

**ABSTRACTS FOR ISBN 2005**  
**ST KITTS**  
(In alphabetical order by presenting author)

**Adolescent decision-making: much more than an oxymoron**

*Abigail Baird*

Psychological and Brain Sciences, Dartmouth College

The ability to think counterfactually about the consequence of one's actions represents one of the hallmarks of the development of complex reasoning skills. This talk will review both behavioral and neuroscientific data exploring the role that counterfactual thinking plays in reasoning about the consequences of one's actions, especially as it pertains to the developing mind of the adolescent. Based on the assimilation of both behavioral and neuroscientific data, a brain-based model will be described that provides a theoretical framework for understanding the emergence of counterfactual reasoning ability in the developing mind.

**Cognitive Control: This time, again, with feeling**

*Marie Banich*

University of Colorado

In this talk, I will present brain imaging data supporting a model of how top-down cognitive control is implemented by both lateral and medial prefrontal regions of the brain. I will discuss how this circuitry varies depending on 1) the nature of the information on which such control is to be exerted, and 2) emotional and personality characteristics of the individual. In particular, I will discuss how engagement of brain regions involved in cognitive control varies for emotional as compared to non-emotional information. I will also discuss how both the manner and degree to which cognitive control is implemented varies as a result of personality characteristics and/or psychiatric diagnosis. Finally, I will discuss some recent behavioral studies that speak to the nature of the cognitive mechanisms involved in the repression or amplification of information, and potential differences in these processes for emotional as compared to non-emotional information.

**Frontal cortex, strategy, and memory in rhesus monkeys**

*Mark G. Baxter*

Department of Experimental Psychology, Oxford University

I will show some (very) preliminary data from the beginning stages of a research program whose ultimate goal is to examine the neurochemical substrates of strategy implementation and memory in the frontal cortex. Most would agree that the frontal cortex is critical for higher-order aspects of cognition and behavior, although there are disputes about localization of function within the frontal cortex, and data on the neurochemical underpinnings of frontal function are particularly limited. Our monkeys are currently training on two tasks, one of strategy implementation and one of episodic (scene) memory. Postoperative testing will also include a test of goal-directed behavior. Effects of dorsolateral and orbital prefrontal lesions on these tasks

will be compared. I am interested in people's input on what "strategies" and "rules" are, as well as thoughts on localization of function within prefrontal cortex, and the comparability of prefrontal function in humans and nonhuman primates.

### **Role of the pulvinar in higher visual functions.**

*Christian Casanova\**, *Martin Villeneuve*, *Maurice Ptito*  
Ecole d'optométrie, Université de Montréal, Canada

Thalamic nuclei have long been considered as passive relay stations for sensory signals en route to the cerebral cortex, where higher level processing occurs. In recent years, it has been proposed that thalamic nuclei may actively participate in the processing of specific information in conjunction with cortical areas. In support of this hypothesis, we recently discovered that neurons in the main extrageniculate visual nucleus, the pulvinar, exhibit higher-order visual properties that were, until now, only associated with higher-order cortical areas. Pulvinar neurons can indeed code the veridical direction of a moving plaid pattern, indicating that these cells can integrate ambiguous signals into a coherent percept. Subsequently, using positron emission tomography (PET), we have investigated the possibility that the human pulvinar is also involved in plaid-defined higher-order motion integration. Plaid patterns were presented to normal observers in two conditions (coherent vs. transparent) created by varying the relative spatial frequency of the two gratings comprising the plaid. Regions of interest analysis revealed a significant activation of the pulvinar in the coherent condition supporting the notion that the human pulvinar nucleus is involved in higher-order motion processing. Plaid pattern activation was also observed in the medial temporal gyrus (area MT/V5), a motion area with strong anatomical connections to the pulvinar. These last data provide the first direct evidence that the human pulvinar is involved in complex motion integration, as previously shown in animal models, and further support the existence of cortico-thalamo-cortical computational networks involved in higher-order visual processing.

\* Guest

### **Active fixation control and the superior colliculus.**

*Daniel Guitton\**  
Montreal Neurological Institute, McGill university, Montreal, Canada.

By definition, fixation occurs when the visual axis is immobile in space. In this condition, gaze can be either "parked" idly or accompanied by an active or attentive fixation process. We have shown that there is a specialized zone in the rostral pole of the superior colliculus whose cells, called "fixation neurons" (SCFNs) discharge tonically when a cat fixates a food target or a monkey fixates a light spot for which it is penalized for breaking fixation. The tonic fixation activity of SCFNs ceases, or "pauses", during eye saccades made by head-fixed monkeys or eye + head gaze saccades made by head-free cats and monkeys. We have recorded from SCFNs in experiments where monkeys make gaze shifts in the dark to previously seen targets and gaze trajectories are perturbed. In this paradigm, the time to reach the target is prolonged and there is an equivalent increase in SCFN pause duration such that their fixation discharge is only reinstated when gaze in the dark reaches the remembered

target location. The reason for this discharge pattern has been clarified by recent electrophysiological studies in the laboratory of Y Shinoda (Tokyo) that have shown that SCFNs project to brainstem neurons that inhibit saccades. Thus, when a monkey fixates attentively, tonic SCFN activity prevents intrusive saccades.

\* Guest

### **A specific role for the human hippocampus in relational retrieval: Effects of encoding and reinstatement of study episode**

*K. S. Giovanello, D. Schnyer, M. Verfaellie*

Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Department of Psychology, Harvard University

Previous research has demonstrated that the hippocampus plays a critical role in the successful retrieval of newly formed associations (Giovanello et al., 2004). In the current study, we used event-related fMRI to examine: (1) whether hippocampal activation is due to exact reinstatement of previously learned associations or to flexible retrieval of learned associations and (2) whether hippocampal activation associated with successful relational retrieval is contingent upon relational encoding. At study, participants viewed word pairs and were instructed to encode the items of each pair non-relationally (i.e., covertly generate a sentence for each of the two words) or relationally (i.e., covertly generate a sentence that relates the two words). At test, participants saw intact pairs (IP), reversed pairs (RevP), and recombined pairs (RecP), and were asked to indicate whether the two words were previously seen together regardless of the order of presentation. The results revealed that: (1) the hippocampus is involved in successful retrieval of relational information even in the absence of exact reinstatement of the study episode (RevP>RecP), but that additional hippocampal activation is observed during exact reinstatement (IP>RevP); and (2) that the hippocampus is involved in relational retrieval, regardless of whether stimuli are encoded relationally or not. However, when flexible retrieval is required, hippocampal activation is greater for information encoded relationally than for information encoded non-relationally. These results are consistent with the notion that the hippocampus is involved in retrieval of relational information independent of whether initial information is reinstated. Further, such hippocampal activation occurs even in the absence of intentional relational encoding.

### **Item versus associative recognition memory in patients with developmental amnesia**

*Anna-Lynne R. Adlam<sup>1,2</sup>; Antonio Incisa della Rocchetta<sup>3</sup>; Michelle de Haan<sup>1</sup>; Faraneh Vargha-Khadem<sup>1</sup>; Mortimer Mishkin<sup>4</sup>;*

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Previous studies of developmental amnesia (DA), have reported an impairment on multi-trial tasks of object-place and voice-face associative recognition but not one

trial single item or intramodal associative recognition tasks (Vargha-Khadem et al., 1997). These findings suggest that the hippocampus supports cross-modal and object-place associative recognition, but not single item or intramodal associative recognition, consistent with recent models of medial temporal lobe (MTL) function (e.g., Mishkin et al., 1997; Aggleton and Brown, 1999). The first experiment reported in this paper aimed to replicate these findings in a larger group of patients with DA than previously reported (n = 12), relative to a group of age-, sex- and IQ-matched controls. The second experiment aimed to further examine the role of the hippocampus in object-place memory using a newly devised task of one trial object-place recognition memory. Whilst the results of Experiment 1 largely replicated the previous findings, deficits were also found on the multi-trial intramodal associative recognition task involving unfamiliar faces and place-only recognition. Furthermore, in Experiment 2, the patients with DA were impaired at recognising the location of objects (both object-place and place-only recognition memory) when presented with single arrays for study and subsequent recognition after a two-minute delay. These findings suggest that the hippocampus is required for some types of associative recognition when the memory load is high, but also for object-place associative recognition independent of size of memory load.

### **What perimenopause and estrogen do to emotional memory**

*Jeri Janowsky*

Oregon Health & Science University

Estrogen receptors are found in memory regions of the brain such as the amygdala and medial temporal lobe. Using two different models, we have investigated the role of estradiol loss and replacement on emotional memory in women. In one study of we compared the perception of emotions and memory for emotional stimuli in women with high and low perimenopausal symptoms. In the second model we compared emotional memory in postmenopausal women with and without estrogen replacement. There were no group differences in perception of affective stimuli. However, memory for negative information was lower in those with symptoms or without estrogen replacement. This may be due to estrogen's actions on the amygdala's modulation of memory. This work will be discussed in relation to studies of the brain basis of emotional memory and emotional memory in aging.

### **Is laterality of cerebral function subserved by structural asymmetry?**

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Functional laterality in the human brain has been well established since the time of Broca and Dax, but the extent to which this relates to structural asymmetry is unclear. Brain torque (rightward frontal asymmetry and leftward occipital asymmetry) has been reported to be greater in males than females and in right than left handed individuals (Bear et al, 1986), and leftward planum temporale asymmetry has been

supposed to relate to leftward ‘dominance’ for language (Geschwind and Galaburda, 1968). This supposition has been widely referenced as evidence of a structural substrate for language laterality but has not been directly tested. Here we have automatically quantified brain torque and planum temporale asymmetry in a group of 33 healthy controls (16 male) and used fMRI to assess language and motor laterality. No significant correlations were found between fMRI and behavioural laterality indices, or between language and motor laterality. Average activation was significantly more lateralised when using right than left hand for finger tapping ( $F=5.2$ ,  $p<0.001$ ). A significant correlation between fMRI laterality for right finger tapping and brain torque ( $r=0.48$ ,  $p=0.016$ ) was observed. Planum temporale asymmetry correlated with fMRI language laterality in males ( $r=0.51$ ,  $p=0.043$ ) but not females. We provide some evidence to support a relationship between functional laterality and structural asymmetry, but the correlations are not strong and, in the case of language, depend on sex. These results will be discussed in the wider context of structure-function relationships, equivalence between measures of laterality and importance of taking sex into account.

### **Recollective experience altered by stimulation of the hypothalamus in man: A case study with some provocative findings.**

*Mary Pat McAndrews*

University Health Network, University of Toronto

NF, a 50 year-old man with a long term history of obesity, participated in an experimental therapeutic trial of hypothalamic deep brain stimulation for weight loss. Monopolar stimulation was used with the following parameters: 2.8V bilaterally, 130 Hz, and 60 microseconds. Although there was only a modest effect of stimulation on weight loss, there were some unanticipated effects on recollective experience in this man.

Acute stimulation during electrode positioning evoked a reported experience of *déjà vu*. During subsequent programming (5 mos post-operative), he continued to experience these sensations acutely when electrodes were tested at higher voltage (~5 V), although these were not reported at the lower amplitude used for long-term continuous bilateral stimulation. Neuropsychological testing was conducted at baseline and after three weeks of stimulation. Notable improvements were seen on some memory tests (CVLT, spatial working memory) with scores changing from low average to high average, but there was no change in other measures. After four months of stimulation, we conducted a double-blind study over the course of a few weeks in which NF performed an associative recognition task found to be sensitive to medial temporal functioning. He was tested under three conditions across three test sessions: no stimulation, typical monopolar stimulation, and bipolar stimulation. On each occasion he studied 80 word pairs and made recognition decisions as to whether each test pair was (1) same pair, recombined pair, new words and (2) associated with recollective experience [*remember* decision] or not [*know* decision]. Recognition performance improved slightly under bipolar stimulation but – of most interest – he showed a striking difference in the recollective aspect (proportion of items evoking a *remember* response under typical monopolar stimulation: 27% with no stimulation, 38% bipolar, 72% monopolar). Implications of these findings for hypothalamic/medial temporal circuitry and recollection will be open for debate.

## **What does functional imaging reveal about the role of the medial temporal lobe in autobiographical memory ?**

*Mary Pat McAndrews, Donna R. Addis, Morris Moscovitch, Randy McIntosh*

Department of Psychology, University of Toronto

Results from lesion and functional imaging studies confirm that the medial temporal region (hippocampus [HC] in particular) plays a key role in autobiographical memory (AM). However, questions remain about the exact characteristics of AM or processes engendered by AM retrieval that may be the primary determinants of hippocampal engagement. Of equal importance, the connectivity between HC and other cortical regions in the AM network has been little explored. Here, we present imaging results from both univariate and multivariate (connectivity) analyses that address these questions in healthy controls and some more preliminary imaging findings from patients with temporal lobe epilepsy. Some of the key results are: (1) temporal specificity (unique versus repeated events) does not correlate with degree of hippocampal involvement or with functional connectivity in between HC and other brain regions; (2) characteristics of remembered events such as amount of detail and personal significance do modulate hippocampal activation and they also segregate different patterns of effective connectivity in the AM network; (3) there is reduced activation of HC in cases of unilateral epilepsy although the patterns are complex; (4) the left HC in particular appears to represent a “convergence zone” or hub of activation in the network whose engagement is correlated with objective performance on AM tasks.

## **Processing Deficits Associated with Neonatal Hypoxic-Ischemic Injury in Rats**

*Melissa M. McClure, Glenn Rosen R. Holly Fitch*

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Hypoxia-ischemia (or HI) refers to reduced blood oxygenation and/or a diminished amount of blood perfusing the brain, and is associated with premature birth/very low birth weight (VLBW). HI represents a common cause of injury to the perinatal brain, and a significant number of premature/VLBW infants go on to demonstrate cognitive/behavioral deficits, with particularly high incidence of disruptions in language development. Auditory processing deficits, in turn, have been suggested to play a causal role in the development of language impairments. Specifically, the inability to identify fast elements in speech is purported to exert cascading detrimental effects on phonological discrimination, processing, and identification. Using a rat model of HI coupled with a prepulse inhibition behavioral paradigm, we found rapid auditory processing deficits in rats similar to those seen in children with language impairment. Specifically, unilateral HI injury induced on P1, P7, or P10 led to deficits in rapid auditory processing, as well as impaired performance on the Morris Water Maze. In a subsequent study, unilateral P1 HI animals and bilateral P4 HI animals were also found to show impaired rapid auditory processing ability in the juvenile period, but only the bilateral subjects showed an impairment that persisted into adulthood. Anatomically, area measures of the hippocampus, cortex, ventricles, and corpus callosum were found to correlate with auditory processing ability and maze

scores in HI animals, with smaller structures and larger ventricles associated with worse performance.

### **Dissociable Prefrontal and Limbic Correlates of Affective Working Memory**

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Storage and active maintenance/executive components of "cognitive" working memory have been attributed to ventrolateral and dorsolateral regions of prefrontal cortex (PFC), respectively. Different frontal regions, namely the orbitofrontal cortices (OFC) have been implicated in "affective" working memory -- the maintenance of an emotional representation in the absence of its elicitor. Using fMRI we compared the neural correlates of two analogous delayed response tasks, one requiring emotion maintenance and the other requiring brightness maintenance. On each trial, an image appeared, followed by a retention interval, and then a second image. In the emotion task, participants judged which of the two images was of higher emotional intensity; in the brightness task they judged which image was brighter. A direct comparison of delay period activity obtained in each task revealed lateral OFC during emotion maintenance and ventrolateral PFC during brightness maintenance. Using each participant's relative intensity judgments in the emotion task, we sorted trials in which the first image was experienced as higher in intensity from trials in which the first image was experienced as lower. Limbic activity in anterior cingulate, medial prefrontal, and mediotemporal areas was associated with the maintenance of high, but not low intensity emotions, however OFC did not distinguish these conditions as it was equally active in both. Thus, OFC activation was correlated with the task requirement to maintain emotion, but not with the intensity of the emotion maintained, whereas other limbic activations depended on the emotional intensity of the stored representation. These results suggest separable roles of the OFC and other limbic areas in the active maintenance of emotion representations versus the representation of emotional intensity, respectively.

### **Anterograde and Retrograde Memory after Focal Thalamic Stroke**

*Laurie A. Miller<sup>1,2</sup>, C. Grigora Monasterio<sup>2</sup>, Antony Harding<sup>3</sup>*

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Previous research has revealed that thalamic nuclei, such as the mediodorsal thalamic nuclei (MD) and anterior thalamic nuclei (AT), and also fibers of passage such as the mammillothalamic tract (MTT), play an important role in anterograde and retrograde memory. The fact that the neural connections of the AT and the MD are distinct raises the possibility that these two regions play separable roles in human memory. One theory (Aggleton & Brown, 1999) has proposed that the AT are part of a system (consisting also of the hippocampal formation, fornix, MTT and the mammillary bodies) that is important to the *recall* of anterograde memories. In this theory, a second system consisting of the MD and the rhinal cortices of the temporal lobes is thought crucial to anterograde *recognition* memory. More recently, it has been suggested that the AT and MTT are important to both the recall and recognition of anterograde memories, whereas the MD contribute more to recall than recognition (van der Werf, Jolles, Witter & Uylings, 2003). Neither of these theories make

predictions regarding retrograde memory and the involvement of the thalamus in retrograde memory has been less well studied. It has been proposed that the thalamus may be involved in the retrieval of retrograde memories from diverse cortical networks, with the MD playing a particularly important role in this process (Markowitsch, 1995; Miller et al., 2001). In this study, we compared anterograde and retrograde, recall and recognition memory in 13 patients with focal thalamic stroke and 10 normal control subjects. Overall, the results supported the notion that within the thalamus the AT, MTT and MD are particularly important to memory, and that the ventrolateral and pulvinar nuclei are not. The results indicated that the AT and MTT are involved in the recall and recognition of anterograde memories, and also in the recall of recent retrograde memories. In contrast, the MD seems to be important in the recognition but not recall of anterograde memories, and also in the recall and recognition of retrograde memories, especially for remotely learned material. There was also evidence of lateralized deficits in anterograde memory, with memory for visual material being particularly impaired following damage to the right and verbal memory being impaired following damage to the left side of the thalamus. Studies that include larger numbers of subjects especially with specific AT and MD lesions would help to verify the pattern of findings in our studies.

### **Neural Circuits of the Medial Thalamus and Memory**

*Anna S. Mitchell*<sup>1,3</sup> and *John C. Dalrymple-Alford*<sup>2,3</sup>

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Dense amnesia occurs from localized thalamic injury or the alcoholic Korsakoff syndrome, but the neural basis of the amnesic deficits remains contentious. Initial clinical and animal research focused primarily on the mediodorsal thalamic nuclei. Recent evidence implicates either the anterior or intralaminar thalamic nuclei instead. Based on their significant neural connections, we hypothesized that these thalamic nuclei are associated with different attributes of memory. Highly localized thalamic lesions in rats to three separate medial thalamic aggregates produce dissociable memory impairments. Lesions to the anterior thalamic nuclei disrupted allocentric spatial memory supporting the proposal that these nuclei are critical within the hippocampal memory system. Lateral medial thalamic lesions (the intralaminar nuclei and adjacent lateral segments of the mediodorsal nuclei) primarily impaired memory for egocentric type responding, similar deficits are produced following dorsal striatum or dorsomedial prefrontal cortex lesions. Thirdly, only lesions to a posteromedial thalamic aggregate (the remaining mediodorsal nuclei and the intermediodorsal nucleus) impaired acquisition of a reward magnitude task, previously shown to be sensitive to lesions in the amygdala or agranular insular cortex. Correlational relationships also existed between the extent of brain injury in each of these three thalamic groups and their respective impairments in spatial memory, egocentric responding or the reward magnitude task. In addition, evidence for normal temporal order memory, which is sensitive to medial prefrontal cortex damage, was found in both the anterior and control groups, but not the lateral and posteromedial lesion groups. These new dissociations indicate that different medial thalamic nuclei contribute to distributed neural circuits that are associated with independent attributes of memory and that the variability of amnesic deficits present

in both clinical cases and animal models may be related to the extent and location of specific thalamic injury.

### **Does size matter? Quantitative and qualitative discrepancies between single-subject and normalized-group analysis approaches to fMRI**

*Bradley R. Postle and Eva Feredoes*

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A central question in the cognitive neuroscience of working memory is the nature of prefrontal cortical (PFC) contributions to working memory function. One point of contention is whether PFC contributes to the storage of information in working memory. This question hinges on empirical evidence for load sensitivity and for stimulus domain specificity of delay-period activity in PFC. Single-subject analyses typically find delay-period effects on the order of single percentage points of signal change, but no evidence for load sensitivity or domain specificity. Normalized group analyses, in contrast, typically find delay-periods effects that are an order of magnitude smaller, but that do reveal load sensitivity and domain specificity. So, does size matter?

### **Acute stress, limbic system activity, and the effects of personality differences**

Jens C Pruessner, Katarina Dedovic, Veronika Engert, Najmeh Khalili Mahani, Frances Champagne, Alain Dagher, Michael Meaney & Sonia Lupien

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There is evidence from several studies from our and other laboratories that individual differences in self-esteem modulate the acute cortisol response to stress. Recently, in a study with healthy elderly individuals, we have shown that these acute differences also seem to be linked to long-term effects. We found reduced basal cortisol regulation, with lower cortisol levels in the acrophase of the circadian rhythm, and accelerated hippocampal atrophy with aging in subjects with low self-esteem. Finally, current results from functional neuroimaging studies investigating brain activation during a psychosocial stress task suggest that these differences might originate at the level of the limbic system, where processing of stressful stimuli seems to modulate levels of activation in the hippocampus, amygdala, medial orbitofrontal cortex, and anterior cingulate cortex. These results allow speculation about the modulatory effects of personality on the perception and processing of stress in humans, and the consequences for glucocorticoid exposure and allostatic load. These results further emphasize the need to reevaluate the subjective components of variables defining a stressful situation, and their relation to personality traits.

### **Neural Implementation of Response Selection: Implications for Models of Cognitive Control**

*Eric H. Schumacher*

Georgia Institute of Technology

Response selection is a process responsible for choosing an appropriate response representation among competing alternatives given one's current bottom-up and top-down contextual biases. It is central to a wide variety of human behaviors. Despite

its ubiquity, the neural mechanisms underlying response selection remain unclear. This uncertainty stems in part to the complexity of the tasks used in previous research. Such complexity limits our ability to interpret results, and thus to understand the nature of this elementary cognitive process. To overcome this limitation, I have undertaken a series of fMRI experiments using relatively easy perceptual-motor tasks, allowing a more thorough investigation of the neural mechanisms underlying response selection. The results of these experiments demonstrate that distinct neural processors mediate response selection for different types of visual stimuli, challenging cognitive theories promoting a unitary response-selection mechanism; that practice does not affect the neural substrate of response selection, but functional reorganization occurs for other task-related processes, suggesting that changes in behavioral performance with practice are unlikely to be due to changes in response selection; and finally that response selection can be subdivided into distinct cognitive and neural sub-processes. These data highlight the utility of functional neuroimaging data in informing conceptual models of human cognition.

### **Blindness and the Frontal Eye Fields**

*Alexander A Stevens & Arun Garg*

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The neural mechanism underlying the ability to selectively attend to a particular location remains unclear and is the subject of considerable debate. A network of several areas in frontal and parietal cortex has been implicated with the frontal eye fields (FEF) thought to play a vital role. Here we show that the functions of the putative FEF in humans is are intact in under conditions where planning eye movement is presumably irrelevant: in congenitally blind subjects. Using a auditory spatial adaptation of a cued location task we found that both blind subjects and sighted controls showed highly similar FEF activity with some notable exceptions. These results seem to suggest that the human FEF, as localized and measured with fMRI, plays a role that is inconsistent with the premotor theory of saccade planning and more consistent with a supramodal role in attention.

### **Role of the anterior thalamic nuclei in a hippocampal circuit underlying conditional learning**

*Viviane Sziklas*

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There is now a large body of evidence that damage to the anterior thalamic nuclei can result in a persistent memory disturbance which impairs the ability to store or bring to recollection spatial information. First, lesions to these structures impair the ability to remember which ones of several locations have been visited within a short period of time, i.e., spatial working memory tasks. Second, such lesions impair place learning, namely, the capacity to learn to navigate to a particular location. These deficits are similar to those observed after damage to the hippocampal system. Despite the apparent similarity of the deficits following damage to the anterior thalamic nuclei and the hippocampal formation, and the close anatomical connectivity between them, evidence from my laboratory suggests that these structures contribute *differently* to memory processing on at least one class of spatial learning, conditional

associative learning, which requires the ability to form arbitrary associations between specific visual stimuli and particular places. The aim of this presentation is to examine the selectivity of deficits following damage of the anterior thalamic nuclei and to clarify their unique contribution to this fundamental capacity to learn relationships between stimuli and the spatial contexts in which they are embedded. I will review work which examines the extent to which the anterior thalamic nuclei are involved in conditional learning and discuss the generality of their role in an extended hippocampal circuit underlying spatial memory. I will argue that while different neural stations within the extended hippocampal circuit, such as the anterior nuclear group, may play a role in spatial learning, the role of this latter region in such learning may be highly selective.

### **An Integrated Analysis of the Anterior Thalamus and Connected Regions in Rats**

*Seralynne D. Vann & John P. Aggleton*

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In the past, both the anterior thalamic nuclei and the mammillary bodies have often been treated as unitary structures with single functions. The anterior thalamic nuclei, however, contain three nuclei (dorsal, medial, and ventral) while the mammillary bodies comprise two main nuclei (lateral and medial). The nuclei in both structures differ in terms of their anatomical connections and electrophysiological properties. The lateral mammillary nucleus projects only to the anterior dorsal thalamic nuclei and, in rats, both of these nuclei contain head-direction cells. The medial mammillary nucleus, however, projects to the anterior medial and anterior ventral thalamic nuclei. While these nuclei do not contain head-direction cells they do have a larger number of theta responsive cells. These two parallel routes between the mammillary bodies and anterior thalamus suggest that these two systems may support different functions. These functions, however, could be co-ordinated, thereby giving the impression of a unitary function. By using a combination of techniques it is possible to test hypothesised roles of these two systems, based on their anatomical and electrophysiological properties. The techniques used include making selective neurotoxic lesions and immediate-early gene imaging. Immediate early gene imaging has very high spatial resolution making it an ideal technique for looking at small structures, such as the anterior thalamus and mammillary bodies, as well as their subnuclei. This technique makes it possible to see the involvement of these structures in normal animals performing a spatial task. The lesion studies then complete the picture by showing how the removal of these structures, or subregions within the structures affect performance on spatial tasks. Results of these studies will be discussed and will be put into the context of the two separate systems. Finally, selective lesions and gene imaging can be combined in order to determine the effects of lesions on other brain regions. This has been done with anterior thalamic lesions (both neurotoxic and radiofrequency) and these lesions have a widespread effect on a number of limbic brain regions that are also implicated in spatial memory. The most striking effect of anterior thalamic lesions is found in the retrosplenial cortex, with an almost complete loss of Fos-stained cells in layer 2 of the retrosplenial cortex. This retrosplenial cortex hypoactivity highlights the need to take more widespread effects into account when interpreting lesion effects.

## **Brain activity during speaking with and without altered auditory feedback in developmental stutterers**

*Kate Watkins<sup>1</sup>, Steve Davis<sup>2</sup> and Pete Howell<sup>2</sup>*

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Altering auditory feedback to self-generated speech either with respect to time (delayed auditory feedback) or pitch (frequency-shifted feedback) is effective for enhancing fluency in people who stutter. We investigated the effects of these two types of altered feedback on the brain activity associated with producing and hearing one's own speech. Three groups of healthy adolescents were scanned at 3T: 5 with persistent developmental stuttering (PDS); 4 with a documented history of developmental stuttering but considered recovered on recent testing (RDS); and 9 fluently-speaking controls. Functional images were acquired after 7-s silence which followed a period where subjects read sentences aloud (96 images in total). Speech was recorded and fed back to the subjects via a real-time digitizer. Feedback was either (i) normal (ii) delayed by 200ms or (iii) frequency-shifted by half an octave upwards. Statistical maps were generated to show the brain areas active during speaking under normal feedback across the three groups. These areas included the sensorimotor and premotor cortices bilaterally, the superior temporal cortex bilaterally, the supplementary motor cortex, the anterior cingulate cortex and the cerebellum. The mean activity in these areas was calculated for each condition and each subject separately; analyses of variance examined the main effects of, and interactions, between group (PDS, RDS and controls), condition (delayed, frequency-shifted, normal auditory feedback) and hemisphere (left vs. right). Across all conditions and compared to controls, the PDS group had 1) significantly *less* activity in the sensorimotor and premotor cortices bilaterally, the supplementary motor area and the anterior cingulate cortex and 2) significantly *more* activity in the cerebellum; the RDS group were not significantly different to the controls or the PDS group. For all three groups, there was significantly more activity under delayed auditory feedback compared to frequency-shifted and normal feedback in the supplementary motor area; both delayed and frequency-shifted feedback produced more activity in the superior temporal cortex bilaterally compared to normal feedback. Finally, for all three groups and across all conditions, there was significantly more activity in the left superior temporal cortex than the right. Reading sentences out loud in the scanner resulted in activation of a network of motor and sensory areas involved in speech production and perception. The group with PDS showed underactivity of the cortical motor areas involved in speech production and, in contrast, significant overactivity of the cerebellum. Delayed feedback associated with increased activity in the supplementary motor area, which may relate to fluency. The small RDS group tended to show patterns of activity similar to controls but they did not significantly differ from either group; further subjects are required.

## **Functional and structural subdivision of the human thalamus; studies on memory**

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The thalamus plays a role in declarative memory. It remains unclear, however, to which memory processes it contributes and which are the crucial structures within the thalamus involved in memory. We performed a group analysis of cases of thalamic infarction, proven with MR imaging, using experimental and established neuropsychological tests. We performed a lesion-overlap study in standardized stereotactic space of patients sharing a certain deficit, corrected for the lesion distribution of patients without such deficits and determined the regions of interest using an atlas of the human thalamus. The ‘amnesic syndrome’, a deficit of episodic long-term memory with relative sparing of intellectual capacities and short-term memory, is associated strongly with damage to the mammillo-thalamic tract (the afferent fiber tract of the anterior nuclei). Damage to the intralaminar nuclei affects complex, but not simple, speeded processing. Combined lesions of the medial dorsal nucleus, midline nuclei and/or intralaminar nuclei accompany executive dysfunctioning.

We propose the following dissociation of functions in the thalamus, in keeping both with anatomical data derived from tract tracing studies in rats and human connectivity data obtained using Diffusion Tensor Imaging: firstly, the anterior and mediodorsal nuclei are involved in processing the contents of the stimuli for storage and recall. The anterior nuclei influence the selection of material to be stored and remembered, whereas the mediodorsal nucleus is involved in the coordination and selection of the strategies used to retrieve material. Secondly, the intralaminar and midline nuclei and specifically the lateral and ventral components, maintain a necessary state of the cortical regions involved in the ongoing memory processes. The two types of function subserved by these groups of thalamic nuclei, focussing on contents vs. state, need to work in parallel to mediate and allow memory functioning, respectively.

## **From action perception to social behavior in autism: A role for the mirror neuron system ?**

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It has been suggested that social impairments observed in individuals with autism spectrum disorder (ASD) can be partly explained by an abnormal mirror neuron system (MNS). Mirror neurons are cells in premotor area F5 that discharge when a monkey executes or sees a specific action or when it hears the corresponding action-related sound. Evidence for the presence of a MN system in humans comes in part

from studies using transcranial magnetic stimulation (TMS), where a change in the amplitude of the TMS-induced motor evoked potential during action observation has been demonstrated. Together, these data suggest that actions are understood when the representation of that action is mapped onto the observer's own motor structures. In order to determine if the neural mechanism matching action observation and execution is anomalous in individuals with ASD, TMS was applied over the primary motor cortex (M1) during observation of intransitive, meaningless finger movements. We show that overall modulation of M1 excitability during action observation is significantly lower in individuals with ASD. In addition, we find that basic motor cortex abnormalities do not underlie this impairment. These data lend experimental support to the notion of a dysfunctional MNS in ASD and suggest the involvement of mirror neurons in the adequate development of social behavior.

### **Crossmodal plasticity in congenital blindness.**

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The failure of one sensory input to grab the information present in the environment causes changes in the function of the corresponding cortical area. This area can therefore be driven by other sensory inputs through a phenomenon coined cross-modal plasticity. This cross-modal plasticity has been described in animal model such as hamsters and ferrets and also in humans. We will present here 1) anatomical and behavioural data obtained on hamsters illustrating this phenomenon; 2) behavioural and brain imaging data on human blindness using a sensory substitution device that allows subjects to use their tongue in lieu of the eyes. Our data show that 1) blind as well as blindfolded controls can learn a "visual" task using their tongue and to do so only blind recruit their visual cortex. Moreover, our TMS studies of the occipital cortex of the same subjects indicate a somatotopic remapping of the tongue onto the visual cortex, in blind subjects only. Finally, in highly proficient Braille readers, TMS of the visual cortex produces parasthesia in the fingers that also follow a clear somatotopy. These results indicate that training-induced plasticity has a central role in specifying the functional architecture of sensory cortex.