ARC CENTRE OF EXCELLENCE IN COGNITION AND ITS DISORDERS

CCD Memory Program

Inaugural Symposium

THURSDAY 31st OCTOBER

Neuroscience Research Australia

This Symposium provides an opportunity to hear eminent researchers, postdoctoral fellows and PhD students present their work on various aspects of memory. The day showcases research using animal models, neuroimaging and clinical approaches to examine theories of memory and its disorders, and avenues for remediation.

Keynote speakers: **Prof Rick Richardson**, ***UNSW;*** **A/Prof Elise van den Hoven**, ***UTS;*** and **A/Prof Sarah Wilson, *UniMelb***.

The CCD Memory Program Symposium is a full day event held at Neuroscience Research Australia, Barker St, Randwick, Sydney. Attendance is free of charge, however registration is requested for catering purposes.

RSVP. Please register with Sarah Homewood for catering purposes.
Email: s.homewood@neura.edu.au or phone: 9399 1134 by **30th Sept.**

We look forward to seeing you there.

The CCD Memory Program Symposium Organising Committee

A/Prof Olivier Piguet
Dr Sunny Lah
Dr Laurie Miller
Dr Fiona Kumfor

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FRONTIER
Frontotemporal Dementia Research Group

CCD Memory Program Symposium

Abstracts

Session 1: Disorders of Memory

Keynote Presentation: Effects of Early Life Stress on Memory Development
Prof Rick Richardson
School of Psychology, the University of New South Wales

Research first reported nearly 50 years ago demonstrated that infant, or young animals (including humans) exhibit profoundly faster rates of forgetting (i.e., infantile amnesia) than do adults. Such findings suggest that adverse experiences should have less of an impact on the young than on adults (i.e., young animals should be especially resilient because they rapidly forget these adverse experiences). However, epidemiological evidence has clearly documented that adverse early-life experiences are particularly important for the development of later psychopathologies (such as anxiety disorders). This apparent paradox might be resolved if exposure to chronic stress early in life affects the maturation of the memory system, leading to long-lasting fear memories in these infants. In several recent studies we have found exactly this pattern; that is, infant rats exposed to early-life stress (e.g., repeated bouts of maternal separation) exhibit adult-like fear retention. Further, we have demonstrated that these effects can be mimicked by exposing the mother to the stress hormone corticosterone in their drinking water (in lieu of the separation procedure). These findings suggest that early-life exposure to stress and stress hormones may act as a general signal that can alter the developmental trajectory of emotional memory systems and potentially place animals at greater risk for the development of anxiety.

Accelerated Long-Term Forgetting in Children with Epilepsy
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Objective: Research on accelerated long-term forgetting (ALTF) has largely focussed on adults with temporal lobe epilepsy (TLE), with relatively little attention given to children. This study aimed to determine the extent of ALTF in children with generalised or partial epilepsy.
Participants and Methods: The study included 43 children with epilepsy [idiopathic generalised epilepsy (IGE, n=20), and temporal lobe epilepsy (TLE, n=23)] and healthy control subjects (NC, n=58), matched on sex distribution, age and SES, but not IQ (IGE and TLE < NC). Participants completed a battery of neuropsychological tests, including learning a list of words to criterion. They were asked to (i) recall the words after short (2 and 30 min) and long (7 days) delays, and (ii) recognize the words after the long delay.
Results: A two-way analysis of covariance (group x time, using IQ as a covariate) found a significant interaction ($p < .05$), a main effect of delay ($p < .001$) but not group. Planned contrasts revealed no between-group differences in the reduction of the proportion of words recalled from the 2-min to the 30-min delay. However, compared to the control group, the IGE and TLE participants displayed a significant drop in the proportion of words recalled at the 7-day delay, relative to the 30-min delay ($p < .01$). Both the IGE ($p < .01$) and TLE ($p < .001$) groups made significantly more recognition errors compared to the control group following a 7-day delay.

Conclusions: Surprisingly, ALTF was evident in children who had generalised seizures, in addition to those with partial seizures. This suggests that generalised seizures may also disrupt long-term consolidation.

"As time goes by" – The Neural Correlates of Recent and Remote Autobiographical Memory Retrieval

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Remembering personally relevant events from the past is a complex process subtended by a distributed network of regions in the brain. The neural substrates of autobiographical memory retrieval (ABM) are those harbouring significant pathology in frontotemporal dementia (FTD), a progressive neurodegenerative disorder. Here, we explored the neural correlates of recent and remote autobiographical memory retrieval in 11 behavioural variant FTD (bvFTD), 10 semantic dementia (SD), and 15 Alzheimer's disease patients (AD) and 20 matched Controls. Whereas bvFTD patients showed equivalent deficits for recent and remote retrieval, dissociations were evident in AD and SD. AD patients showed disproportionate deficits for recent relative to remote memory, whereas SD patients showed the converse profile. Voxel-based morphometry analyses of structural brain scans revealed important commonalities and differences in the brain regions necessary for recent and remote ABM. Remote ABM retrieval correlated with predominantly left lateralised structures including the hippocampus, with extensive lateral temporal and frontopolar involvement. Recent ABM retrieval was associated with the integrity of the right hippocampus, bilateral frontal poles, and left posterior cingulate cortex. This study reveals novel insights into the neural substrates of recent and remote ABM retrieval. Regions specialised for semantic processing appear particularly important for older memories, whereas midline cortical regions are differentially implicated for retrieval of recent events. Our findings corroborate the view that the hippocampus plays a permanent role in the retrieval of episodic memories across the lifespan, with lateralisation effects evident contingent on the recency of the remembered event.

Session 2: Neural correlates of memory

Exploring prefrontal cortex contributions to memory deficits in bvFTD

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Behavioural variant frontotemporal dementia (bvFTD) is the second leading cause of early-onset dementia, after Alzheimer's disease (AD). Patients with bvFTD present with a range of symptoms, notably decline in social behaviour and personal conduct, ritualized activity, loss of empathy, emotional blunting and executive dysfunction. While episodic memory deficits are a well-established early feature of AD, the diagnostic criteria for bvFTD mandate a predominantly dysexecutive cognitive profile, with relative sparing of episodic memory and visuospatial skills. Although an amnestic presentation still remains an exclusion criterion for diagnosis of bvFTD, recent evidence has questioned the integrity of episodic memory in bvFTD, where recall performance is impaired to the same extent as in AD. While these deficits appear to be mediated by divergent patterns of brain atrophy, there is evidence to suggest that certain prefrontal regions are implicated across both patient groups. In this study we sought to further elucidate the prefrontal contributions to memory impairment in bvFTD and AD, by examining the relationship between performance on

measures of episodic memory recall and neuropsychological measures typically tapping into either dorsolateral or ventromedial prefrontal cortex functions. Voxel-based morphometry analysis was used to investigate the neural substrates of these relationships. Our results suggest that episodic memory deficits in bvFTD and AD are underpinned by divergent prefrontal mechanisms. However, we argue that these differences are not adequately captured by existing neuropsychological measures.

Functional Involvement of the Papez Circuit in Long-Term Contextual Memory

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Intact episodic memory has long been associated with hippocampal integrity and activity. Nevertheless, the hippocampus is only one relay station of the Papez circuit, with the functional contributions of the other relay stations virtually unknown. We investigated the contributions of Papez circuit regions to immediate and remote (4-week) contextual memory retrieval. Functional neuroimaging results showed that all Papez circuit regions were activated for recent and remote memories but that they varied in their contribution as a function of the post-encoding delay. In particular, hippocampus and mammillary bodies revealed dissociation for recent vs. remote memory, with the hippocampus showing higher activation for recent memories and the mammillary bodies for remote memories. These findings suggest a shift of retrieval activation to extra-hippocampal structures with consolidation of contextual information.

Material Specificity and Alpha-Band Lateralisation: Effects of Verbalisation and Perceptual versus Mnemonic Demands

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Neuropsychological measures of verbal memory appear to characterise the impact of left temporal lobe damage, but nonverbal measures do not reflect right temporal lobe damage reliably, possibly due to their ability to be verbalised. Cognitive neuroscience models of the complex relationship between visual perception, memory and right hemisphere activity in the healthy brain could also usefully inform clinical test development for lateralised functions. We measured hemispheric bias (HB) using event-related alpha EEG (8-13 Hz) during encoding and recognition memory tasks. The effects of material-specific memory (verbal versus spatial) on perceptually equalised tasks (hybrid verbal-spatial stimuli) were compared to effects of material-specific perceptual processing (verbal versus spatial versus hybrid verbal-spatial) on mnemonically equalised tasks. The use of verbal labels to aid memory was measured with a surprise post-test rating task. Against predictions, all conditions exhibited right HB, with no difference due to material effects of memory or perception. The right HB was particularly strong during encoding and in upper alpha (10-13 Hz) compared to lower alpha (8-10 Hz), consistent with previous research. The pattern of correlations suggested independent spatial and verbal right HB effects during encoding but not recognition. Greater use of verbal labels was a very strong predictor of verbal learning and was correlated with non-HB alpha changes. These findings suggest that right HB effects are associated with novel visual memory of both verbal and nonverbal materials regardless of visual form, verbalisability, and hold promise for the development of novel spatial and verbal clinical measures to assess right hemisphere impairment.

Could Memory Impairment in Dementia Reflect High-Level Perceptual Impairment?

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Episodic memory begins with perception. How the neural correlates of perception and memory overlap is unclear. The medial temporal lobes (MTL) sit at the apex of a hierarchical stream of information flow and receive input from different perceptual processing streams. The MTL is crucial for episodic memory processing but an increasing number of reports implicate the MTL in perceptual processing. It is unclear however, how MTL substructures contribute to the perception and memory of different kinds of stimuli. We conducted two functional magnetic resonance imaging experiments to investigate MTL contributions to perception and recognition of verbal and non-verbal stimuli. For verbal stimuli, we observed that the left perirhinal cortex and left hippocampus were recruited during perception and recognition respectively. For non-verbal stimuli, the right perirhinal cortex was asymmetrically recruited during both perception and recognition. In a third experiment, we utilised voxel based morphometry to identify regions of brain atrophy associated with poor performance on these tasks in patients with Alzheimer's disease and semantic dementia. Atrophy in the left perirhinal cortex and hippocampus was associated with poor performance on the verbal memory task and atrophy in the right perirhinal cortex was associated with poor performance on the non-verbal task. Our results suggest that 1) structures of the MTL are recruited during both perception and recognition memory, 2) there is a functional asymmetry with left and right MTL structures recruited for verbal and non-verbal stimuli respectively and 3) atrophy in the MTL regions implicated in our functional imaging results is associated with impaired task performance in patients with dementia.

Session 3: Memory rehabilitation

Keynote Presentation: Materialising Memories: Combining Psychology and Design

A/Prof Elise van den Hoven
School of Design, the University of Technology Sydney

Personal remembering can be heavily influenced by external factors, such as people, locations and things. These things can be physical, digital or a combination of both, such as digital photographs displayed on a physical screen. Together these media and media carriers can act as memory cues, which in turn can be purposefully created for the support of remembering experiences. The aim of this presentation is to show the potential of this new multidisciplinary research area, combining design, psychology and technology, and which I refer to as Materialising Memories. I will illustrate my design research through the presentation of design case studies.


Photo credit: Joris Zaalberg

Self-Cuing and Cross-Cuing Processes in Memory

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Memory cues can come from a range of sources – including our own thoughts and feelings, our interactions with others, and our environment. Memory cues may have important consequences for memory retrieval processes and qualities. The links between the characteristics of cues, the source of cues, the process of memory retrieval, and the qualities and phenomenology of what is retrieved are important across a range of research domains, both theoretical and more applied. In cognitive models of autobiographical memory, the nature of memory cues influence the process by which memories are retrieved, such that personally relevant cues result in high rates of rapid, effortless, direct retrieval. But we know little about how these different retrieval processes might influence the qualities of what is remembered. In collaborative recall research, cross-cuing between remembering partners has been a hypothesised process which has been difficult to identify in the lab when testing groups of strangers remembering non-personal stimuli. But we know little about possible cross-cuing in groups where partners can provide each other with more idiosyncratic, personally-relevant cues. In memory and ageing research, rich cues are found to overcome memory problems associated with cognitive decline. But we know little about the potential characteristics and sources of such rich cues in the day-to-day life of older adults. In this talk, I aim to sketch the links between these disparate literatures. I describe recent research, studies in progress, and planned future research which seek to more clearly identify the role of self-cuing and cross-cuing processes in memory.

Considering the evidence that virtual spatial navigation can help to rehabilitate memory: Where do we go from here?

Cara Wong[1] & Laurie Miller[1]
[1]Neuropsychology Unit, Royal Prince Alfred Hospital

The seminal studies on London taxi drivers (Maguire et al, 2000; 2006) suggest that spatial navigational learning is directly correlated with structural change in the hippocampus. In addition, a few interventions that have emphasised the use of topographical memory indicate improvements in hippocampal functioning (Valenzuela et al., 2003; Caglio et al., 2012). This research, along with the emerging use of virtual reality (VR) technology has vast implications for memory rehabilitation. VR and video games have been increasingly used in cognitive assessment and rehabilitation, and have advantages including enhanced motivation, a safe environment for practice, control over stimulus delivery and high ecological validity. Unfortunately, there is little research directly investigating whether spatial navigation training (virtual or otherwise) can change underlying neural substrates and improve cognitive abilities in patients with memory disorders. This presentation will summarise the existing evidence and the issues involved. In addition it will present a proposal for a pilot study that uses practice with virtual navigation to change hippocampal functioning and thereby rehabilitate memory more generally in neurological patients.

Session 4: Memory processes

Keynote Speaker: Music memory: Current Concepts and Research Challenges
A/Prof Sarah Wilson
School of Psychological Sciences, the University of Melbourne

Music has been dubbed the 'food of neuroscience' as it provides a powerful stimulus for broadly activating the brain via multiple networks underpinning music listening, responding and performance. This means that musical memories provide a rich tapestry of information about human memory processes and their instantiation in the brain. In particular, they provide insights into how we relive auditory and kinesthetic sensory experiences through imagery, as well as recall and execute complex motor sequences (procedural memories). The recognition and identification of music offers insights into the neurocognitive basis of episodic and semantic memories, including how the music and language systems interact when we recall our favorite songs. Combined with rare musical skills such as 'perfect pitch', this provides a salient paradigm to study 'material specificity' in memory. Music also has well-established effects on the emotional and reward networks of the brain, providing a unique paradigm for investigating the recall of musical emotions and how these might shape our autobiographical memories and social identity. Moreover, through the motivating effects of reward, music provides a powerful stimulus to promote new learning and memories, and may 'prime' the brain for neuroplasticity. Drawing on this rich tapestry, this talk will review our knowledge of the many and varied facets of music memory and its associated brain networks, providing insights into our current understanding of human memory functioning. Current research challenges in the music memory field will also be considered, including how these might advance our understanding of human memory into the future.

Remembering Together Makes us True Believers: The Origins of Shared Memories and Shared Beliefs
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Memory research has primarily focused on how individuals form and maintain memories across time. However, less is known about how groups of people working together can create shared memories of the past. In this talk, I will discuss my research which demonstrates how the very act of collaboration induces people to reorganize their knowledge of the past, particularly the associations they have among pieces of knowledge related to the memory. As a result, the former discussants not only possess shared memories, but also similar knowledge associations within those memories. The presence of these shared knowledge associations has important implications for understanding how groups of people may come to form shared beliefs about the world. During belief formation, people tend to rely on knowledge retrieved from memory when evaluating aspects of the world as true, particularly by considering the knowledge associations they possess that are relevant to the belief. I will discuss preliminary research which examines whether sharing similar knowledge associations as a result of collaboration leads people to form similar beliefs.