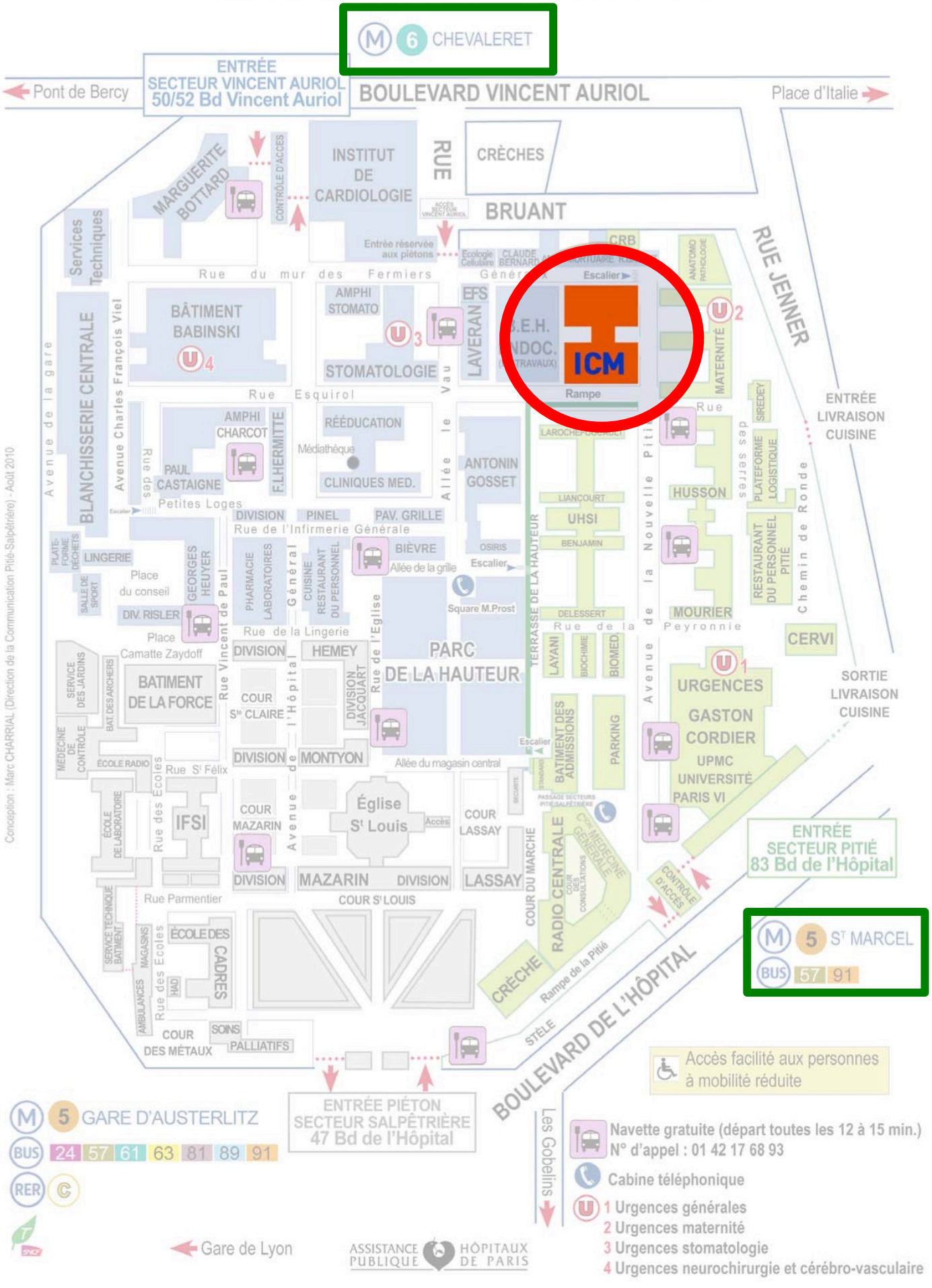
- From **Rue Bruant** (small side entry): next to metro station **Chevaleret** (**metro line 6**). As you walk from this entry to the ICM, you will have to climb a flight of stairs.



Secondary entry from **Rue Bruant**

Main entry from **Boulevard de l'Hôpital**

GROUPE HOSPITALIER UNIVERSITAIRE
LA PITIÉ SALPÊTRIÈRE - CHARLES FOIX



Tour Zamansky (Jussieu campus, Sorbonne University)

On Wednesday evening, the social event will take place at the top floor of the Tour Zamansky on the Jussieu Campus of the Sorbonne University. The venue is situated at a 20-minute walking distance from the ICM. The Tour Zamansky is one of the few tall buildings in Paris' inner city, offering a stunning view over the Seine River and the city center.

The entry to the Jussieu Campus faces the metro station "Jussieu" (metro lines 7 and 10).

Tour Zamanksy, Sorbonne Université
4 place Jussieu 75005 Paris, France

Accessing the internet on site

To access the Wi-Fi at the ICM, you will need to log in using the open Wi-Fi:

Wi-Fi name:	**Open-ICM**
Password:	**Welcome@icm2019**

/!\ Please make sure to connect to "Open-ICM", not to "ICM-GUEST"!

POSTERS

1-20	Title	Authors (A-K)
1	Decision making improves across adolescent development in the rat: implications for orbitofrontal circuit development	Neema Moin **Afshar,** Alexander Keip, Daeyeol Lee, Jane Taylor, and Stephanie Groman
2	Economic Decisions through Circuit Inhibition	Sébastien **Ballesta** and Camillo Padoa-Schioppa
3	Distinct local and long-range cortical dynamics in an adaptive decision-making task	Abhishek **Banerjee,** Giuseppe Parente, Jasper Teutsch, and Fritjof Helmchen
4	Anatomical Connectivity of Orbitofrontal Cortex Subdivisions	Ines V. **Barreiros,** Tim E. J. Behrens, Mark E. Walton, and Marios C. Panayi
5	The construction and deconstruction of suboptimal preferences through range-adapting reinforcement learning	Sophie **Bavard,** Aldo Rustichini, and Stefano Palminteri
6	Activation and disruption of a neural mechanism for novel choice in monkeys	Alessandro **Bongioanni,** Davide Folloni, Lennart Verhagen, Jérôme Sallet, Miriam Klein-Flügge, and Matthew Rushworth
7	Intracerebral correlates of mood fluctuations and their impact on choices	Romane **Cecchi,** Philippe Kahane, Anca Nica, Jiri Hammer, Agnès Trébuchon, Jean-Philippe Lachaux, Emmanuel Barbeau, Bruno Rossion, Mathias Pessiglione, and Julien Bastin
8	Noradrenergic modulation of the orbitofrontal cortex mediates behavioral flexibility in rats	Juan Carlos **Cerpa,** Margot Dehove, Angélique Faugère, Mathieu Wolff, Alain Marchand, Etienne Coutureau, and Shauna Parkes
9	The experience-description gap in the human brain	Fabien **Cerrotti,** Vasilisa Skvortsova, Valentin Wyart, and Stefano Palminteri
10	The ventromedial prefrontal cortex signal : a common neural currency for reward, effort and confidence	Nicolas **Clairis** and Mathias Pessiglione
11	Impact of n-3 PUFA deficiency on executive control: putative implication of cortical dopaminoceptive signal.	Andrea **Contini,** Chloé Arrondeau, Roman Walle, Véronique De Smedt-Peyrusse, Etienne Coutureau, Guillaume Ferreira, Fabien Ducrocq, and Pierre Trifilieff
12	The contribution of different subregions of macaque orbitofrontal cortex to probabilistic learning	Megan **Fredericks,** Richard Saunders, Elisabeth Murray, and Peter Rudebeck
13	A critical role of the amygdala on the influence of interoception during decision-making.	Atsushi **Fujimoto,** Elisabeth A. Murray, and Peter H Rudebeck
14	The impassable gap between experienced and described values	Basile **Garcia,** Maël Lebreton, Sacha Bourgeois-Gironde, and Stefano Palminteri
15	The orbitofrontal cortex is necessary for novel but not established economic choice.	Matthew **Gardner,** Davied Sanchez, Jessica Conroy, Jingfeng Zhou, Andrew Wikenheiser, and Geoffrey Schoenbaum
16	Retrospective and Prospective Inferences of Fear in the Orbitofrontal Cortex	Dilara **Gostolupce,** Belinda Lay, and Mihaela Iordanova
17	Testosterone Causes Decoupling of Orbitofrontal Cortex-Amygdala Relationship While Anticipating Primary and Secondary Rewards	Valentin **Guigon,** Chen Qu, Simon Dunne, Agnieszka Pazderska, Thomas Frodl, John J. Nolan, John P. O'Doherty, and Jean-Claude Dreher
18	Targeted stimulation of human orbitofrontal networks disrupts outcome-guided behavior	James D. **Howard,** Rachel Reynolds, Devyn E. Smith, Joel L. Voss, Geoffrey Schoenbaum, and Thorsten Kahnt
19	Relationships between serotonin transporter rate and brain activity associated with learning of social ranks: a simultaneous TEP([11C]-DASB)-fMRI study in humans	Rémi **Janet,** Annabel Losecaat Vermeer, Gabriel Belluci, Soyoung Park, Romain Ligneul, Christoph Eisenegger, and Jean-Claude Dreher
20	Representations of Reward and Abstract Structure in OFC Neurons During a Two Dimensional Auditory Task	Akash **Khanna,** Matthew Gardner, Nishika Raheja, and Geoffrey Schoenbaum

POSTERS

21-35	Title	Authors (K-Z)
21	Error monitoring in interval production in rats	Tadeusz W. **Kononowicz,** Virginie Van Wassenhove, and Valérie Doyere
22	Distinct neural substrates modulate fear overexpectation and extinction learning	Belinda **Lay,** Audrey Pitaru, Nathan Boulianne, and Mihaela Iordanova
23	Inter-individual variability in the neural correlates of valuation	Maël **Lebreton,** Stefano Palminteri, and Kaustubh Raosaheb Patil
24	Differential functional connectivity underlying asymmetric reward-related activity in human and non-human primates	Alizée **Lopez-Persem,** Léa Roumazeilles, Davide Folloni, Kévin Marche, Elsa Fouragnan, Nima Khalighinejad, Matthew Rushworth, and Jérôme Sallet
25	Conservatives show reduced disconfirmatory evidence integration in value-based decision-making	Anis **Najar,** Marc Pichot De La Marandais, Martial Foucault, Coralie Chevallier, and Stefano Palminteri
26	A system-level computational model of decision-making and learning in the lateral and medial sub-regions of Orbitofrontal Cortex	Bhargav Teja **Nallapu** and Frédéric Alexandre
27	Contribution of the orbitofrontal cortex to model-based inference about specific stimulus-reward relationship	Masaaki **Ogawa,** Seiya Ishino, Kota Tokuoka, Tadashi Isa, Brian Allen, Amy Chuong, Edward Boyden, Naoya Oishi, Im Sanghun, and Takeshi Yamada
28	Neurocomputational mechanisms of strategic decision making during unsignaled competitive and cooperative social interactions	Rémi **Philippe,** Rajesh P. N. Rao, Koosha Khalvati, and Jean-Claude Dreher
29	The effects of selective flavor-nutrient conditioning on choice behavior and autonomic arousal following crossed-surgical disconnection of the orbitofrontal cortex and amygdala in rhesus macaques	Maia **Pujara,** Jaewon Hwang, Nicole Ciesinski, Charday Long, Dawn Lundgren, and Elisabeth Murray
30	Prediction and prevention of compulsive behaviors by closed-loop optogenetic recruitment of striatal interneurons	Christiane **Schreiweis,** Lizbeth Mondragon, Jean-Luc Zarader, and Eric Burguière
31	Outcome preferences dynamically alter representations of reward probability in prefrontal-limbic circuits	Frederic M **Stoll** and Peter H Rudebeck
32	Behavior and learning based on imagined outcomes in a human Pavlovian over-expectation task recruits the orbitofrontal cortex	Jana **Tegelbeckers,** Geoffrey Schoenbaum, and Thorsten Kahnt
33	Testing orbitofrontal state and value representations during generalization	Avinash **Vaidya,** Johanny Castillo, and David Badre
34	Impaired learning from conflicting action outcomes in obsessive-compulsive disorder	Aurelien **Weiss,** Lindsay Rondot, Luc Mallet, Philippe Domenech, and Valentin Wyart
35	High trait anxious individuals represent aversive environment as multiple states: a computational mechanism behind reinstatement?	Ondrej **Zika**, Katja Wiech, Nicolas Schuck

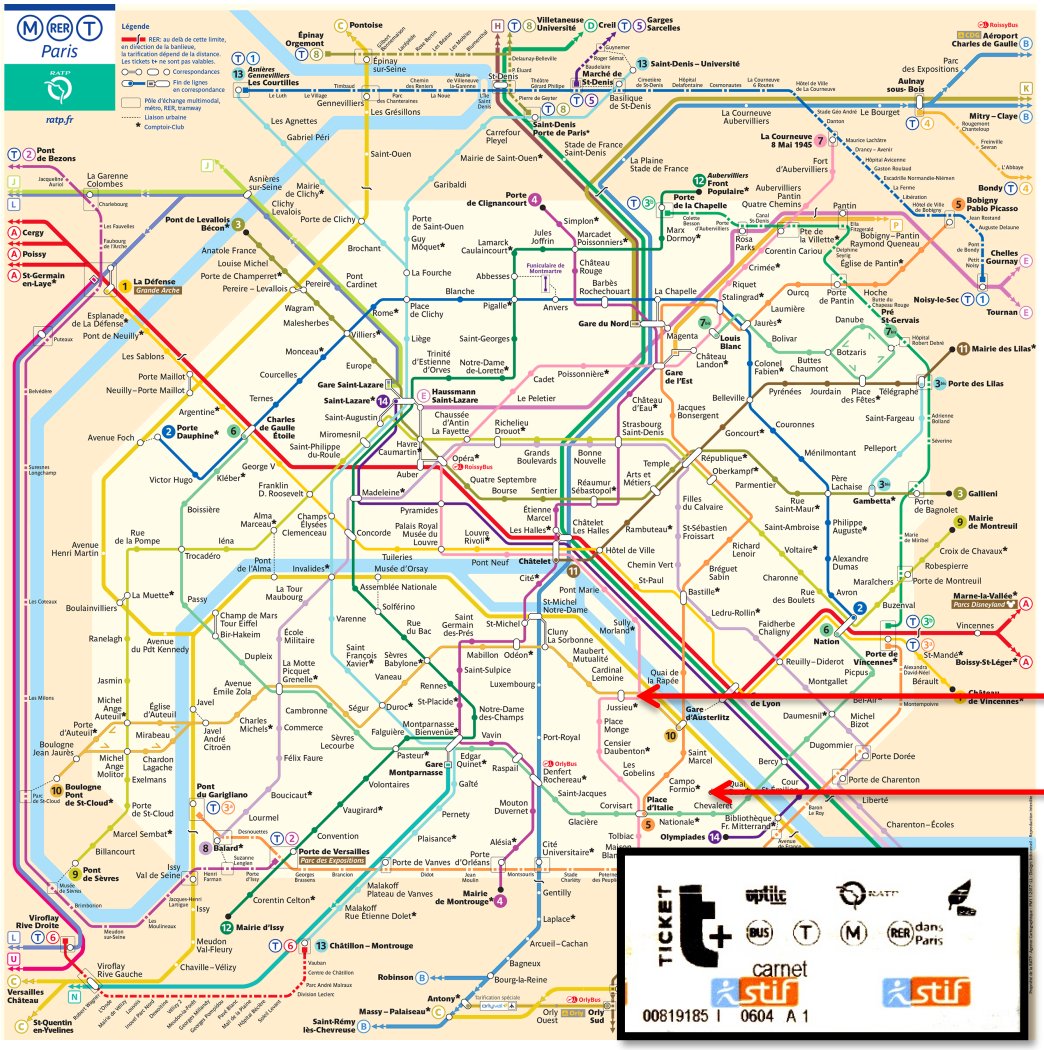
VISITING PARIS

PUBLIC TRANSPORT

For detailed information about your journey to and from the airport, see this page on the OFC website.

You can move around in Paris using the metro, bus, tram, or RER (something in between a metro and a suburb train: faster than metro, but with fewer stations). To plan your trip, simply use Google Maps or the official public transportation website.

The easiest way to move around is by metro, as Paris has a dense network and regular service (see map below). However, many stations are only about 250 meters apart, so you may also consider walking (note that it does not matter whether you cross the entire city or just hop off after two stations – you pay the same price for a single ticket). Please beware of the pickpockets on the metro, keep hold of your bags at all times, and try not to look like easy targets to them (a.k.a. tourists).

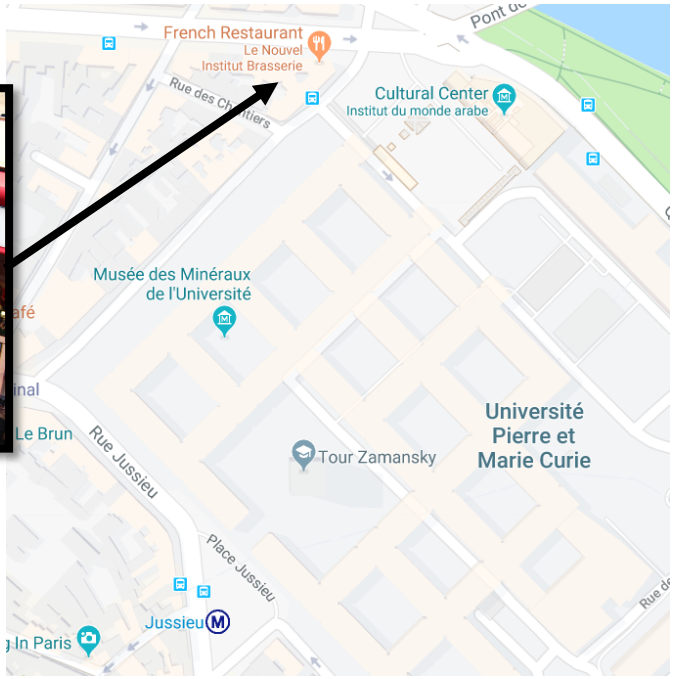


For each journey, you will have to buy a “T+ Ticket” (shown above) that you must hold on to during your trip in order to pass through the gates; you can dispose of the ticket once you leave the station. Tickets get date-stamped once you enter a station or bus and cannot be re-used afterwards. You can use the same ticket if you transit from the metro to the RER or vice versa, but if you transit from metro or RER to a bus or tram, you have to use a new ticket. So, as you can imagine, you will use up many tickets rapidly if you move around a bit. Therefore, it may be more economical to buy a pack of 10 or more tickets at once. Note that there are different price categories: if you only move around within Paris, you can get the “dans Paris” ticket for 1,90€ (or 14,90€ per 10), but if you are going outside Paris (this includes the suburbs), you will need a ticket that includes the banlieues, which is a little bit more expensive. Be sure to buy the correct ticket at the vending machines (fines range from 35€ to 375€).

FOOD AND DRINKS

Needless to say that France is known for its exquisite cuisine. This does not, however, mean that your every meal will be delicious, served by gentle waiters, and represent good value for your money. Be critical of the restaurant or brasserie you select, or make an informed choice based on recommendations from LeFooding or TimeOut Paris.

On **Wednesday, November 13,** our social event will take place in the Tour Zamansky, offering a beautiful view over Paris' city center. The event will end at 22:00, which may be a bit early for some. For a potential afterparty, the brasserie "Le Nouvel Institut" seems partiularly well-suited. Located at just 5 minutes' walking distance, this bar sells pints of beer for only 3€!



SIGHTSEEING

If the Tour Zamansky doesn't give you enough of a view of the city, you can get a bird's-eye view of Paris from top of the Eiffel Tower, the Tour Montparnasse, the Arc de Triomphe, or the Centre Pompidou. To access any of these sites, you will have to pay (and probably queue…), so you may therefore want to consider the view from in front of the Sacré Coeur basilica in the elevated area of Montmartre.

Paris also has an impressive amount of museums to visit. These include the famous Louvre, the beautiful Musée d'Orsay, or the permanent and temporary exhibitions of the Grand Palais. But, do also consider having a look at some other museums more specifically dedicated to movies, magic, ethnology, Picasso, contemporary art, modern art, or photography. And there's plenty more…

Less intellectual, but ever-so-easy on the eye, are the glamorous Opéra Garnier, some of the most beautiful leaded windows in the world in the Sainte Chapelle, or the macabre Catacombs of Paris.

If you are an European citizen under 26 years old, you can get into most of these places for free. Important for everyone: be sure to reserve your tickets (even if they are free of charge) online, to avoid queueing.

More commercial ways of spending your money are amply available at Paris' well-known department stores Le Bon Marché, Le Printemps, and the Galeries Lafayette, or the large Les Halles mall.

And if you really just want to see the city without standing in line or paying for entry, take a stroll and be sure not to miss the Place des Vosges (4th arrondissement), Place Vendôme (1st), the gardens of the Palais Royal (1st), Rue Montorgeuil (2nd), and the many little streets and passages. Consider taking a guided tour, some of which are free.

PART 2 – TALK ABSTRACTS

WEDNESDAY 13 NOVEMBER

CAMILLO PADOA-SCHIOPPA (9:30 – 9:50)

Department of Neuroscience, Washington University School of Medicine, St-Louis, MO, USA

Causal links between OFC activity and economic decisions

I will present the results of two experiments that established causal links between neuronal activity in OFC and economic decisions.

PETER RUDEBECK (9:50 – 10:10)

Neuroscience Department, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Reward identity and probability encoding in prefrontal-striatal-amygdala circuits

Optimal decision-making requires an understanding of the identity of the outcome, good or bad, big or small, that will follow a particular choice. It also requires an understanding of the probability of receiving that outcome. Both orbitofrontal (OFC) and ventrolateral prefrontal cortex (PFC) have been implicated in these decision processes, but their precise roles and the neural mechanisms engaged are unclear. Here I will describe experiments designed to provide mechanistic and circuit level understanding of how OFC and VLPFC represent outcome identity and probability information. We recorded neural activity within OFC, VLPFC and amygdala as well as parts of the striatum while monkeys chose between different visual stimuli predicted different outcomes, distinct fruit juices, at different probabilities. We show that VLPFC preferentially encodes reward probability, whereas outcome identity is encoded in to a similar degree in both OFC and VLPFC especially when monkeys exhibit a preference for a specific outcome. Recordings in amygdala suggest that VLPFC and amygdala form a functional circuit for computing reward probability during decision-making. Thus, our data provide mechanistic insight in how separate parts of ventral PFC represent different decision-related information, both of which are required for optimal decision-making.

SUSANNE AHMARI (10:10 – 10:30)

Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA, USA

Characterization of OFC activity patterns associated with distinct OCD-relevant behaviors

Human neuroimaging studies in obsessive compulsive disorder (OCD) consistently demonstrate abnormal patterns of activity in orbitofrontal cortex (OFC). However, the directionality of these neural activity abnormalities is dependent on behavioral state. For example, impaired OFC recruitment is typically observed during tasks probing perseverative decision-making including reversal learning, whereas OFC hyperactivity is found during symptom provocation. Because it is not possible to determine whether overlapping or distinct neural ensembles are associated with distinct OCD-relevant behaviors and activity patterns in humans, we turned to the Sapap3 knockout mouse (KO) model. In prior work we found that Sapap3 KOs display behavioral disturbances relevant to distinct behavioral states in OCD: perseverative grooming and impaired reversal learning (Manning et al, 2019). Sapap3-KOs are therefore a useful platform for precisely characterizing OFC activity associated with distinct OCD-relevant behaviors using in vivo calcium imaging. Male and female mice were injected with virus encoding fluorescent calcium indicator (AAV5-hysn-GCaMP6f) and implanted with gradient-index (GRIN) lenses in lateral OFC (LOFC) to visualize neural activity using Inscopix miniature microscopes (n=12KO/8 wildtype (WT) littermate controls, ~5 months of age). Calcium imaging was performed during grooming assessment and reversal learning, and aligned to behaviors of interest (correct/incorrect responses, initiation/termination of grooming). Time spent engaged in compulsive grooming varied across individual KOs (7-70% of time spent grooming). A subset of KOs (n=6) showed elevated perseverative incorrect responding during reversal learning; no correlation was seen between this behavior and levels of perseverative grooming. Consistent with predictions from the literature (Burguiere et al, 2013) and our previous work (Corbit et al, 2019), perseverative grooming was associated with an increased percentage of inhibited neurons in LOFC in Sapap3-KOs ($R2=0.49$, $p<0.01$). In contrast, perseverative

incorrect presses during reversal learning were associated with an increased percentage of activated LOFC neurons in Sapap3-KOs (R2=0.52, p=0.008). Finally, preliminary analyses suggest that the proportion of LOFC neurons inhibited during correct responses is associated with acquisition of the new rule following reversal in KOs (R2=0.83, p<0.002) but not WTs (R2=0.55, p<0.15). Together, these data suggest a model in which decreased activity within one subpopulation of OFC neurons leads to excessive grooming, while increased activity in another subpopulation of OFC neurons leads to increased perseverative lever pressing. Ongoing experiments are determining whether these subpopulations represent LOFC neurons with distinct projection targets.

Lesley Fellows (11:00 – 11:20)

Department of Neurology & Neurosurgery, McGill University, Montreal, Canada

OFC contributions to discovering value

Even apparently simple choices, like selecting from a breakfast buffet, involve options characterized by multiple attributes. Orbitofrontal cortex (OFC) has been implicated in making optimal choices in the face of this complexity. However, the mechanisms involved remain unclear. I will present evidence from studies of people with focal damage affecting the OFC. These findings support the claim that OFC makes a necessary contribution to attending to and learning about potentially reward-predicting attributes of the environment, particularly under conditions of complexity: i.e. when the environment contains multiple candidate predictors, or when the reward contingencies are probabilistic. This region is also critical for making value judgments and value-based choices of complex, multi-attribute objects, notably when value is conferred by the relationships between attributes. Together, these findings point to a nuanced role for OFC in discovering and recognizing value under conditions of environmental complexity. How these results might relate to object recognition in the ventral visual stream and relational mapping hippocampus will also be discussed.

Stephanie Groman (11:20 – 11:40)

Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA

Orbitofrontal circuits control multiple reinforcement-learning and addiction-relevant

Subjective value is a central concept in neuroeconomics. It is tracked in ventral fronto-striatal circuits, and variation in ventromedial prefrontal (vmPFC) value-related signals can predict choice. Real-world options are typically characterized by multiple attributes, some or all of which could contribute to a global value estimate. What brain mechanisms underpin value “construction” from multiple attributes?

Introduction: There is evidence that some individuals are more susceptible to developing substance abuse disorder, which may be linked to neurobiological differences that are present prior to drug use. The identity of these differences, however, remains unknown because most investigations into addiction susceptibility mechanisms have been conducted in humans and/or animals exposed to drugs of abuse, which result in robust neurochemical alterations that likely overshadow the subtle, pre-existing variation mediating susceptibility. Our recent work, using computational approaches, has found that individual differences in reward-mediated updating of decisions are uniquely associated with future drug-taking behaviors, whereas decision-making deficits following drug self-administration are due to selective disruptions in the updating of choices following no reward outcome (Groman et al., 2019). These data suggest that the neural circuits mediating addiction susceptibility may differ from those that are affected by chronic drug use. Here, we used a viral approach to investigate the function of anatomically-defined orbitofrontal circuits in reinforcement-learning and addiction-relevant behaviors in rats.

Methods: Adult, male rats (N=80) were trained to make decisions in a three-choice, probabilistically reinforced, reversal-learning task. Anatomically distinct orbitofrontal cortical (OFC) circuits were targeted by combining a floxed diphtheria toxin (DT) receptor virus with a retrograde Cre virus to selectively express DT receptors either in OFC neurons projecting to the nucleus accumbens (N=40) or amygdala neurons projecting to the OFC (N=40). Individual circuits were ablated by systemic administration of DT (30 ug/kg; i.p.). Decision making was reassessed in a subset of rats (N=40) to investigate the role of OFC circuits in computationally distinct reinforcement-learning processes. The remaining rats (N=40) were trained to self-administer methamphetamine (0.05 mg/kg/infusion) in 5 h, daily sessions for 30 days. Drug self-administration behaviors were then examined under probabilistically delivery of electric foot shocks and followed by tests of motivation and relapse-like behaviors.

Results: Ablation of OFC neurons projecting to the nucleus accumbens impaired decision-making processes by disrupting the use of negative outcomes to guide subsequent choices ($p<0.001$) and lead to greater self-administration of methamphetamine only under punishment ($p<0.01$). Ablation of amygdala neurons projecting to the OFC also impaired decision-making, but this was due to a disruption in the use of positive outcomes to guide subsequent choices ($p<0.001$). Moreover, ablation of amygdala neurons projecting to the OFC resulted in greater levels of cue-induced reinstatement and responding under a progressive ratio schedule ($p<0.05$).

Conclusions: These data demonstrate that anatomically-defined OFC circuits – that are linked to different computational steps – are involved in distinct aspects of addiction-relevant behaviors. Our ongoing work is using viral approaches to investigate the circuit-specific signaling mechanisms that are linked to drug-taking behaviors in order to identify novel molecular targets for the prevention and treatment of addiction.

MATHIAS PESSIGLIONE (11:40 – 12:00)

Institut du Cerveau et de la Moelle épinière, INSERM, Sorbonne Université, Paris, France

Bridging the gap between electrical and hemodynamic OFC value signals

One of the core functions assigned to the OFC is the valuation of potential action outcomes. Although this valuation has been endorsed both by monkey electrophysiology and human neuroimaging, the two literatures have drawn somewhat different conclusions. A first difference relates to the relationship between OFC activity and subjective value expressed in choices or likeability ratings. A positive linear link has been repeatedly observed with population-level hemodynamic response in human fMRI studies, while a more complex pattern has been revealed in monkey electrophysiology studies, including all sorts of relationships with single-unit spiking responses. Based on simulations of a simple neural network that projects multiple features onto a single value dimension, I will show that single-unit and population levels can be reconciled. Indeed, summing over all units can provide a univariate value signal, even if unitary activity is not correlated with value in any systematic manner. A second difference relates to the anatomical location of value signals. While meta-analyses of fMRI studies point to the medial OFC, many electrophysiological studies have observed value signals in the lateral OFC. Based on iEEG recordings in epileptic patients, I will show that electrical value signals in the human lOFC share the same core functional properties as previously demonstrated in the mOFC hemodynamic value signals. Indeed, value signals in both regions are 1) anticipatory (predicting upcoming value judgement, 2) generic (providing value for different categories of outcome), 3) automatic (signaling value even when useless for the ongoing task), and 4) quadratic (signaling both linear and squared value, which is a good proxy for confidence). All these core properties of the OFC value signal are fundamental to explain irrational value judgements such as the misattribution bias.

ERIN RICH (15:00 – 15:20)

Neuroscience Department, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Stable and dynamic representations of value in orbitofrontal cortex

The ability to associate positive and negative outcomes with predictive stimuli allows us to make optimal decisions. These stimulus-value associations are kept up to date by comparing an expected value with the experienced outcome, so that expected values must be held in mind when a stimulus and its outcome are separated by a delay. Little is known about the neural mechanisms that hold value representations online across delays, but temporarily remembering task-relevant information has been extensively studied in the context of item-specific working memory. Different hypotheses have suggested this ability requires either persistent or transient neuronal activity, with stable or dynamic representations respectively. To test these different hypotheses in the context of value representations, we analyzed the spiking activity of neurons in the orbitofrontal cortex while monkeys performed a task in which cues predicted rewards delivered after a short delay. Features of all hypotheses were simultaneously present in prefrontal activity. Thus, mixed dynamics supported robust, time invariant value representations while also encoding the information in a temporally specific manner. We posit that this hybrid coding might be a critical mechanism supporting flexible cognitive abilities.

Christina Gremel (15:20 – 15:40)

Department of Psychology, UC San Diego, La Jolla, CA, USA

Thalamic mechanisms supporting OFC-based value updating

The orbitofrontal cortex (OFC) supports the ability to update the value our decisions, however, the cell-type and circuit mechanisms supporting this computation are not clear. Thalamic projections to cortex have been hypothesized to support cortical computations, as well as provide sensory, and perhaps motivational, information. I will present findings from our investigations into the contribution of mediodorsal thalamic (MdT) inputs to OFC. Previous works have shown OFC supports incentive learning, or the process through which motivational states assign value to the goals of our actions. We found chemogenetic attenuation of MdTOFC projections disrupts both the updating and inference of a value change. In vivo photometry of OFC projection neurons shows calcium transients increases during epochs of decision-making, but a notable decrease during consummatory processes. In contrast, calcium photometry of MdT terminals in OFC shows marked calcium transient increases reflecting learned associations or decisions predictive of reward proximity. Intriguingly, we also see increased calcium activity of MdT terminals in OFC during consummatory processes. This contrast between MdT terminal activity in OFC and OFC projection neuron activity led us to examine the functional role of MdT on OFC activity. Using whole-cell physiology, we found that MdT inputs into OFC support a disynaptic inhibitory gating of OFC projection neuron firing rate. The magnitude of this disynaptic inhibition appears greater in food-restricted than sated mice. This raises the hypothesis that MdT input into OFC may enforce precise spiking timing important for value-based computations. In support of this, optogenetic activation of MdT terminals in OFC specifically during consummatory processes necessary for value updating, increased the magnitude of incentive learning. Together, our data suggests a mechanism through with motivational state gates thalamic support of an OFC-based computation.

Vincent McGinty (15:40 – 16:00)

Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ, USA

A population approach to choice prediction in the OFC

A fundamental goal in neuroeconomics is to identify how neural representations of value relate to value-based decisions. Although the value-coding neurons of the primate orbitofrontal cortex (OFC) have long been scrutinized in this role, we still lack a complete understanding of their contribution to behavior. In particular, we do not fully understand choice prediction in the OFC: how variability in the neural representation of value co-varies with choice behavior on a trial-by-trial basis. In this talk, I will describe a population approach to choice prediction, leveraging the simultaneous activity of many OFC neurons recorded during the performance of a sequential two-alternative economic choice task. One key question that I will address is the predictive leverage afforded by the representations of economic goods per se, in comparison to other potential reference frames, such as the sequence of stimulus presentation.

Thorsten Kahnt (16:30 – 16:50)

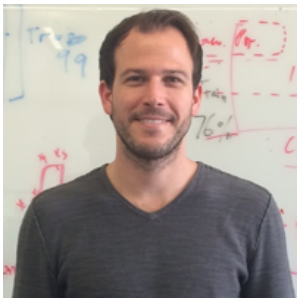
Feinberg School of Medicine, Northwestern University, Chicaco, IL, USA

Inference-based behavior depends on outcome-specific expectations in orbitofrontal cortex

Research across species has shown that the orbitofrontal cortex (OFC) is critical for decision making. However, it is less clear what computations are carried out in this region that make it so important for this function. Recent work from our lab and others has suggested that the OFC signals expectations about specific outcomes. Here we present evidence that these expectations are critical for behavior that is based on inferred or simulated outcomes, as opposed to behavior that can be based on direct experience alone. Specifically, we show that disrupting OFC activity using targeted transcranial magnetic stimulation selectively disrupts choices that require inference, without affecting value-based choices that can be based on direct experiences. Together these findings suggest that the OFC contributes to adaptive decision making by representing a model or cognitive map of the task environment that allows individuals to infer or simulate the value of future outcomes when direct experience is lacking.

Erie Boorman (16:50 – 17:10)

Department of Psychology, UC Davis, Davis, CA, USA



Map making: Constructing, combining, and navigating abstract cognitive maps

The cognitive map is thought to enable model-based inferences from limited experience that can even guide novel decisions–a hallmark of goal-directed behavior. It has been proposed that the orbital frontal cortex (OFC) and the hippocampal-entorhinal (HC-EC) system may contain such a cognitive map, even for non-spatial task spaces. We tested whether the OFC and HC-EC system organize abstract and discrete relational information into a cognitive map to guide novel inferences. Subjects learned the status of people in two separate unseen 2-D social hierarchies defined by competence and popularity dimensions. Although only one dimension was ever behaviorally relevant, multivariate activity patterns in OFC and the HC-EC system were robustly and linearly related to the Euclidian distance between individuals in the mentally reconstructed 2-D space, such that more proximal individuals were represented progressively more similarly. Within OFC we observed a medial-lateral differentiation, such that activity patterns in medial and central OFC reflected the Euclidian distance, whereas those in lateral OFC reflected the behaviorally-relevant 1-D rank distance alone. Hubs created unique comparisons between the two hierarchies, enabling inferences between novel pairs of individuals. We found that both behavior and neural activity in OFC reflected the Euclidian distance to the retrieved hub, which was reinstated in HC. These findings reveal how abstract and discrete relational information is represented, combined, and navigated in the OFC and HC-EC system to generate novel inferences in the human brain.

Tianming Yang (17:10 – 17:30)

Institute of Neuroscience, Shanghai Neuroeconomics Collective, Shanghai, China

Orbitofrontal Cortex Plays A Limited Role in Value Computation During Decision Making

During value-based decision making, the value associated with each option is computed and compared. It has been suggested that the orbitofrontal cortex (OFC) plays important roles in this process and produces decisions. We examined the representation of reward value in the OFC during decision making in macaque monkeys with a probabilistic reasoning task. In this task, the monkeys had to make decisions by computing the reward probability associated with each option by accumulating evidence from sequentially presented visual stimuli. We found that the OFC neurons encoded the reward probability associated with individual visual stimuli. However, this representation of reward probability in the OFC was transient and disappeared with the offset of each visual stimulus. The OFC neuronal activity did not reflect the process of reward information accumulation during decision making. Our results indicated that the OFC plays a more limited role in value-based decision making than previously suggested.

THURSDAY 14 NOVEMBER

JOHN P. O'DOHERTY (8:30 – 8:50)

Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA, USA

The construction of value: attribute-based value integration in orbital and medial prefrontal cortices

A core notion in economics and psychology is that animals and humans assign value to stimuli in the world and use this information to guide their behavior. Over the past 15 years, we have obtained evidence from numerous neuroeconomics studies that value is encoded in the brain, for diverse kinds of stimuli, tasks and contexts. Value signals have been found in medial orbital, adjacent medial prefrontal cortex and elsewhere in the human brain not only for the prospect or receipt of monetary rewards, but also for food, prospective romantic partners, attractive faces, and even for the aesthetic appreciation of art. However, a fundamental question remains: how are these value signals actually constructed by the brain? Here I will review a series of studies aimed at addressing how value signals are constructed by integrating over underlying attributes from which a given stimulus is composed. I will show that across multiple stimulus types, including food stimuli, art, good bundles and even strategies for exploration, integration of attributes occurs leading to an overall value computation in the medial prefrontal cortex. These findings suggest a hierarchical process of value-integration in which features of increasing complexity are combined as one transitions from feature-space into value-space.

ALICIA IZQUIERDO (8:50 – 9:10)

Department of Psychology, UC Los Angeles, Los Angeles, CA, USA

Orbitofrontal cortex in adjusting to changes in reward delay and probability

Neural activity in rodent or nonhuman primate orbitofrontal cortex (OFC) signals both stimulus value and an expected range of possibilities for reward, or risk. These neural responses update following changes in value and are modulated by reward history. Previously we found that rat ventromedial OFC is causally involved in building expectations about the range of expected delays-to-reward acquired over longitudinal experience (Stolyarova & Izquierdo, 2017). Intriguingly, recent studies show that monkey OFC may not integrate different reward attributes (i.e. delay, probability), but may instead maintain orthogonal representations of these attributes (Yang and Murray, 2018) for integration elsewhere. Inspired by this evidence, we ask the following questions: i) are there common mechanisms by which OFC learns/adjusts to changes in probability vs. delay attributes? and ii) is there specialization for this in rat OFC, or does another region in rat frontal cortex (i.e. anterior cingulate cortex, ACC) perform a similar function? In this talk I will review results from different experiments in our lab aimed at understanding the role of OFC in learning under different forms of reward uncertainty. Rats were trained to first discriminate visual stimuli and then adjust to changes in probabilities-of-reward or delays-to-reward associated with those stimuli following inhibitory (hM4Di, Gi) DREADDs in ventral OFC. We found that rats need an intact OFC to adjust to changes in either delay or probability attribute. Furthermore, across both attributes, OFC-inhibition resulted in a pattern of "confirmation bias:" animals learn more from expected than unexpected feedback, and engage in more WinStay and less LoseShift strategies overall. Our parallel experiments with ACC DREADDs inhibition suggest substantial overlap with OFC in adjusting to changes in both attributes, with ACC as more specialized for learning about better-than-expected changes and OFC serving a more general function in learning about both better- and worse-than-expected changes in reward. Collectively, these results support the notion that OFC may encode essential information for generating representations about expected delays and probabilities. This information may then be used by ACC to mediate adjustments when meaningful changes occur. I will end with a discussion of ongoing experiments in which we are imaging, recording, and disconnecting ACC and OFC during these tasks.

Shauna Parkes (9:10 – 9:30)

Institut de Neuroscience Cognitives et Intégratives d'Aquitaine, CRNS, Université de Bordeaux, Bordeaux, France

OFC tracks changes in action-outcome contingencies in rats

Appropriate decision-making is critical for adapting to a changing environment. Every day we make decisions based on internal goals and the expectation that a given action will lead to goal achievement. Such decisions are experimentally defined as "goal-directed." The ability to behave in a goal-directed manner requires knowledge about the causal relationship between an action and its outcome as well as knowledge about the current value of that outcome. Previous studies have shown that inactivation of the ventral and lateral regions of OFC (vlOFC) in rats does not disrupt the ability to initially acquire action-outcome associations or to select actions based on the current value of their consequences. However, we demonstrated that inactivation of vlOFC does render rats incapable of properly updating previously encoded action-outcome associations and using these new associations to guide choice behaviour. This effect relies on interactions between vlOFC and the submedius thalamic nucleus, as disconnecting these structures also produces a specific impairment in adaptive responding following reversal of the action-outcome associations. Interestingly, no impairment was observed when vlOFC was disconnected from its other thalamic partner, the mediodorsal thalamus. Finally, I will present some ongoing research investigating the contribution of dopaminergic and noradrenergic inputs to the OFC in tracking changes in action-outcome associations.

Kate Wassum (10:00 – 10:20)

Department of Psychology, UC Los Angeles, Los Angeles, CA, USA

Corticolimbic circuitry in reward learning and pursuit

To make adaptive decisions we must cast ourselves into the future and consider the outcomes of our potential choices. This prospective consideration is informed by our memories. I will discuss our lab's recent work investigating the neural circuits responsible for encoding, updating, and retrieving reward memories for use in the considerations underlying decision making. We have taken a multifaceted approach to these investigations, combining recording, circuit dissection, and behavioral tools. Our results are indicating that the orbitofrontal cortex and basolateral amygdala work in a circuit to regulate the encoding and retrieval of reward memories to ensure adaptive reward pursuit. The cognitive symptoms underlying addiction can result from a failure to appropriately learn about and/or anticipate potential future events, making these basic science data relevant to the understanding and potential treatment of addiction to drugs or alcohol.

Catharine Winstanley (10:20 – 10:40)

Department of Psychology, University of British Columbia, Vancouver, BC, Canada

Cue-biased risky choice and the orbitofrontal cortex

Rewarding events in commercial gambling games are typically accompanied by highly salient sound and light stimuli. We have shown previously that adding reward-concurrent audiovisual cues to laboratory-based gambling tasks designed for both rats and humans significantly increases choice of risky, disadvantageous options. However, the neurocognitive mechanism through which sensory cues enhance risky choice is unclear. Computational modeling of acquisition data from the rat gambling task (rGT) suggest the cues do not increase learning from rewarding outcomes, but instead diminish the impact which losses have on an option's value. Whereas lesions to the orbitofrontal cortex (OFC) slow acquisition of the standard "uncued" version of the rGT, such that a preference for the most lucrative option emerges more slowly, inactivation of the OFC during initial learning sessions lead to a more optimal pattern of choice. As such, computational processes within the OFC as to the expected value of risky options may be compromised by the presence of reward-concurrent cues. Risky choice on the cued version of the rGT can also be improved by a 5-HT2C antagonist and atomoxetine. Both these drugs can also improve reversal learning, a process in which the OFC has also been implicated. Indeed, the ability of 5-HT2C antagonism to facilitate reversals appears to be OFC-dependent. Collectively, these data indicate that the OFC may be a critical location through which reward-paired cues promote risky choice in the rGT, and manipulations which target OFC function may prove useful in preventing this deleterious effects of cues.

MIRIAM KLEIN-FLÜGGE (10:40 – 11:00)

Department of Experimental Psychology, University of Oxford, Oxford, UK

Multiple neural mechanisms of knowledge acquisition

Humans and animals learn from reward but they also learn by observing statistical relationships in the world. It is the coalescence of these learning mechanisms that shapes our ability to produce complex goal-directed behaviours. While much is known about the neural encoding of updating signals during learning, there is relatively little knowledge on where and how learnt representations are stored. The first study I will present explores the neural representations or 'associative structures' created by multiple different learning mechanisms using human fMRI. We find that knowledge encoded via model-free RL is dissociable, neurally, from the encoding of statistically learnt relationships. One advantage of acquiring relational knowledge is that it allows us to behave adaptively in new situations and make inferences about never previously experienced options. In the second study I will examine whether macaque monkeys can make inferences about novel choice options and show that they recruit a hexagonal map-like coding scheme to represent relationships in an abstract option space.

FRIDAY 15 NOVEMBER

STEVE KENNERLEY (9:30 – 9:50)

Department of Clinical and Movement Neurosciences, University College of London, London, UK

Dynamic computations supporting information search and choice in prefrontal cortex

Real-world choices are typically guided by multiple shifts in attention between choice alternatives. The order, duration and frequency of shifts in visual attention can strongly influence the eventual decision made. However, decision paradigms in neuroscience have been predominantly conducted with central or uncontrolled fixation, thus overlooking the importance of attention in shaping decision-related computations. Attention filters how information enters decision circuits, thus affecting the temporal dynamics of several decision-related computations, including stimulus identification, valuation, comparison to previously attended alternatives, and action selection. Dissociating the neural substrates of decision-related computations may therefore require synchronizing neural activity with attentional focus. Here I will discuss results across prefrontal cortex (PFC) neurons during an attention-guided decision-making task. From the first saccade to decision-relevant information, a triple dissociation of decision- and attention-related computations emerged in parallel across PFC subregions, with the OFC population encoding information about both stimulus identity and attended value. As subjects gathered more information about a choice, OFC activity reflected value comparison between currently and previously attended information. Our findings show how anatomically dissociable PFC representations evolve in parallel during attention-guided information search, supporting computations critical for value-guided choice.

LAUREN ATLAS (9:50 – 10:10)

National Center for Complementary and Integrative Health, NIH, Bethesda, MD, USA

Orbitofrontal contributions to expectancy, learning, and pain

The orbitofrontal cortex is implicated in value-based learning for both appetitive and aversive outcomes. In this talk, I will review the role of the OFC/VMPFC in expectancy-based modulation of pain and aversive learning. We find that value-based signals in the OFC update with instruction during aversive reversal learning, whereas the amygdala seems to respond to aversive outcomes irrespective of instructions. I will also present new work measuring causal influences of OFC/VMPFC on expectancy effects on pain. We find that human patients with OFC/VMPFC lesions show larger expectancy effects on pain, and reduced pain-related autonomic activity. I will discuss the implications of these findings for our understanding of the role of the OFC in value-based learning, higher order knowledge, aversive experience, and subjective pain.

JAY GOTTFRIED (10:10 – 10:30)

Department of Neurology, University of Pennsylvania, Philadelphia, PA, USA

What Tim Hath Wrought: Following Your Nose to Find Your Way

A singular aspect of odors is their ability to travel through the air over long distances. In this manner, the sense of smell can gather valuable predictive information about an odorous object, enabling animals to navigate either toward or away from an odor source as needed. Notably, in contrast to the "what" questions of olfaction, the role of the olfactory system in spatial navigation is less well studied, though no less important. Elegant neurobiological studies on odor navigation have been conducted in insects and birds, but there are very limited neural data available in mammals, including humans. In this presentation, I will discuss our recent work showing that human subjects can orient within a 2-D abstract space defined by odor mixtures varying in perceived intensity. Intriguingly, even though subjects were not actively navigating through a physical environment, "grid-like" neural representations of this odor intensity space emerged in human ventromedial prefrontal cortex, entorhinal cortex, and piriform cortex, highlighting a novel mechanism by which the human brain can construct an olfactory cognitive map. I will also present new preliminary data suggesting that subjects can learn to navigate a virtual reality (VR) arena in which the only informative sensory cues are olfactory. These studies bring fundamental understanding to the capacities and constraints of human olfactory navigation, and highlight neural mechanisms by which the olfactory system tracks and locates odor sources in odiferous environments.

DANIELA SCHILLER (11:00-11:20)

Neuroscience Department, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Navigating social space

How do we place ourselves within a social structure? Social encounters provide opportunities to become intimate or estranged from others and to gain or lose power over them. The locations of others on the axes of power and intimacy can serve as reference points for our own position in the social space. The goal of our research is to uncover the neural encoding of these social coordinates. This talk will describe recent experiments tracking the online neural encoding of the perceived locations of others relative to us through dynamic interactions with multiple peers. The talk will also describe initial attempts to uncover a "grid-like" representation of social space, as well as preliminary findings from studies testing these predictions in psychiatric patients presenting with a broad dimensional range of psychopathology. Altogether, the results suggest that navigational computations are potentially crucial for representing and tracking dynamic social relationships, and imply that beyond framing physical locations, the OFC, the hippocampus and related regions compute a more general, inclusive, abstract, and multidimensional cognitive map consistent with its role in episodic memory.

MASAYUKI MATSUMOTO (11:20 – 11:40)

Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

Value-to-choice signal transformation in midbrain dopamine neurons and orbitofrontal neurons during economic decision-making in monkeys

In economic decision-making, we first evaluate the value of offered options and then decide whether or not to choose them using the value information. To uncover the neural basis of economic decision-making, it is critical to understand how the brain transforms value information into choice commands. Although previous studies have focused on the roles of prefrontal regions (e.g., the orbitofrontal cortex, OFC) in the value-to-choice transformation, the whole picture of the neural network underlying this process remains elusive. Here, we investigated whether and how midbrain dopamine neurons, a subcortical center for reward processing, contribute to the value-to-choice transformation. We designed an economic decision-making task in which monkeys were required to decide to choose or not to choose an option based on its value immediately after the option was offered, and recorded single-unit activities from dopamine neurons as well as OFC neurons, for comparison, in the animal performing the task. We found that dopamine neurons represented diverse signals related not only to the option's value but also to the animal's choice behavior; some dopamine neurons represented the value of the offered option, some represented whether the animal would choose or not choose the option, and some represented the combination of the value and choice behavior, i.e., these neurons represented the value only when the monkey decided to choose the option (we henceforth call this signal "choice-dependent value"). We next analyzed the time course of these dopamine signals, and found that these signals were observed at different timing. Shortly after the onset of the option, the value signal rapidly appeared, followed by the choice-dependent signal. The choice signal arose at last. This time course of the three signals is well consistent with the time course of the value-to-choice transformation, and we also observed the same time course in the OFC. Notably, the last choice signal appeared before the monkey executed a motor action to choose the option in both dopamine neurons and the OFC. Our findings show that dopamine neurons and OFC neurons share the same signal dynamics corresponding to the value-to-choice transformation, and provide evidence suggesting that not only prefrontal regions but also the subcortical dopamine system regulates the value-based choice formation.

MEHDI KHAMASSI (11:40 – 12:00)

Institut des Systèmes Intelligents et de Robotique, CNRS, Sorbonne Université, Paris, France

Hippocampal replay and preplay through the lenses of model-based reinforcement learning

Apology - I would like to apologize since my talk will be mostly about the hippocampus, but will nevertheless include some OFC data. I think these can contribute to the study of how the hippocampus and the orbitofrontal cortex may interact during offline inference processes to update stimulus values.

Abstract - Hippocampal offline reactivations during reward-based learning, usually categorized as replay and preplay events, have been found to be important for performance improvement over time and for memory consolidation. Recent computational work has linked these phenomena to the need to transform reward

information into state-action values for decision-making and to propagate it over time and space. Nevertheless, it is still unclear whether an integrated reinforcement learning mechanism could account for the variety of hippocampal reactivations, including variety in order (forward and reverse reactivated trajectories) and in the places within the environment where they occur (reward site or decision-point). I will present a new model-based bidirectional planning model which accounts for a variety of hippocampal reactivations. The model combines forward trajectory sampling from current position and backward sampling through prioritized sweeping from reward location until the two trajectories connect. This is repeated until stabilization of state-action values (convergence), which could explain why hippocampal reactivations drastically diminish when the animal's performance stabilize. Forward reactivations are prominently found at decision-points while backward reactivations are exclusively generated at reward sites. Moreover, the model can generate imaginary trajectories that are not allowed to the agent during task performance. I will finish the presentation by briefly discussing how an extended version of the model can represent Hpc-OFC communication during offline preplay/inference, and how this can be related to experimental data in rodents.

MATTHEW SHAPIRO (15:00 – 15:20)

Neuroscience Department, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Visualizing goal-modulated neuronal coalitions in distributed circuits

In 2017, Howard Eichenbaum argued that the brain mechanisms of cognition would be best pursued at the level of cell assemblies--population coding. By recording neuronal ensembles as animals performed a well-characterized contextual memory task, he found that single cells responded to the same set of cognitive and behavioral task features across brain areas. For example, both hippocampal and orbitofrontal (OFC) single neurons distinguished locations and outcomes, and commonly showed "mixed selectivity," responding to specific outcome-location associations. Population coding differed: hippocampal ensembles distinguished location better than outcome; OFC ensembles vice versa. Why should different brain areas respond to overlapping task features with different coding hierarchies? This talk will discuss how OFC and hippocampal ensembles evolve and interact during learning, and how hierarchical coding could promote interactions among these and downstream brain areas.

BETSY MURRAY (15:20 – 15:40)

National Institute of Mental Health, NIH, Bethesda, MD, USA

Macaque orbitofrontal cortex is necessary for developing and sustaining autonomic arousal in anticipation of positive emotional events

Neurophysiological studies have shown that neurons in orbitofrontal cortex (OFC) of macaques signal several aspects of reward, including the sensory properties of reward (e.g., taste, flavor), the magnitude of reward, and the probability of receiving reward. Further, the encoded reward properties are inextricably linked to the stimuli that predict them, as evidenced by OFC neuronal signaling of specific anticipated rewards based solely on the presence of different predictive stimuli. Yet macaque OFC is not necessary for many types of stimulus-reward learning, including deterministic or probabilistic instrumental learning, and either deterministic or probabilistic stimulus reversal learning (Murray and Rudebeck, Nat Rev Neurosci, 2019). To probe the potential contributions of OFC to other aspects of stimulus-reward learning we turned to an appetitive Pavlovian task and used a measure of sympathetic autonomic arousal, pupil dilation, as our measure of learning. Specifically, we compared the acquisition of changes in pupil diameter (PD) to a CS+ in rhesus monkeys (Macaca mulatta) that had sustained bilateral excitotoxic lesions of OFC (n=4) and unoperated controls (n=4). Monkeys were trained on a task in which Pavlovian trace-conditioning of stimulus-reward associations was superimposed on instrumental conditioning of active visual fixation. The visually presented CS+ was followed by a trace interval, which was in turn followed by 0.5-ml fluid reward. The CS- was followed by an unfilled interval and no reward was delivered. PD was measured with an eye-tracking device. Learning was reflected by the emergence of a differential pupil response to the CS+ and CS-. Criterion was set at four consecutive sessions with differential pupil responses to the CS+ vs. CS- during the CS period. As expected, controls acquired conditioned autonomic responses within a few sessions. Relative to controls, monkeys with OFC lesions required more sessions to attain criterion. In fact, whereas controls attained criterion with 10 sessions or so, three out of the four monkeys with an OFC lesion failed to acquire criterion within roughly 50 training sessions. The same operated monkeys showed normal responses to changes in luminance and to the receipt of unsignaled reward. Thus, the OFC lesion did not have a global influence on pupil function. In addition, when monkeys were given an instrumental task with parameters matched to the Pavlovian task, the groups learned at the same rate. We conclude that the macaque OFC is essential for developing and sustaining autonomic arousal in anticipation of positive emotional events.

Joni Wallis (15:40 – 16:00)

Department of Psychology, UC Berkeley, Berkeley, CA, USA

Orbitofrontal–hippocampal interactions during reward-guided learning

Neuronal oscillations in frontal cortex have been hypothesized to play a role in the organization of high-level cognition. Within orbitofrontal cortex (OFC), there is a prominent oscillation in the theta frequency (4-8 Hz) during reward-guided behavior, but it is unclear whether this oscillation has causal significance. One methodological challenge is that it is difficult to manipulate theta without affecting other neural signals, such as single neuron firing rates. A potential solution is to use closed-loop control to record theta in real-time and use this signal to control the application of electrical microstimulation to OFC. Using this method, we show that theta oscillations in OFC are critically important for reward-guided learning and that they are driven by theta oscillations in hippocampus. The ability to disrupt OFC computations via spatially localized and temporally precise stimulation, could lead to novel treatment strategies for neuropsychiatric disorders involving OFC dysfunction.

Alison R. Preston (16:30 – 16:50)

Departments of Neuroscience, Psychology, and Psychiatry, University of Texas, Austin, TX, USA

Hippocampal–prefrontal cortex interactions support formation of cognitive maps of space, time, and concepts

We acquire knowledge by connecting events that are experienced at different times and places, forming cognitive maps that represent the commonalities among and differences between individual events and their elements. In this talk, I will present evidence from virtual reality experiments in humans that show the hippocampus and prefrontal cortex form cognitive maps of space that exaggerate spatial similarities and differences. I will further show how distorted maps of space bias individuals' perception of temporal boundaries, demonstrating generalization of knowledge across domains. Using neurocomputational approaches, I will present evidence that hippocampal and prefrontal cognitive maps reflect abstract representational geometries that code the regular structure of the environment, promoting generalization through inference. I will end by showing that prefrontal cortex supports efficient formation of abstract, conceptual knowledge through a process akin to goal-directed dimensionality reduction. Collectively, these data show how neural representations extend knowledge beyond direct experience to allow for adaptive decision making in new contexts.

Tim Behrens (16:50 – 17:10)

Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

The Tolman–Eichenbaum Machine

Apology - I realise that this is not strictly about OFC, and apologise, but I feel vindicated for 2 reasons. First, the meeting is dedicated to Howard. Second, with the recent demonstrations of OFC being involved in representing state space locations, many of the things that we say about entorhinal cortex should be relevant to the OFC folk. Actually there is a chance, I will be able to present an example of this at the end of the talk.

Abstract - The hippocampal-entorhinal system is important for spatial and relational memory tasks. We formally link these domains; provide a mechanistic understanding of the hippocampal role in generalisation; and offer unifying principles underlying many entorhinal and hippocampal cell-types. We propose medial entorhinal cells form a basis describing structural knowledge, and hippocampal cells link this basis with sensory representations. Adopting these principles, we introduce the Tolman-Eichenbaum machine (TEM). After learning, TEM entorhinal cells include grid, band, border and object-vector cells. Hippocampal cells include place and landmark cells, remapping between environments. Crucially, TEM also predicts empirically recorded representations in complex non-spatial tasks. TEM predicts hippocampal remapping is not random as previously believed. Rather structural knowledge is preserved across environments. We confirm this in simultaneously recorded place and grid cells. I realise that this is not about OFC, and apologise, but I feel vindicated for 2 reasons. First, the meeting is dedicated to Howard. Second, with the recent demonstrations of OFC being involved in representing state spaces, many of the things that we say about entorhinal cortex should be relevant.

YAEL NIV (17:10 – 17:30)

Department of Psychology, Princeton Neuroscience Institute, Princeton University, Princeton, NJ, USA

Hippocampus–OFC interactions in building a cognitive map of task space

Prominent theories of orbitofrontal function have focused on a role in representing value and economic decision making. However, converging data suggest a wider role in representing an oft-overlooked building block of reinforcement learning and decision making: a representation of the task as a sequence of "states". In this talk, I will present evidence from a non-value-based experiment that suggests that the orbitofrontal cortex represents the current state in a cognitive map of the task. Like a way-finder maps app, this representation is especially critical when external stimuli do not uniquely identify one's location. I will then discuss a potential role for offline hippocampal replay in honing these orbitofrontal state representations.

PART 3 – POSTER ABSTRACTS