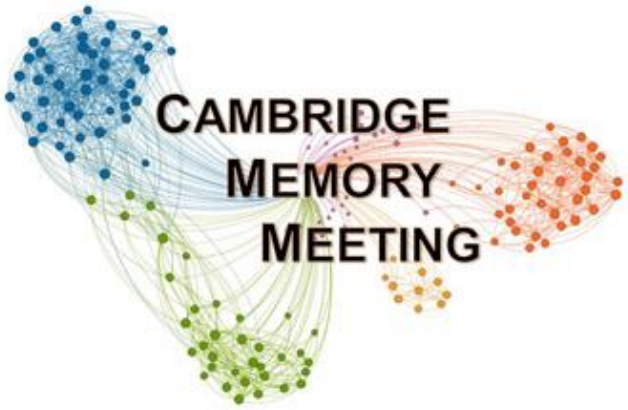
Cambridge Memory Meeting 2019



Thursday 4th April 2019

Buckingham House Conference Centre, Murray Edwards College, Cambridge

Website: www.cammindlab.com/cambridge-memory-meeting-2019

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Welcome

Welcome to the 8th annual Cambridge Memory Meeting! This year's meeting is being hosted jointly by the MiND Lab (PI: Amy Milton) and CAMBLab (PI: Lucy Cheke) in the Department of Psychology, and the Cahill Lab in the Department of Physiology, Development and Neuroscience. The goal of this meeting is to encourage interaction between Cambridge researchers specialising in the neuroscience or psychology of learning and memory, whether at the basic, preclinical or clinical levels. The meeting provides Principal Investigators, postdoctoral researchers and graduate students with the opportunity to share their research in an informal environment.

This year the meeting has been generously sponsored by **Alzheimer's Research UK** and the **Department of Psychology**.

Programme at a glance

Time	Speaker	Title:
9:30	Arrival and morning refreshments	
10:00	**Plenary lecture:** Prof Alan Baddeley	Working memory: Ambling and stumbling towards the multicomponent model
11:00	Dace Apšvalka	Controlling unwanted memories: the medial septal pacemaker suppression hypothesis
11:25	Elisa Galliano	Neuronal plasticity: beyond the usual suspects
11:50	Alex Clarke	The dynamics of semantic knowledge within the anterior temporal lobes
12:15	Lunch and Posters	
13:30	**Plenary lecture:** Prof Clea Warburton	Interleaving brain wide neural circuits for recognition memory
14:30	Mona El-Sayed Hervig	Dissociable roles of rat medial and lateral orbitofrontal cortex in visual reversal learning
14:55	Coffee	
15:25	Gido van de Ven	Hippocampal offline reactivation consolidates recently formed cell assembly patterns during sharp wave-ripples
15:50	Carolin Sievers	Encoding variability: when pattern reactivation does not benefit context memory
16:15	Jörn Alexander Quent	Using immersive reality to examine the U-shaped relationship between schema and memory performance
16:40	Speed Meeting session:	Let's work that memory! Participants, especially new members of Cambridge Memory Labs, are invited to introduce their work on memory in three minutes, no preparation or supports necessary - sign-up sheet at entrance!
17:05	Closing remarks and thanks from Organisers	
17:15	After Meeting Drinks – Tables at The Architect Pub	

Abstracts - Talks

Alan Baddeley, University of York

Working memory: ambling and stumbling towards the multicomponent model

The way in which ideas develop into experiments, experiments into concepts and concepts into theory typically bears little resemblance to the neat progression that appears in journal articles and books. I was reminded of this in writing a rather strange book, "Working Memories: Postmen, Divers and the Cognitive Revolution" which led, among other things, to my reflecting on the way in which the multicomponent model of working memory originated and then developed over the next 40 years. I will use the development of the model to talk about the interaction of theoretical and applied research and different approaches to the development of scientific theories.

Dace Apšvalka, MRC CBU

Controlling unwanted memories: the medial septal pacemaker suppression hypothesis

The ability to control unwanted thoughts and memories is essential to mental health and wellbeing. Prior research suggests that stopping intrusive memories involves top-down control by the prefrontal cortex and subsequent inhibition of hippocampal retrieval processes. Moreover, the efficacy of this fronto-hippocampal inhibitory pathway depends on hippocampal GABA to enable memory suppression. Specifically, higher resting concentration of hippocampal GABA has predicted better mnemonic control. These findings raise questions about the mechanisms through which hippocampal GABA enables the suppression of unwanted memories. The prefrontal cortex itself does not have direct connections to the hippocampus. Therefore, the question is, what is acting on the GABAergic interneurons in the hippocampus during memory suppression? Based on animal research, we hypothesise that the medial-septal nucleus in the basal forebrain is critically involved in the memory inhibition process. Our preliminary results support the hypothesis. When stopping intrusive memories, activity in the medial-septal nucleus is suppressed, potentially causing hippocampal tonic inhibition and disabling the memory recall.

Elisa Galliano, Department of Physiology, Development and Neuroscience

Neuronal plasticity: beyond the usual suspects

Alex Clarke, Department of Psychology

The dynamics of semantic knowledge within the anterior temporal lobes

Clea Warburton, University of Bristol

Interleaving brain wide neural circuits for recognition memory

Successful judgement of the prior occurrence of a stimulus may be achieved by remembrance of a stimulus and its associated information, such as the location in which the stimulus was previously

encountered. We have shown previously that object-in-place associative recognition memory in rodents depends on a brain wide neural network in which the hippocampus (HPC) and medial prefrontal cortex (mPFC) are key regions. Both the HPC and mPFC have bidirectional connections with the nucleus reuniens of the thalamus (NRe). Here I present data from in my lab in which we have utilise optogenetic and pharmacogenetic techniques to dissociate the neural pathways between the NRe, HPC and PFC that mediate object-in-place recognition memory and for object temporal order judgements. These experiments reveal the roles of different NRe-HPC and NRe-mPFC pathways during encoding and retrieval and highlight the importance of the NRe as a crucial node within a recognition memory network.

Mona El-Sayed Hervig, Department of Psychology

Dissociable roles of rat medial and lateral orbitofrontal cortex in visual reversal learning

Much evidence suggests that reversal learning is mediated by cortico-striatal circuitries with the orbitofrontal cortex (OFC) playing a prominent role. The OFC is a functionally heterogeneous region, but potential differential roles of lateral (lOFC) and medial (mOFC) portions in visual reversal learning have yet to be determined. We investigated the effects of pharmacological inactivation of mOFC and lOFC on a deterministic serial visual reversal learning task for rats. For reference, we also targeted other areas previously implicated in reversal learning: the prelimbic (PrL) and infralimbic (IL) prefrontal cortex, and basolateral amygdala (BLA). Inactivating mOFC and lOFC produced opposite effects; lOFC impairing, and mOFC improving, reversal performance - only in the perseverative phase. Additionally, mOFC inactivation enhanced negative feedback sensitivity, while lOFC inactivation generally diminished feedback sensitivity. mOFC and lOFC inactivation also produced different effects on novel visual discrimination learning; lOFC inactivation paradoxically improving learning, and mOFC inactivation having no effect. We also observed dissociable roles of the OFC and the IL/PrL. Whereas the OFC inactivation affected only perseveration, IL and PrL inactivation improved learning overall. BLA inactivation improved the late phase of reversal learning. These results support opponent roles of the rodent mOFC and lOFC in deterministic visual reversal learning.

Gido van de Ven, Department of Engineering

Hippocampal Offline Reactivation Consolidates Recently Formed Cell Assembly Patterns during Sharp Wave-Ripples

The ability to reinstate neuronal assemblies representing mnemonic information is thought to require their consolidation through offline reactivation during sleep/rest. To test this, we detected cell assembly patterns formed by repeated neuronal co-activations in the mouse hippocampus during exploration of spatial environments. We found that the reinstatement of assembly patterns representing a novel, but not a familiar, environment correlated with their offline reactivation and was impaired by closed-loop optogenetic disruption of sharp wave-ripple oscillations. Moreover, we discovered that reactivation was only required for the reinstatement of assembly patterns whose expression was gradually strengthened during encoding of a novel place. The context-dependent reinstatement of assembly patterns whose expression did not gain in strength beyond the first few minutes of spatial encoding was not dependent on reactivation. This demonstrates that the

hippocampus can hold concurrent representations of space that markedly differ in their encoding dynamics and their dependence on offline reactivation for consolidation.

Carolin Sievers, Department of Psychology

Encoding variability: When pattern reactivation does not benefit context memory

A growing body of evidence suggests that neural pattern reactivation supports successful memory formation across multiple study episodes. Previous studies investigating the beneficial effects of repeated encoding typically presented the same stimuli repeatedly under the same encoding task instructions. In contrast, repeating stimuli in different contexts is associated with superior item memory, but poorer memory for contextual features varying across repetitions. In the present functional magnetic-resonance imaging (fMRI) study, we predicted dissociable mechanisms to underlie the successful formation of context memory when the context in which stimuli are repeated is either held constant or varies at each stimulus presentation. Twenty participants studied names of famous people four times, either in the same task repeatedly, or in four different encoding tasks. This was followed by a surprise recognition memory test, including a source judgement about the encoding task. Behaviourally, different task encoding compared to same task encoding was associated with fewer correct context memory judgements but also better item memory, as reflected in fewer misses. Searchlight representational similarity analysis revealed fMRI pattern reactivation in the posterior cingulate cortex to be higher for correct compared to incorrect source memory judgements in the same task condition, with the opposite pattern being observed in the different task condition. It was concluded that higher levels of pattern reactivation in the posterior cingulate cortex index generalisation across context information, which in turn may improve item memory performance during encoding variability but at the cost of contextual features.

Alex Quent, MRC CBU

Using immersive reality to examine the U-shaped relationship between schema and memory performance

The literature on schema and memory suggests that schema-congruency and schema-incongruency can benefit memory performance. A recent study (Greve et al, in press) confirmed this, by finding that memory was as a U-shaped function of congruency, with best memory for highly congruent (expected) or highly incongruent (unexpected) events. However, this paradigm used simple, experimentally-acquired rules, which may not generalise to the richer and well-established schemas, such as what objects to expect in a kitchen. To test for this generalisation, we ran a series of immersive virtual reality experiments, in which participants explored a virtual kitchen containing various objects at different locations with respect to the kitchen furniture. The expectancy of finding each object at that location varied parametrically based collected ratings. As predicted (see https://osf.io/4sw2t/), we replicated the U-shaped function of object-location memory (recognition and recall) as a function of the expectancy each object's location. Furthermore, there was preliminary evidence that the two extremes of this continuum were supported by different types of memory (Remember responses for unexpected and Know responses for expected locations). The results are interpreted in terms of a neuroscientific model called SLIMM (schema-linked inter-actions between medial prefrontal and medial temporal regions; van Kesteren et al, 2012).

Abstracts - Posters

Giulia Barsuola, MRC CBU

A novel autobiographical think/no-think paradigm to elicit and control the involuntary recall of autobiographical intrusive negative memories: behavioural evidence

Introduction: The flow of human thoughts is frequently plagued by unwanted cognitive activity, which has the unfortunate power to interfere with task performance, planning, social behaviour, and many other aspects of our lives, playing also a major role in psychopathology. Drawing on Benoit's Imagine/No-Imagine study based on personally relevant future fears, we developed the Autobiographical Think/No-Think paradigm, a modified version of Anderson's Think/No-Think task based on autobiographically grounded word pairs to study the intrusions of recurrent upsetting memories. This represents the first attempt to use intrusion ratings in an Autobiographical Think/No-Think study, enabling us to elicit the recall of autobiographical intrusive involuntary memories in a controlled way.

Materials & Methods: 40 participants were tested for this behavioural study. Unlike most studies, no standardised materials were used. Participants were instructed to generate a list of twenty-two upsetting intruding personal events happened in the past three years and to select two key words before completing the pre-TNT phase, the TNT phase, and the post-TNT phase.

Results & Conclusions: We predicted that memories would frequently intrude into awareness involuntarily initially, but that with repeated attempts to stop retrieval, intrusion frequency would decline. Our one-way ANOVA analysis confirmed that intrusions declined significantly from the first block to the fourth. These preliminary results indicate that participants gained increasing control over the intrusions of unwanted memories. Post experimental questionnaires, phenomenological perspectives on intrusions, and Skin Conductance measurements will shortly be added to this study, providing novel and insightful views on this topic.

Panyuan Guo, Department of Psychology

Memory development in middle childhood

Laura Marsh, MRC CBU

Positivity bias in past and future episodic thinking: relationship with anxiety, depression and retrieval induced forgetting

Positivity biases in autobiographical memory and in episodic future thinking are considered important in mental wellbeing, and are reduced in both anxiety and depression. It has been proposed that the inhibitory processes underlying retrieval induced forgetting (RIF) may contribute these biases, via forgetting of negative material.

In this study, we measured individual differences in RIF, and examined how this related to positivity biases in past and future thinking. We also examined whether this relationship was influenced by anxiety and depression levels, and ruminative tendencies.

Reduced positivity in past and future thinking was associated with greater levels of anxiety, depression and rumination, and reduced ability to generate specific episodes. In general, greater levels of RIF significantly predicted more positive memory valence. However, for participants with high depression scores, greater levels of RIF were associated with more negative memory biases.

These results indicate that RIF plays a role in healthy positivity biases, but that this relationship may depend on an existing positivity bias. We suggest that the habitual retrieval positive material can lead to RIF of associated negative items, but, in the context of repetitive negative recall in depression, the opposite may occur; positive alternatives are weakened or forgotten.

Subbulakshmi Sankarasubramanian, MRC CBU

Seeking the supramodal inhibitory control network in the brain: the role of the right DLPFC and the basal ganglia in memory and motor control.

Memory inhibition and motor inhibition can be seen as fundamentally similar processes involving the stopping of prepotent responses. Various studies have hinted at a supramodal inhibitory control network in the brain which is engaged in the suppression of both unwanted memories and actions. A recent meta-analysis study showed that there are indeed overlapping cortical and sub-cortical regions which get activated in both memory and motor control tasks (Guo et al, 2018). In this study, we chose to investigate the role of the potential key players in this control network namely the right dorsolateral prefrontal cortex (DLPFC) and the basal ganglia.

33 healthy young adults were recruited for the study, and they performed two sessions inside the 3T scanner- an inhibitory motor task and a version of the Think/No Think memory inhibition task.

The univariate group level analysis revealed that the conjunction of regions of activation seen in both the right DLPFC and the basal ganglia for the two inhibitory tasks closely overlap with the regions previously identified in the meta-analysis. Further analysis (DCM) would help investigate if this network can then be artificially 'entrained' by non-invasive brain stimulation to see if memory and motor control can be enhanced especially in people having difficulties in controlling unwanted memories. The possibility of aiding better cognitive memory control training though motor control training, can also be investigated.

Joanna Szypula, Department of Psychology

Memory of a recent meal can regulate consumption: the role of memory ability, depth of recall and mode of recall

Previous literature suggests that recalling a recent meal, relative to a less recent one, can reduce subsequent consumption (i.e. the 'meal-recall' effect). This study attempted to replicate this effect, by assessing participants' biscuit consumption (N=77) during a bogus taste test in two separate sessions, before which they had either recalled a meal they had on the same day, or a meal they had on a previous day. The central aim of the study was to explore whether factors that might affect the quality of a meal-memory, particularly individual differences in memory ability and depth of memory interview, would influence the relationship between recalling a recent meal and subsequent consumption. To this end, only participants with a low or high memory ability were recruited for the study, and were allocated to either an unguided or a guided-recall condition. In the

unguided-recall condition, participants were asked to recall what they ate, whereas in the guided condition they were prompted for further details regarding their meal. In order to assess the robustness of the meal-recall effect, the effect of the mode of recall was also assessed, by asking the participants to recall their meal either out-loud through an interview with the experimenter or by writing their recollection down on the computer. Contrary to the initial hypotheses, it was found that only the written-recall group demonstrated the meal-recall effect, whereas the verbal-recall group did not. Moreover, this was specific to the written-recall, unguided group. The written-recall, guided group's snacking seemed to increase after recalling a meal from the same day, relative to recalling a meal from the previous day. Memory ability did not influence the magnitude of the meal-recall effect. It was also observed that in the verbal-recall group, total biscuit consumption was higher for the unguided group, than for the guided group. No significant differences in total intake between unguided and guided groups were observed in the written-recall group. The results of this study provide preliminary evidence that the meal-recall effect could potentially be used as a weight management intervention, but also highlight that the effect might be prone to interference from some contextual factors.

Jiaqi Zou, Department of Psychology

Modelling anxiety in rats: investigating rodent ultrasonic vocalisations and corresponding brain activation

In a fear conditioning tasks, a sub-population of rats have been noted to produce 22-kHz ultrasonic vocalisations (USVs) across a number of studies. Recently, 22kHz USVs were proposed as a valid behavioural measure of anxiety. The hypothesis of this study is that rats who emit 22kHz USVs in a Pavlovian conditioned-fear paradigm are hypervigilant relative to non-vocalising counterparts. As such, this research intends to develop and refine an animal model of hypervigilance using USVs and explore the neuroanatomical underpinnings of this response. Rats were trained in a cued fear-conditioning procedure, in which a tone (CS) predicted an unavoidable footshock (US). USVs and freezing were measured across a conditioning phase and a subsequent test phase. The CS was modified at test to reduce its detectability and salience, in order to screen for hypervigilance. Further investigation into the association between ultrasonic calling and freezing was conducted by dividing rats into groups of vocalisers and non-vocalisers and analysing the effect of vocalisation separately for the original tone group and modified tone group. In addition, a traditional test of 'anxiety', the elevated plus maze (EPM) was used. The relationship between individual scores in the EPM and other variables were correlated using Pearson's correlation coefficient. Immunohistochemistry was performed to establish which brain regions were activated, by the expression of freezing and/or vocalisation. The results suggest that the nature of the anxiety experienced during a fear-conditioning procedure is qualitatively different to that elicited by the elevated plus maze. Moreover, rats that vocalised froze significantly more during the test of fear learning despite having acquired conditioning to a similar level as non-vocalisers, and as such represent a population that susceptible to exaggerated fear/anxiety responding.