Cambridge Memory Meeting

Tuesday, 13 May 2014, 9.30 am - 5:00 pm

Lecture Theatre, MRC Cognition and Brain Sciences Unit, 15 Chaucer Road

Website: http://www.mrc-cbu.cam.ac.uk/cambridge-memory-meeting-2014/

Contact: camm2014@mrc-cbu.cam.ac.uk

Welcome!

Welcome to the annual Cambridge Memory Meeting. The aim of this Cambridge-wide meeting is to encourage more interaction between the many local groups working on the psychology/ neuroscience of memory in its many forms, both human and non-human.

The idea is for a friendly, informal meeting in which students, postdocs and program leaders can present their research in a supportive environment, helping us all find out about related work taking place on our doorsteps, and highlighting areas for future collaboration.

Directions

The Cognition and Brain Sciences Unit is located on Chaucer Road, just off Trumpington Road. Talks shall take place in the Main Lecture Theatre with posters presented in the West Wing Seminar Room; there will be signage to direct you. Please note that parking is extremely limited in the surrounding area; for this reason we strongly recommend that attendees plan on arriving via train, bike or bus. Should special circumstances apply, please contact the conference organizers at the address provided on the front page.

Schedule

9:30 AM	**Arrival and Morning Coffee**
10:00 AM	**Talk Session 1**
10:00 - 10:20 AM	Dennis Chan, Clinical Neurosciences *Diagnostic differentiation of mild cognitive impairment due to Alzheimer's disease using a hippocampus-dependent test of spatial memory*
10:20 - 10:40 AM	Cristina Blanco, MRC CBU *Classification of Alzheimer Disease stages using structural neuroimaging*
10:40 - 11:00 AM	Michael Hornberger, Clinical Neurosciences *How specific are episodic memory deficits to Alzheimer's disease?*
11:00 AM	*Break*
11:20 - 11:40 AM	Sian Beilock, University of Chicago *At the intersection of working memory and emotion: The case of the high-stakes test*
11:40 - 12:00 PM	Rik Henson, MRC CBU *Effects of ageing on recollection, familiarity and priming: evidence from the CamCAN project*
12:00 -12:20 PM	Karen Campbell, CamCAN *The hyper-binding hypothesis: Age differences in attentional control and the implications for associative memory*
12:20 PM	**Poster session during sandwich lunch** Rachel Goodwin, Alexandra Trelle, Elisa Cooper, Ella James, Sujeong Yang, Andrea Greve, Chihun Kim, Keshani Jayaweera

2:00 PM	**Talk Session 2**
2:00 - 2:20 PM	Brianne Kent, Department of Psychology *The hippocampus and spatial pattern separation*
2:20 - 2:40 PM	Martha Hvoslef-Eide, Department of Psychology *Prefrontal adrenergic manipulations influence spatial working memory in rats*
2:40 - 3:00 PM	Emma Cahill, Department of Psychology *Investigation of novel molecular targets for memory intervention therapy*
3:00 - 3:20 PM	Barbara Wilson, Oliver Zangwill Centre *The past, present and future of a paging system to reduce everyday memory problems*
3:20 PM	*Break*
3:40 - 4:00 PM	Ana Catarino, MRC CBU *Memory control deficits in post-traumatic stress disorder*
4:00 - 4:20 PM	Yasemin Yazar, Department of Psychology *A role for angular gyrus in the subjective experience of remembering*
4:20 - 4:40 PM	Charan Ranganath, UC Davis *States of curiosity modulate learning of neutral information via the mesolimbic dopaminergic circuit*
4:40 PM	**Closing Remarks and Pub Social**

Talk Abstracts

1. Dennis Chan, Clinical Neurosciences

Diagnostic differentiation of mild cognitive impairment due to Alzheimer's disease using a hippocampus-dependent test of spatial memory

The hippocampus is one of the earliest brain regions to exhibit neurodegeneration in Alzheimer's disease (AD) and as such tests of hippocampal function have the potential to detect AD in its earliest stages. Based on the theory that the hippocampus is critically involved in allocentric spatial memory, this study applied a short test of spatial memory, the 4 Mountains Test (4MT), to determine whether test performance a) can differentiate MCI patients with and without CSF biomarker evidence of underlying AD b) can distinguish patients with mild cognitive impairment (MCI) and mild AD dementia in different cultural settings. Healthy controls (HC), patients with MCI and mild AD dementia were recruited from study sites in UK and Italy. Study numbers were: HC (UK 20, Italy 10), MCI (UK 21, Italy 14), AD (UK 11, Italy 9). Nineteen UK MCI patients were grouped into CSF biomarker-positive (n=10) and biomarker-negative (n=9) subgroups. Place memory performance was impaired in both UK and Italy MCI and AD patients. Test performance additionally differentiated between MCI biomarker-positive and biomarker-negative subgroups ($p = 0.001$). A 4MT score of <8/15 was associated with 100% sensitivity and 93% specificity for detection of early AD (MCI CSF+ve and mild AD dementia) in the UK population, and with 100% sensitivity and 70% specificity for detection of MCI and AD in the Italy sample. 4MT performance correlated with hippocampal volume and cortical thickness of the precuneus. These findings demonstrate the potential of spatial memory testing for detecting early AD and of the 4MT as a cross-cultural diagnostic tool suitable for widespread use across different clinical settings.

2. Cristina Blanco, MRC CBU

Classification of Alzheimer Disease stages using structural neuroimaging

Alzheimer Disease (AD) is the most common form of neurodegenerative disease, characterized by progressive cognitive decline with an early and prominent impairment of episodic memory. Cerebral atrophy occurs long before the clinical manifestation of

AD and the identification of these biological changes is critical to improve diagnostic accuracy and treatment. Therefore, several magnetic resonance imaging (MRI) analysis methods have been proposed to automatically discriminate different stages of AD and predict cognitive decline related to the disease. Nonetheless, evidences of the structural changes that might predict future memory and cognitive decline in AD vary widely depending on the MRI analysis methods and classification technique applied. In this study, we analysed T1-weighted MRI scans of 66 participants divided into four groups by baseline diagnosis as probable Alzheimer (pAD), mild cognitive impairment (MCI), worried-well (WW) and older controls (OC). Our main aims were to: (1) Evaluate the specificity and sensitivity of volume-based analyses of global, subcortical and cortical features, in their ability to predict cognitive decline in pAD and (2) Identify critical brain regions for the classification of pAD and its prodromal stages. Our results show that volume based MRI analyses can classify different AD stages based on anatomical data acquired at a phase when clinical diagnosis might be uncertain. At initial stages of the

3. Michael Hornberger, Clinical Neurosciences

How specific are episodic memory deficits to Alzheimer's disease?

Episodic memory deficits are seen as a hallmark feature of Alzheimer's disease (AD) pathology. Not surprisingly, there is increasing interest in measuring episodic memory deficits and its neural correlates as early as possible in AD and its prodromal syndromes due to the advent of novel disease modifying therapies. I will present data suggesting that episodic memory deficits may be not as specific to AD as currently suggested. Instead other neurodegenerative pathologies can present with similar episodic memory and associated neuroimaging deficits. More importantly, I will proposed novel memory and cognitive measures which might have greater AD specificity and will allow earlier diagnosis and disease tracking in AD in the future.

4. Sian Beilock, University of Chicago

At the Intersection of Working Memory and Emotion: The Case of the High-Stakes Test

For many people, the desire to perform their best in academics is high. Consequences for poor performance, especially in examinations, include poor evaluations by mentors, teachers, and peers; lost scholarships; and relinquished educational opportunities. But, why do poor performances occur in those very situations where students are set on

doing their best? What cognitive and neural processes drive less-than-optimal outcomes when the pressure is high? And, can we use knowledge about how cognitive control is altered under stress to help everyone show what they know on important tests? In this talk, I will discuss behavioural and brain imaging work examining how students' knowledge and general cognitive abilities (e.g., working memory capacity) interacts with emotional factors (e.g., a fear of test taking) to impact performance in academic arenas such as math. These findings are used to motivate simple test-taking interventions aimed at alleviating the negative impact of high-stakes situations on academic performance.

5. Rik Henson, MRC CBU

Effects of ageing on recollection, familiarity and priming: evidence from the CamCAN project

Memory problems are among the most common complaints as we grow older. These problems relate mainly to difficulties encoding new, lasting memories (rather than retrieving older memories). Such 'anterograde, long-term memory' is believed to reflect multiple processes however, supported by distinct neural networks, which may have differential life-span trajectories. Furthermore, though memory for emotional material is generally better than for neutral material, the relative advantage of positive-versus negatively-valenced material is believed to change with age ('positivity-bias'). As part of the Cam-CAN project (www.cam-can.com), we report preliminary results from a memory experiment run on over 100 population-representative individuals approximately equally distributed from 18 to 88 years of age. We found that 'recollection' - the ability to recall the background picture with which an object was previously paired – was dramatically impaired by age, even when partialling-out Cattell-derived estimates of IQ, suggesting that the memory problem does not simply reflect general intellectual decline with age. Perceptual 'priming' on the other hand – the advantage in identifying a degraded image of an object previously seen – showed no evidence of an age effect. This "spared" form of memory occurred when using the same metric as recollection, and when priming was clearly above chance for all ages. Finally, though recollection was better for negative than positive pictures, and for positive than neutral pictures, for all ages, there was only a trend for a relative sparing of memory for positive versus negative material. These results are consistent with different brain networks supporting these different types of memory, possibly with differential potential for reorganisation or compensation with age; issues that are currently being explored with concurrent structural and functional MRI data on the same individuals.

6. Karen Campbell, CamCAN

The hyper-binding hypothesis: Age differences in attentional control and the implications for associative memory

A prominent theory of cognitive aging suggests that older adults are less able to form new associations and this leads to poorer performance on a variety of learning and memory tasks. In this talk, I will discuss a series of findings that make the unique suggestion that age differences in associative memory may be due, at least in part, to interference from excessive binding. Older adults, with their lessened attentional control, inadvertently form associations between co-occurring targets and distracters, as well as across successive events in time. These results suggest an age-related hyper-binding phenomenon, whereby older adults obligatorily encode seemingly extraneous co-occurrences in the environment, which may later interfere with or, in certain circumstances, benefit older adults performance on subsequent tasks.

7. Brianne Kent, Department of Psychology

The hippocampus and spatial pattern separation

Pattern separation is the computational process thought to underlie the ability to separate memories for similar events into discrete non-overlapping representations. Spontaneous Location Recognition (SLR) is a behavioural task designed to assess spatial pattern separation in rats. Our lab has shown that performance on SLR is dentate gyrus (DG)-dependent and sensitive to manipulations of plasticity mechanisms. Using SLR, we conducted a series of experiments to evaluate the role of brain-derived neurotrophic factor (BDNF) and immature neurons for spatial pattern separation. Using intracranial infusions, we identified BDNF as critical for encoding/consolidation of pattern-separated memories and performance on SLR (Bekinschtein et al., 2013). We then used a lentiviral approach to inhibit neurogenesis in adult male rats by inhibiting Wnt signaling, a principal regulator of adult hippocampal neurogenesis (Lie et al., 2005). Rats with inhibited neurogenesis were impaired on the SLR task, but only when objects were placed in similar locations. Infusing BDNF into the DG improved performance on SLR in the control group, but not in the LV-dnWnt rats with inhibited neurogenesis, suggesting that consolidation of pattern-separated memories requires the action of BDNF on immature neurons. We then evaluated the effects of increasing neurogenesis, by elevating acyl-ghrelin levels in rats. Ghrelin is an orexigenic peptide known primarily

for its growth hormone releasing properties, but also affects synaptic plasticity and hippocampal neurogenesis. Treating rats with acyl-ghrelin (14 days, i.p. 10ug/kg) enhanced both adult hippocampal neurogenesis and performance on SLR when tested 8-10 days after the end of treatment.

8. Martha Hvoslef-Eide, Department of Psychology

Prefrontal adrenergic manipulations influence spatial working memory in rats

Prefrontal adrenergic receptors have been extensively linked to spatial working memory performance. Specifically, agonists of the alpha1 and alpha2 adrenergic receptors have been shown in aged (naturally catecholamine depleted) rats to cause impairments and enhancements of spatial working memory performance respectively. It is unclear, however, whether this finding extends to young rats with a different baseline level of adrenergic firing. The current study sought to establish whether spatial working memory could be enhanced in young rats through alpha1 and alpha2 agonists microinfused into the medial prefrontal cortex. The touchscreen continuous Trial-Unique Non-matching to Location (cTUNL) task was used to optimise the translational value of the study. Infusions of the alpha1 agonist phenylephrine significantly improved performance scores, whilst no effect on performance was observed following infusions of the alpha2 agonist guanfacine. The study suggests that the alpha1 receptor, rather than the alpha2 receptor, plays a role in agonist-induced cognitive enhancements when administered to young, healthy rats.

9. Emma Cahill, Department of Psychology

Investigation of novel molecular targets for memory intervention therapy

Memories are not permanently stable once consolidated; rather, when retrieval is induced by exposure to a reminder cue, the active memory is rendered labile by a destabilisation process. Drug addiction and post-traumatic stress disorder are thought to involve maladaptive persistent memories. A novel therapeutic strategy is to disrupt the memory, when in the active state, with the use of amnestic agents targeting specific neurochemical processes. Both drug and fear reminders engage the dopamine system, but whereas some molecular substrates involved in the retrieval and destabilisation of fear memory have been characterised, drug memories have yet to be investigated. Herein, we propose a combination of behavioural and molecular analysis to further our

understanding of how to achieve diminution of intrusive and maladaptive memories, by identifying molecular mechanisms of retrieval and destabilisation of memories.

10. Barbara Wilson, Oliver Zangwill Centre

The past, present and future of a paging system to reduce everyday memory problems

Neuropage is a paging system designed to assist people with memory and/or planning problems so that they can be more independent in carrying out everyday tasks (Hersch & Treadgold 1999). It was developed by a neuropsychologist working together with the father of a young man who had sustained a traumatic brain injury (TBI) .We started evaluating NeuroPage in 1994 and a pilot study was published in 1997. Two single case studies showing how the pager could reduce costs for health and social services appeared in 1998 and 1999. A randomised control trial demonstrating the effectiveness of Neuropage was published in 2001. As a result of this RCT, the local health authority set up a clinical service providing Neuropage to people throughout the United Kingdom. We showed the pager was effective for survivors of TBI (2005), stroke (2008), encephalitis (2007) and for children (2009). One study (2003) looked at the characteristics of people using the clinical service and the type of messages received. The clinical service is still running and a ten year follow up study to determine how the latest users of the service differed from the original users appeared in 2011. Since 2007, people could choose to have their reminders sent via mobile phone or by pager (17/40 users chose a mobile phone). There was no difference in age between the telephone users and the pager users, but those using a pager were less likely to have sustained a TBI and were more likely to be longer post insult. We have recently looked at those people who have used the service for many years. We analysed the characteristics of 11 long term (LT) users and compared them to previous cohorts. The mean length of time for service use was 1.06 years (first cohort) and 3.4 years (second cohort). The eleven LT users, 7 of whom were male, used the service for a mean of 9.45 years (range 5-13 years). There were no significant differences in age, or time between insult and use of the service. More LT users were female. Fewer of the LT users had sustained a traumatic brain injury and, of course, there was a difference in the length of time the service was used. For all users, reminders about medication, food and orientation were the most frequent messages sent. LT users were more likely to require messages concerned with finances and less likely to require messages about taking rest. Clinical details about the LT users are sparse, the Neuropage service is focussed on providing a solution for the functional consequences of memory impairment. Future clinical and research work in collaboration with CAMM colleagues could include

gathering anatomical & physiological data to help us understand better processes underlying these lasting memory impairments, and potentially, how they change over time. This presentation concludes with a discussion of how the service might develop in the future.

11. Ana Catarino, MRC CBU

Memory control deficits in post-traumatic stress disorder

Previous research in healthy volunteers has shown that people are able to voluntarily suppress unwanted memories, a process supported by increased neural activation of right dorsolateral prefrontal cortex. This project extends previous research by investigating voluntary memory suppression of aversive images. It employs a Think/No-Think paradigm where pictures of neutral objects are paired with emotionally negative scenes. Results of the first experiment, in healthy volunteers, show that people are able to suppress memories of aversive images. Furthermore, results show that the suppress effect is larger for people with higher self-perceived thought control abilities. The second experiment recruited individuals with post-traumatic stress disorder (PTSD), a psychiatric condition that develops after exposure to a severe traumatic event and is characterized by symptoms such as intrusive memories and flashbacks. Results show that people with PTSD are less able to suppress memories of aversive images, when compared to a control group of trauma-exposed individuals.

12. Yasemin Yazar, Department of Psychology

A role for angular gyrus in the subjective experience of remembering

Neuroimaging studies of recollection demonstrate consistent left lateral parietal activation, particularly around angular gyrus (AnG). This is surprising because patients with parietal lesions are not amnesic, with parietal lobe lesion studies traditionally focusing on problems with visuospatial attention and visually-guided action. However, recent evidence indicates that such patients may show impairments in subjective aspects of memory as demonstrated, for example, by reduced confidence in their recollections and reduced vividness and amount of detail recalled. As patient studies have limited anatomic specificity, we here used continuous theta-burst stimulation (cTBS) to focally induce temporary disruption in AnG in a source memory recollection task. Following AnG stimulation, we found selectively reduced subjective confidence in participants accurate recollections, thus establishing a causal link between AnG and the

subjective experience of recollection. Next, we investigated what processes might underlie subjective recollection, proposing that AnG might mediate the integration of multimodal memory features into a conscious representation. Disrupting AnG with cTBS selectively reduced source accuracy when integrating memory features from different modalities compared to within-modality integration. This suggests that AnG may indeed support processes that integrate memory features from different cortical areas into conscious representations enabling the subjective experience of remembering.

13. Charan Ranganath, UC Davis

States of curiosity modulate learning of neutral information via the mesolimbic dopaminergic circuit

People find it easier to learn about topics that interest them, but little is known about the psychological or neural mechanisms by which intrinsic motivational states affect learning. We demonstrate that curiosity – intrinsic motivation that drives learning in daily life – enhances learning of both intrinsically motivating material and neutral material. A state of high curiosity that preceded the presentation of interesting information was associated with enhanced activity in key regions of the dopaminergic circuit (i.e. the dopaminergic midbrain and the nucleus accumbens). Crucially, we observed that curiosity leads to enhanced learning of not only interesting information, but also of temporally contiguous neutral material. Such learning benefits were related to anticipatory brain activity in the dopaminergic circuit and the hippocampus. These findings highlight the importance of initiating intrinsic motivation ahead of learning in order to create more effective learning experiences.

Poster Abstracts

P1. Rachel Goodwin, Oliver Zangwill Centre

Evaluation of NeuroText for people with multiple sclerosis

Background and aims: Memory problems are reported in 40-60% of people with multiple sclerosis (MS) (Rao et al., 1993), they can affect independence in activities of daily living and may limit their ability to benefit from rehabilitation. Previous research in the field of memory rehabilitation for people with MS is inconclusive and of poor quality (das Nair et al., 2012). There is good evidence to support the use of NeuroPage, a memory aid service in people with acquired brain injury (Wilson et al., 2001). The aim of this study is to evaluate the effectiveness of the NeuroPage service for people with MS who have memory problems. Method: A multicenter, single-blind randomised controlled crossover design will be used. Treatment efficacy will be determined by comparing treatment (memory texts) to an active control (social texts) on a range of measures, including subjective memory reports and mood. Sample size was calculated at 66 participants, accounting for drop-outs. The intervention has been named NeuroText for clarity, in light of the increasing use of texts on phones, and the decreasing use of pagers. The active control has been developed to ensure that it is the specific content of the memory messages that serve as a memory aid, rather than the act of simply receiving a message working as a prompt. Group (treat first versus control first) by time (baseline, post-treatment) analyses of covariance will be conducted, with baseline performance as a covariate. Results will be available in 2015.

P2. Alexandra Trelle, Department of Psychology

Identifying age-invariant and age-limited mechanisms for enhanced memory performance: A closer look at the self-reference effect in younger and older adults

Cognitive ageing is characterized by a marked decline in episodic memory. However, research suggests that older adults can gain significant mnemonic benefits from the provision of orienting tasks that facilitate meaningful elaboration of study material. Moreover, it has been suggested that orienting tasks that reference the self might provide a greater memory enhancement for older adults, relative to general semantic processing. To test this, we measured recall and recognition of concrete nouns that

were processed in relation to the self or to general semantic knowledge. We additionally crossed this self-semantic manipulation with the amount of elaborative processing, as determined by whether the orienting task required only a yes/no decision or a more open-ended description. We found that all participants exhibited a substantial enhancement in memory performance following the use of orienting tasks that increased the amount of elaborative processing, irrespective of whether the item was related to the self or general knowledge. Furthermore, younger, but not older, adults showed an additional boost to subsequent memory by associating a unique autobiographical (i.e, self-referential) context with each study item, though this benefit was only evident during free recall. These findings point to limitations in the efficacy of memory strategies among older adults, perhaps due to age-related reductions in attentional resources and cognitive control. However, they also highlight the substantial enhancement of both recall and recognition memory that results from using prior knowledge to elaborate on, and presumably better differentiate, study events; an advantage that is maintained across the lifespan. Contrary to previous suggestions, this benefit does not appear to be greater when referencing self-relevant information, but holds true for any well-developed knowledge structure.

P3. Elisa Cooper, MRC CBU

What can you do despite hippocampal damage? Preliminary findings from the Cambridge Hippocampal Panel

The importance of the hippocampus in declarative memory is well-known, but there have been recent claims that it is also important for certain types of short-term memory, priming and even perception. In order to investigate such issues, we have compiled a panel of 8 patients with acquired amnesia to date (aged 39-69) whose MRIs show hippocampal damage resulting from hypoxia or encephalitis. For 7 of these individuals, we acquired further MRI images, including 1mm isotropic T1-weighted MPRAGE images on a 3T scanner. We found reduced anterior hippocampal and/or amygdala grey-matter volume relative to a large number of matched controls, but no evidence of significant volume loss elsewhere. A neuropsychological test battery showed mild (in 1 individual) to severe (in the other 7 individuals) impairments in delayed verbal and non-verbal recall. On tests of recognition memory for words or faces, 3 revealed no deficit, 1 showed mild impairment and 4 had moderate-to-severe impairment. All but one individual showed normal performance on the majority of measures of executive function (e.g., verbal fluency), short-term memory (e.g., digit span) and mood (e.g., HADS). A number of more focused laboratory experiments have also been performed;

to date no evidence has been found of impairments in visual perception or stimulus-response learning in priming, nor any benefit of fast-mapping. The Cambridge Hippocampal Panel offers the opportunity for group-based tests of what is spared, as well as impaired, following hippocampal damage.

P4. Ella James, MRC CBU

Tetris game-play reduces intrusive memories of trauma via reconsolidation blockade mechanisms

One's memory of a traumatic event becomes consolidated within hours. These memories can then flash back repeatedly into the mind's eye, causing distress. We show that the reconsolidation process can be blocked using a simple cognitive task, thereby reducing intrusive memories. Our hypothesis is that reactivating visual trauma memory (to initiate reconsolidation) and then engaging in a visuospatial cognitive task will reduce intrusive memory frequency, via competition for visual memory resources during reconsolidation. We find that, 24 hours after experimental trauma memory reactivation followed by Tetris computer game-play reduced the frequency of intrusive memories over the next week. Furthermore, this effect depended upon reconsolidation mechanisms, as both memory reactivation and playing Tetris were required to reduce subsequent intrusions. These data suggest that non-invasive procedures may be used to prevent the recurrence of intrusive memories of trauma.

P5. Sujeong Yang, John van Geest Centre for Brain Repair

Enhancement of plasticity by perineuronal net removal restores memory in a transgenic mouse model of tauopathy

Microtubule-associated protein tau forms intacellular aggregates in many neurodegenerative diseases known as tauopathies. Alzheimers disease (AD) is the most prevalent tauopathy and cause of dementia. Reduction of perineuronal nets (PNNs) has shown to significantly enhance object recognition (OR) memory. As recognition memory is one of the prime deficits in dementias, we asked whether PNN attenuation can restore OR memory in human tauopathy models. The effects of PNN reduction were investigated in two models with tau hyperphosphorylation, aggregation and neurodegeneration: a transgenic mouse model in which the mutant P301S tau is expressed in neurons (Tg P301S), and a model in which an adeno-associated virus expressing P301S tau (AAV-P301S) was injected in perirhinal cortex (PRh), a region

critical for OR memory. Both models show profound loss of OR memory despite only 15% neuronal loss in the Tg P301S and 26% in AAV-P301S-injected mice. Recordings from PRh slices showed a diminution in synaptic transmission following temporal stimulation at 3 months of age in Tg P301S mice. PNNs were then degraded by injecting chondroitinase ABC (ChABC) into PRh and animals were tested for OR memory 1 week later. Although ChABC digestion did not affect tau hyperphosphorylation or aggregation in the PRh, both OR memory and synaptic transmission were restored to normal levels in the two animal models of tauopathy. The findings indicate that increase in plasticity by manipulation of PNNs offers novel therapeutic approaches to treat memory loss in neurodegenerative disorders.

P6. Andrea Greve, MRC CBU

Predicting learning when learned predictions are violated

Predicting future events from prior experiences is essential for adaptive behaviour and decision making. The recently proposed Predictive Interactive Multiple Memory Systems (PIMMS) framework suggests that unexpected events (violations of prior predictions) play a key role in memory encoding. Here we present a series of behavioural investigations that examine whether prediction errors (PE) do indeed enhance learning of novel scene-face associations. All experiments contained a training phase during which unrelated scenes and faces were repeatedly presented for a varying number of times to induce a range of predictions for particular face-scene pairings: High PE (four or six scene-face repetitions), Baseline (with one scene-face presentation) or Low PE (six changing scene-face presentations). Participants performed a speeded gender judgement task. After training trials, there was a critical study trial, in which a trained scene was presented with a completely new face (i.e, any predictions were violated). In the test phase, memory for the critical faces was assessed with a 3 AFC test, in which the 3 choices for a given scene were all from the study trials (i.e, not training trials). Our data show that such novel associative learning was indeed modulated by the history of trained expectations, with significantly better memory for items encoded under High PE than under Low PE. A second experiment confirmed superior memory in the High PE condition relative to Baseline. Furthermore, the degree of speeding in gender judgement RTs across scene-face training repetitions (a measure of acquired prediction strength) was correlated across participants with subsequent memory success; confirming better learning/memory of novel items that violate stronger predictions. Our neural network simulations demonstrated that memory performance for PE driven learning should rank from: high PE > Baseline > Low PE conditions, in line with our findings, whereas

standard Hebbian learning predicts: Baseline > High PE > Low PE. Thus, our pattern of empirical results favoured models of prediction-error learning over standard Hebbian learning. Although we consider potential alternative explanations of the results, our data are generally in agreement with key assumptions proposed by the PIMMS framework.

P7. Chihun Kim, MRC BCNI

New automated touchscreen location and object-location tasks for the mouse: effects of lesions of the hippocampus

Tasks such as Trial-unique Delayed Nonmatching-to-Location (TUNL) and Paired-Associates Learning (dPAL) have been developed to test spatial and object learning in automated touchscreen operant chambers. To date, these tasks have been primarily used in rats (Talpos et al, 2009, Psychopharmacology, 205, 157-168; Talpos et al, 2010, Neurobiology of Learning and Memory, 94, 341-352). In this study, we adapted and optimised these tasks for use in mice and confirmed the hippocampal dependency of these paradigms with bilateral excitotoxic lesions. In addition, a new version of PAL (cpPAL) is presented, in which discrimination problems are presented in two separated areas in the touchscreen chamber. For TUNL, 32 male C57Bl/6 mice were trained on the task. Based on the final performance level, the mice were assigned to a lesion or a sham group. The lesion group received bilateral dorsal hippocampal injections of NMDA before being tested for post-surgical performance. For dPAL and cpPAL, the subjects were 24 male C57Bl/6 mice; half of the mice received NMDA lesions of the hippocampus and half were shams. The number of screen locations used for TUNL was reduced from 14 locations for rats to five locations for mice. dPAL was used without major modification, but for cpPAL a divider was inserted to divide the testing chambers into two spatial contexts. When (re) acquiring the tasks after surgery, we found that in all three tasks both hippocampal lesioned and sham animals were able to learn across sessions ($P<0.01$), but only for the TUNL task was there a significant difference between lesion and shams groups ($P<0.001$). When the performance of the last three sessions of (re) acquisition was averaged, we found that hippocampal lesions significantly impaired performance ($P<0.01$) in TUNL and also dPAL, but not in cpPAL. However the number of errors committed per session was significantly higher in the lesion group in all three tasks ($P<0.05$), confirming a role for the dorsal hippocampus in these tasks. In summary, we have successfully developed and optimised touchscreen tasks to examine spatial and object-location learning and memory in the mouse. As in the rat version of the tasks, intact hippocampal function is required for normal task performance.

P8. Hirosha (Keshani) Jayaweera, University of Sydney

Neuropsychological and neuroimaging correlates of concomitant of late life depression and mild cognitive impairment

Background: Mild Cognitive Impairment (MCI) is common in late-life depression (LLD) and predicts conversion to dementia. Hippocampal atrophy also occurs in LLD, and is associated with memory loss. However, few studies to date have concurrently examined these inter-relationships in individuals with remitted or mild depressive symptoms.

Method: 152 older participants (mean age = 64.0) meeting criteria for lifetime Major Depression but with only remitted or mild depressive symptoms were recruited. Standardised psychiatric and neuropsychological assessments were conducted and MCI diagnoses were consensus rated. Magnetic resonance imaging was conducted and hippocampal volumes were determined.

Results: MCI was diagnosed in 75.7% of the patients, and non-amnestic profiles were most prominent (54.6%). The left hippocampus was significantly smaller in MCI compared to those without MCI ($t=2.09$, $p=0.04$). For the MCI subgroup, smaller left hippocampal volumes were associated with poorer verbal memory ($r=0.31$, $p=0.014$). Smaller bilateral hippocampal volumes were associated with later ages of depression onset for those with MCI (left: $r=-0.39$, $p=0.002$; right: $r=-0.32$, $p=0.014$) but not for those without ($p>0.05$). Compared to the non-amnestic subtype, amnestic MCI was associated with greater hippocampal atrophy, advancing age, poorer global cognition and greater medical comorbidity ($p<0.05$).

Conclusions: MCI is common in LLD, even when symptoms are remitted or mild. MCI diagnosis is associated with hippocampal atrophy, particularly for those with predominant memory deficits and may be suggestive of neurodegenerative disease trajectory. Longitudinal studies of hippocampal atrophy in LLD and MCI is warranted from a clinical and research perspective.