TALK SESSION I

Rob Blumenfeld

Functional connectivity during working memory maintenance and manipulation

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Studies investigating working memory (WM) have suggested that maintenance and manipulation of information are neurally separable processes. In the prefrontal cortex, ventrolateral prefrontal cortex (VLPFC) has been implicated in WM maintenance, whereas VLPFC and dorsolateral prefrontal cortex (DLPFC) have been shown to be involved in manipulation. Here, we used event-related fMRI to investigate functional connectivity of the VLPFC and DLPFC during verbal WM maintenance and manipulation. On maintenance trials, participants actively maintained sequences of three words across a twelve second delay. On manipulation trials, participants were instructed to reorder sequences of three words (based on the relative size of the referent of each word) across a twelve second delay. During maintenance, posterior regions of VLPFC and DLPFC showed enhanced connectivity with regions of posterior perisylvian cortex that have been associated with phonological rehearsal. In contrast, during WM manipulation, posterior regions of the VLPFC showed enhanced connectivity to the DLPFC, anterior regions of the VLPFC, as well as posterior parietal cortex. DLPFC exhibited heightened connectivity with anterior regions of VLPFC, posterior parietal, anterior cingulate, and retrosplenial cortex. These findings suggest that the prefrontal cortex accesses qualitatively different cortical networks involved in maintenance compared to manipulation.

Brad Buchsbaum

An fMRI study of serial position effects in a Sternberg item-recognition task

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The Sternberg item-recognition paradigm has been studied extensively over the past 40 years as a test of short-term memory. Recently, researchers have used this paradigm in neuroimaging studies in order to investigate the brain basis of the cognitive operations required to perform such a memory scanning task. One aspect of the Sternberg task that has received much attention in the behavioral literature has been the effect of the serial position of the to-be-recognized item (the "probe") on the subject's reaction time (RT). As is the case with other short-term memory tasks such as free and serial recall, U-shaped serial position curves are observed in the Sternberg task, with subjects responding fastest when the probe corresponds to the first (primacy effect) or last (recency effect) items of the memory set. In the present study, we used functional Magnetic Resonance Imaging (fMRI) and a verbal (six one-syllable nouns) Sternberg task to isolate those brain regions whose BOLD response is modulated by the serial position of the memory probe. Serial position effects were observed for auditory stimulus presentation in the inferior frontal gyrus (IFG) and supramarginal gyrus (SMG) bilaterally. In the IFG, the fMRI response decreased linearly with serial position while the reverse pattern (increased response with later serial positions) was observed in the SMG. Inverted-U shaped serial position effects were observed in the middle frontal gyrus (MFG) bilaterally, and the right anterior frontal cortex at the approximate location of Brodmann area 10. Linearly increasing effects were seen in the posterior hippocampus and the anterior cingulate gyrus.

Jesse Rissman

The effects of working memory load on top-down modulation of visual processing

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University of California, Berkeley

Recent fMRI and ERP findings have demonstrated that individuals are able to enhance activity for behaviorally relevant visual stimuli and suppress activity for irrelevant stimuli in stimulus-specific visual association areas (Gazzaley et al., 2005). Unlike typical studies of top-down modulation in which target stimuli are presented simultaneously with distractors, these enhancement and suppression effects were obtained in the context of a working memory task in which the relevant and irrelevant stimuli were presented sequentially. Thus, suppression of the irrelevant stimuli was not driven by competition for visuospatial processing resources, but rather by competition for mnemonic resources. To gain further insights into this interplay between working memory and selective attention, we conducted two complementary fMRI studies. In both studies, we sought to examine how manipulations of working memory load would influence subjects' ability to modulate activity in posterior cortical regions. In the first study, the load manipulation involved increasing both the number of relevant and irrelevant stimuli. In the low load condition, subjects were presented with two faces and two scenes, and depending on the instructions, they had to either remember the faces, remember the scenes, or passively view the stimuli. In the high load condition, three faces and three scenes were presented. In the second study, rather than increasing the number of visual stimuli, memory load was manipulated by auditorily presenting subjects with six digits to memorize at the beginning of each trial. In the high load condition, the digit sequence was random; in the low load condition, the digits occurred in an ascending sequence. After hearing the digits, subjects were presented with two faces and two scenes with the same collection of task instructions described above. In both experiments, fMRI activity levels during the image encoding period of the task in a functionally-defined scene-selective region of interest were used as a marker of top-down modulation. The results from the first study found that increasing the number of faces to be remembered led to an increase in the degree to which activity in this scene-selective region was suppressed below the passive viewing baseline. In contrast, the digit load manipulation in the second study had no effect on the level suppression in this region. Taken together, these findings suggest that one's ability to suppress the neural representation of distracting visual information is facilitated by visual, but not phonological, working memory load. This increased suppression effect could be due to a heightened incentive to inhibit irrelevant visual stimuli when faced with a demanding visual working memory task. Alternatively, the reduced processing of visual distractors in the high image load condition could be conceptualized as an increased withdrawal of attention.

David Badre

Computational modeling and fMRI support for interference in task switching

David Badre
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The ability to shift between different tasks and the representations that govern action is a fundamental requirement for flexible behavior. Despite established behavioral consequences, the sources of task switching costs remain controversial. The present study sought to test the hypothesis that task switch costs reflect proactive interference arising from retrieval of competing representations from long-term memory. In an effort to be theoretically explicit, a novel computational model of task switching was developed that derives switch costs entirely from changes in the model's "long-term" associative structure, rather than from a time-consuming reconfiguration process or transient carry-over of interference. Critically, estimates of conflict computed from the model across task switch manipulations provided quantifiable hypotheses for analyzing data from an fMRI experiment of task switching. An event-related fMRI experiment indexed neural responses while subjects switched tasks (odd/even number judgments and vowel/consonant letter judgments) under differing levels of preparedness and interference. Preparation-related decay of switching effects in left mid-VLPFC (~Brodmann area 45) was accounted for by the model's estimate of conflict among competing conceptual representations. Furthermore, this conceptual conflict pattern dissociated left mid-VLPFC from the response in inferior parietal cortex, which was characterized by the estimated change in conflict computed from a distinct response layer of the model. These data and the associated theoretical framework serve to formally link fMRI response measures with interference theories of task switching, and so provide insights into the sources of task switch costs and the processes by which these costs are overcome.

TALK SESSION II

Patrick Khader

Event-related fMRI reveals content-specific cortical activation during associative long-term memory retrieval

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In two experiments we tested whether visual stimulus material that is assumed to be processed in different cortical networks during perception (i.e., pictures of faces, manmade objects (here cups), and spatial positions) are also topographically dissociable during long-term memory recall. With an extensive overlearning procedure participants learned word-position and word-face associations in Exp. I, and word-position and word-object associations in Exp. II. Each word was combined with either one or two positions/faces/objects. The fMRI was recorded several days later during a cued recall test in which two words were presented in each trial and the participants had to decide whether these were linked to each other via a common mediator, i.e. a position or a face in Exp. I and a position or a cup in Exp. II, respectively. Depending on the number of learned associations, two, three or four associated stimuli had to be compared in a given trial. This kind of a fan-paradigm enforces retrieval from long-term memory without confounding recall with perceptual processes. A broadly distributed network of cortical areas was found to be differently activated during recall of positions, faces and manmade objects, including the parietal and precentral cortex for positions, the left prefrontal, occipito-temporal and posterior cingulate cortex for faces, and the left temporal and prefrontal cortex for cups. These activations included stimulus-specific regions along the dorsal and ventral visual pathways (i.e., the parietal cortex for positions, the occipital and fusiform gyrus for faces, and the middle temporal gyrus for cups). In a subset of the activated areas for each stimulus type the BOLD response was found to increase monotonically with the number of the to-be-re-activated associations, indicating that the activity level of stimulus-specific cell assemblies increased the more representations had to be accessed. These areas also dissociated topographically for positions, faces, and objects. The left superior parietal lobe and bilateral precentral cortex were more strongly activated for positions compared to faces and objects, whereas the left inferior prefrontal cortex was more active for objects, and slightly more active for faces. Furthermore, the posterior cingulate cortex was activated only during face retrieval. Because the activated areas also showed up as stimulus-specific in the general comparison of stimulus type, we conclude that these areas play a crucial role in storing, recalling and comparing stimulus-specific memory representations. The results clearly show that material-specific cortical networks are systematically activated during long-term memory retrieval that overlap with areas also activated by positions and objects during perceptual and working memory tasks. This is consistent with information- processing models of material-specific cortical representations, which are assumed to be established as localized cortical cell assemblies during encoding and reactivated during recall.

Alison Preston

High-resolution fMRI of stimulus-specific novelty encoding and subsequent memory responses in human medial temporal lobe

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The medial temporal lobe (MTL) is critical for declarative memory, though the functions of specific MTL subregions remain underspecified. Given known differences in anatomical connectivity and inputs to particular subregions, MTL substructures may differentially support memory encoding, depending on the content of the experience. Using high-resolution fMRI, the present experiment investigated the topographic organization of stimulus-specific encoding processes in human MTL, focusing on encoding responses related to novelty processing and subsequent memory performance. During scanning, subjects performed a novelty-encoding task on classes of stimuli (e.g., unfamiliar faces and scenes) that differed according to perceptual domain (e.g., visual-object and visuo-spatial). A post-scan recognition memory test assessed memory for stimuli presented at encoding. Analysis of novelty encoding (Novel>Repeated) and subsequent memory (Remembered>Forgotten) responses revealed differential activation along the anterior-posterior axis of MTL cortex. Parahippocampal cortex demonstrated encoding responses associated with novelty and subsequent memory during scene presentation, whereas perirhinal cortex demonstrated such responses during presentation of faces. Heterogeneous novelty-encoding responses within MTL cortex were also revealed by distributed pattern analyses examining the overlap between patterns of activation across stimulus class. Within hippocampus proper (CA1, CA3, dentate gyrus), segregation of stimulus-specific novelty and subsequent memory responses was less differentiated, with hippocampal subfields demonstrating novelty and subsequent memory responses across multiple stimulus classes. These results suggest that MTL contributions to encoding vary across experience, with certain classes of stimuli/events being differentially processed by specific MTL subregions.

Colleen Parks

Aging and noncriterial recollection in the remember-know and confidence-rating procedures

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When trying to remember a specific detail about a prior event, people frequently recollect other, often irrelevant, details. Memory of these details, dubbed "noncriterial recollection" (ncR), elevates familiarity estimates and may operate automatically and independently of "criterial" recollection (Yonelinas & Jacoby, 1996). To date, ncR has been considered unique to the process dissociation procedure, and has been found only in young adults (Toth & Parks, in press). The remember-know and confidence-rating procedures were used to address these issues in young and older adults. ncR elevated familiarity estimates in all groups, but was greater for those with optimal levels of criterial recollection (e.g., young > old). This pattern, along with receiver-operating characteristic evidence, suggests that ncR may operate more similarly to criterial recollection than to familiarity. Overall, the findings demonstrate that ncR is likely to elevate familiarity estimates when operational definitions of recollection are both specific and difficult, regardless of the process estimation method.

Amy Gitcho

Brain imaging predicts cognitive decline in aging: Evidence of preclinical Alzheimer's disease

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There is great interest in using biomarkers to predict who will develop Alzheimer's disease (AD). Studies have investigated individuals with mild cognitive impairment and genetic risks as models of preclinical disease using a variety of imaging modalities. In this study, we used positron emission tomography (PET) and magnetic resonance imaging (MRI) to detect metabolic and structural changes that predict cognitive decline in asymptomatic elderly people (> 60 yrs). The participants in this study were drawn from a subset of the Sacramento Area Latino Study of Aging (SALSA), N=61. These participants received MRI and PET and were neither demented nor cognitively impaired at baseline. The modified mini mental state examination (3MSE) and delayed recall (DelRec) examination were administered at approximate yearly intervals for an average follow up of 3.8 years. The rate of change in the 3MSE/year and DelRec/year were correlated with baseline PET data and MR-measured volumes of entorhinal cortex and hippocampus. Baseline PET metabolism in the left and right parietal lobes and left temporal lobes predicted the rate of change on the 3MSE ($p<0.001$). Six individuals developed incident dementia or cognitive impairment (converters). The left hemisphere regions remained significant when converters were excluded. Left parietal cortex metabolism was associated with DelRec decline, but not when converters were excluded. Both hippocampal ($p=0.03$) and entorhinal cortical regions ($p=0.01$) predicted decline on DelRec over time, and entorhinal cortical volumes remained significant when converters were excluded ($p=0.02$). These brain volumes did not predict 3MSE decline. The results from this study showed that global cognitive test decline is related to temporal and parietal metabolism, and memory test decline is related to medial temporal lobe brain volumes in normal older people. This detection of presymptomatic cognitive decline is consistent with the detection of presymptomatic AD pathology in healthy older individuals.

POSTER SESSION

Jack Day

A "phonological loop" for non-linguistic working memory?

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Previous research has shown that the architecture that characterizes verbal working memory (the phonological loop) is not restricted to the case of speech, but has a nearly-exact parallel in working memory for sign language in fluent signers. Is linguistic expertise necessary for this, or can the equivalent of a "phonological loop" be created on-the-fly, for novel, non-phonological materials? In a series of three experiments we tested working memory for meaningless gestures in non-signers. A new method of stimulus construction was used to minimize verbal labeling. The data show a similarity effect, a length effect, and an articulatory suppression effect, suggesting the use of a sensorimotor rehearsal strategy that resembles the phonological loop. We propose that the key property for the emergence of such a loop is stimulus imitability.

Kristin Geraci

Sharp limits on transfer of motor skills

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Previous research has shown that people can map a motor skill that has been learned by a particular set of effectors on to a new set of effectors. However, this research has generally lacked appropriate controls for perceptual or cognitive learning of the temporal and spatial patterns involved in the task. This presentation argues for limitations of our motor system's ability to transfer motor skills. Specifically, we aimed to find out whether the motor system can use a logically possible mapping (from two fingers to the feet) in a dancing task to enhance motor learning. This condition was compared to a control condition in which no systematic mapping is possible (three fingers to feet). The results give no indication that transfer is aided in any way by the use of analogous effectors. This finding places limits on theoretical claims that have been made about the transfer of motor skills across effectors.

Simona Ghetti

When true memory availability promotes false memory: Evidence from confabulating patients

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The present study examined confabulators' susceptibility to false recall and false recognition. Specifically, we were interested in determining the effects of increased true-memory availability on confabulators' ability to discriminate between true and false memories.
Five confabulating patients were administered the DRM paradigm (Deese, 1959; Roediger & McDermott, 1995). Their performance was compared to that of (a) five non-confabulating amnesics with lesions to the medial temporal lobes, diencephalic regions, or posterior regions, but not in the frontal regions (NF amnesics); (b) four non-confabulating amnesics who had frontal-lobe damage in addition to damage in other memory-relevant areas (F amnesics); and (c) 10 individuals without any form of brain damage.
Participants took part in two testing conditions. In both conditions, they studied 8 lists of semantic associates and free recall was tested after the presentation of each list. In the Standard testing condition, recognition memory was tested after studying all 8 lists; in the Proximal testing condition, recognition memory was tested after studying each of the 8 lists. The order of the Standard and Proximal condition was counterbalanced. In both sessions, participants provided remember/know judgments, and described the content of their recollections.
In all groups, true recognition was higher in the Proximal than in the Standard condition. However, the groups varied in their pattern of false recognition: (1) Confabulators showed higher false recognition of critical lures in the Proximal than in the Standard condition, whereas their false recognition of unrelated lures did not differ between the two conditions; (2) F amnesics' false recognition of both critical and unrelated lures did not differ between the two conditions; (3) NF amnesics' false recognition of critical lures did not differ between the two conditions, but their false recognition of unrelated lures was lower in the Proximal than in the Standard condition; (4) Control participants showed lower false recognition of critical lures in the Proximal than in the Standard condition; false recognition for other distracters was at floor levels in both conditions. Together, these results indicate that confabulators' ability to extract the gist of the lists is preserved, and can be paradoxically promoted if true memories are made more readily available. However, confabulators do not appear to use this gist-based information to reject unrelated distracters.
With respect to the phenomenological experience associated with true and false recognition, results showed that confabulators were as likely as control participants to give remember (R) responses, whereas F and NF amnesics were less likely than control participants to do so. Content analyses of participants' R responses revealed qualitative differences among the four groups. Only confabulators' R responses included significantly more descriptions of thought processes that were irrelevant to the task at stake, and showed, unlike the other groups, virtually no report of contextual information. The relation between the inability to report contextual information and that of rejecting unrelated distracters has important implications for our understanding of the nature of memory deficits exhibited by confabulators.

Ellen Klostermann

The inhibition of memories for performed and learned actions by executive control

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To successfully function in our environment we need to be able to inhibit the retrieval of unwanted, distracting memories using executive control. Previous research by Anderson and Green (2001) has shown that repeated prevention of a retrieval attempt impairs later memory for the item to be retrieved such that those items are forgotten more often than baseline levels. Here, we applied their paradigm to assess two different types of inhibitory control conditions- the repeated prevention of retrieval of actions one has learned and actions one has performed. We found that this paradigm can be used to bring about the successful inhibition of memories for both learned and performed actions, although here inhibiting learned or performed actions did not cause memory to go below baseline levels. Additionally, when the two inhibitory control conditions are compared, memories for performed actions were more susceptible to inhibition than memories for actions that were learned.

Diane Marian

Emotional lexical decision: Effects of gender and priming on attention and memory

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Sex differences in emotional processing are often posited. We used a lexical decision task to explore whether males and females differ in their response time to and memory for emotional and neutral words. Replicating previous findings, memory was better for emotional than neutral words, and both sexes showed this pattern of results. Interestingly, analysis of the lexical decision response times showed a word type by sex interaction; males responded equally fast to both emotional and neutral words, but females were slower to respond to emotional words than to neutral words. Affective priming was assessed by examining how response time to a word was influenced by whether the preceding word was emotional or neutral. The effects of affective priming were consistent across both sexes. Possible explanations for the apparent sex difference are discussed.

Adriane Mayda

Disconnection of working memory processes by cerebrovascular disease.

Adriane Mayda
University of California, Davis

Mild Cognitive Impairment (MCI) is characterized by episodic memory deficits beyond that expected for normal aging, leading to the notion that MCI is a transition state between normal aging and Alzheimer's disease (MCI-AD). Recent evidence, however, finds that MCI is heterogeneous with multiple etiologies, including cerebrovascular disease (MCI-CVD). Behavioral data also show that patients with MCI-CVD have impairments of episodic memory identical to MCI-AD, but it is hypothesized that these deficits result from impaired working memory. White matter hyperintensities (WMH) are a recognized marker for CVD and are correlated with performance on various working memory tasks suggesting that white matter injury may mediate the working memory deficit of MCI-CVD. WMH, however, are non-specific and cannot
reveal the extent of underlying injury. We hypothesize that working memory deficits in individuals with severe WMH are the direct result of white matter fiber tract disconnections between dorsolateral prefrontal cortex and other cortical and subcortical targets. In order to examine this hypothesis, we used diffusion tensor imaging (DTI) to generate fractional anisotropy (FA) maps as a measure of white matter fiber track integrity and correlated local FA values with working memory performance in MCI patients with varying degrees of WMH burden. Atlas based non-linear warping techniques enabled inter-subject averaging and voxel-based correlations with working memory using both a region of interest and whole brain approach. Working memory tasks consisted of a 4-item recognition task and a 2-back test. FA values in several regions of interest were more strongly correlated with performance on the working memory tasks than WMH volumes in the same regions. Performance on the 4-item recognition task was correlated with ROIs along the superior longitudinal fasciculus, suggesting involvement of a frontal-parietal network. Performance on the 2-back task was correlated with a frontal pericallosal ROI, suggesting that frontal-subcortical circuits are involved. These preliminary results indicate that performance on the working memory tasks is impaired when white matter tracts are disrupted, suggesting this as a mechanism by which CVD can impair cognitive function, and that different and discrete white matter tracts may mediate performance on these different working memory tasks.

Rosanna Olsen

The effects of perceptual similarity on item recognition and repetition suppression in the medial temporal lobe

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Declarative memory permits an organism to recognize stimuli as previously encountered. One basis for recognition is item memory strength, which may support the perception of stimulus familiarity. Though the medial temporal lobes are known to be critical for declarative memory, the neural mechanisms supporting differences in memory strength remain poorly specified.
Recent imaging studies have shown repetition suppression effects for old versus new items in the medial temporal cortex (e.g., Henson et al., 2003), effects that may influence the perception of memory strength. For example, Gonsalves, Kahn, et al. (in press) observed that fMRI and MEG measures of medial temporal activation varied according to subjective reports of item memory strength. In that study, participants responded with a "Remember/Know/New" judgment for studied and unstudied face stimuli. BOLD signal in perirhinal and parahippocampal cortex was lowest for remembered (and highly familiar) items and highest for correct rejections (highly unfamiliar) items. This strength-dependent response reduction suggests that repetition suppression in medial temporal cortex is related to the perception of item memory strength. Moreover, MEG data revealed a rapidly emerging (150-300 ms) response that showed a similar monotonic pattern according to perceived memory strength.
While there appears to be a link between repetition suppression in medial temporal cortex and item memory strength, the factors that mediate this effect are unclear at present. Recognition memory models posit that a key factor impacting item memory strength is the global similarity between a test probe and studied items. Accordingly, in the current experiment, high-resolution functional MRI (fMRI) indexed correlates of graded memory strength in the human brain, focusing on the medial temporal cortex (parahippocampal and perirhinal cortex). At study, faces were incidentally encoded during performance of a similarity judgment task. At test (scanned), a subsequent recognition memory test varied study-test perceptual similarity across three classes of memory probes: studied faces, faces that were morphs between a studied and an unstudied face, and unstudied faces. Subjects responded using a five-point confidence scale, indicating whether they recognized the face as old or new (1= sure new, 5= sure old). Behavioral results showed that perceived item strength was modulated by study-test perceptual similarity. Initial fMRI analyses revealed a decrease in medial temporal cortical activation that was sensitive to similarity, and that varied with perceived item strength. Thus, memory strength is affected by study-test similarity and is associated with repetition suppression in medial temporal cortex.

Rebecca Ray

Self-reference effect in children

Rebecca Ray[1], Amy Shelton[2], Nick Hollon[1], James Gross[1] and John Gabrieli[3]
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Behavioral studies have consistently shown that adults remember more information that is encoded when related to the self than information that is encoded semantically or processed by perceptual features. This is referred to as the self-reference effect (SRE; e.g., Craik and Lockhart, 1972). Imaging studies have further identified areas in the medial prefrontal cortex as being involved in self-referential processing (Johnson et al., 2002; Kelley, Heatherton, et al., 2002; Kircher et al., 2000; Ochsner et al, 2004; Ochsner, Ray et al, 2004). Given that structure of the prefrontal cortex is continuing to develop throughout childhood, there is reason to believe that the functional development of a self may be also developing during in this time period. Few behavioral studies have investigated the development of preferential memory for self related information in children. Those previous studies that have spot sampled cross-sections of children and adolescents, have found mixed support for the idea that the self reference effect has any linear relationship to age (Hammen & Zupan, 1984; Halpin, et al, 1984; Pullyblank, et al, 1985). These studies often mixed males and females who might differ in verbal memory development and did not always sample the age spectrum thoroughly. Additionally, studies did not control for the valence or abstract nature of words.
The current study hoped to avoid some of these potentially confounding problems and tested 42 male children spread across the ages of 7 and 13. Each child was tested on two lists of positive words (abstract and concrete) counterbalanced across individuals. Each word was presented in one of four trial types: self-reference (Is this word like you?), close other (Is this word like your Mom?), semantic (Is this a nice word?) or perceptual (Is this word outlined?) and recall was assessed after each list. Memory for words processed in the self-reference trials had a curvelinear relationship with age such that self-referential memory was correlated with age between the ages of 7 and 11 even after controlling for memory ability. However, between 11 and 13 the relationship between flattened out. In addition, this relationship between self-referential memory and age was strongest for abstract words. This suggests that there is a window in which this ability is developing. Further studies investigating the relationship between the development of the prefrontal cortex and the development of self-referential processing may benefit from sampling more densely in this age range in order to understand the relationship of structure and function.

DATA BLITZ

Linda Chao

fMRI evidence of intact distractor inhibition in elderly individuals who do not show negative priming

Linda Chao
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Negative priming (NP) is a decrement in performance observed when a previously ignored stimulus is re-presented as a target. One explanation for the NP effect is that it reflects inhibitory attentional mechanisms that suppress irrelevant, distracting information (Tipper, 1985). Older adults often do not show the NP effect and it has been suggested that this may be indicative of age-associated impairments in inhibitory mechanisms (e.g., Hasher & Zacks, 1988). To test the hypothesis that older adults fail to show NP because they have a reduced ability to inhibit irrelevant, distracting information, the present study used functional MRI to examine the neural fate of ignored stimuli in 9 healthy, elderly adults (mean age: 684.8 years) while they performed a selective attention task with pictures of scenes. We focused our analyses on scene-related activity in the parahippocampal place area (PPA), a region of the medial temporal cortex important for scene processing (Epstein & Kanwisher, 1998). The PPA was independently localized in each subject. As expected, attended scenes producing greater activation in the PPA than unattended scenes. In addition to the fMRI selective attention task, subjects also performed a NP task outside of the scanner. Five subjects exhibited robust NP while 4 subjects did not. When we compared PPA activity to attended and unattended scenes in subjects who showed NP relative to those who did not, we found greater signal differences between attended vs. unattended scenes in subjects who did not show NP than those who did. These results suggest that older individuals who fail to exhibit NP do not have an impaired ability to inhibit distracting stimuli.

Nicole Dudukovic

Prefrontal, parietal, and medial temporal contributions to item and temporal-recency recognition

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Declarative memory supports remembering what events occurred as well as when they were experienced. Few imaging studies have investigated the neural processes supporting retrieval of temporal information, and extant studies have tended not to match test conditions when comparing item and temporal-recency recognition. Some data suggest that recency decisions recruit left prefrontal and parietal regions typically involved in attempts to recollect or retrieve source information, whereas other evidence suggests that recency decisions recruit right prefrontal regions implicated in orienting to item familiarity. While carefully matching test conditions, the present study sought to investigate the neural processes underlying temporal-order retrieval and item recognition. Functional magnetic resonance imaging (fMRI) was conducted while eighteen participants made item recognition and temporal-recency decisions. During each study phase, participants made an abstract/concrete decision for each word in a series. Subsequently, a brief retention interval was filled through engagement in a spatial working memory task. Event-related fMRI data were then collected while participants encountered three-alternative-forced-choice memory retrieval trials, each consisting of two words from the preceding study phase and one novel word. Participants were to either identify the novel item (Novelty trials) or the more recently presented study item (Recency trials). Relative to correct Novelty decisions, correct Recency decisions elicited greater activation in left frontopolar, dorsolateral prefrontal cortex (PFC), and intraparietal sulcus, suggesting that participants attempted to recollect contextual details to guide their recency decisions. Recency decisions also recruited right superior PFC, indicating a putative reliance on visuo-spatial attention in the service of orienting to familiarity. Correct Recency decisions were further associated with greater left ventral precuneus activation than incorrect Recency decisions, which could either reflect more successful attempts to recollect and retrieve contextual information or an enhanced familiarity signal. By contrast, correct Novelty decisions activated right hippocampus to a greater extent than did correct Recency decisions, which may reflect increased novelty encoding. Temporal-order retrieval appears to activate a distributed network of PFC and parietal regions, suggesting that both recollective and familiarity processes may play a role in determining the relative recency of an event.

Daphna Shohamy

Dynamics of medial temporal lobe and basal ganglia activity during associative learning

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Converging evidence indicates that the medial temporal lobe (MTL) and basal ganglia (BG) support distinct forms of memory. The MTL is thought to play an important role in the acquisition of novel stimulus-stimulus associations, while the BG is thought to contribute to the acquisition of implicit, stimulus-response associations. Recent studies further suggest a neural interaction between these systems during learning, though the specific dynamics of this interaction and its implications for memory function remain unknown. The present fMRI study investigated the dynamics of MTL and BG activity while subjects performed an associative learning task. On each trial, subjects viewed a stimulus (a visual scene) and pressed a key to predict one of two outcomes ('dollar bill' or 'dollar coin'), followed by response-contingent feedback. Stimuli were either perfect predictors of an outcome (p=1.0) or probabilistic predictors of an outcome (p=0.7). Assessment of learning-related changes across acquisition revealed changes in MTL activity that were particularly prominent in the probabilistic condition, while changes in the BG were present in the deterministic condition. Analyses of individual differences as a function of learning indicated that better performance on the task was associated with systematic activation decreases in MTL, BG, and prefrontal cortex, while poor learning performance was associated with decreases in MTL, suggesting a stimulus-based learning effect. These results are discussed in the context of recent views of the nature and dynamics of the interaction between memory systems, and the implications of such interactions for memory function. [Supported by an NIMH National Service Research Award, the National Science Foundation, and McKnight Fund for Neuroscience]

Carter Wendelken

Working memory for structured item sets

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An fMRI investigation into the neural subtrates of maintenance for organized item sets was conducted. This was designed to test the hypothesis that dorsolateral PFC and superior parietal cortex are both involved specifically in the maintenance of organization or structure over sets of items in working memory. Subjects were asked to remember sets of letters over an 18-second delay. On some trials -- the organization condition (ORG) -- arbitrary relationships between the letters were indicated with arrows, and subjects were supposed to maintain this relational organization as well as the identity of the letters. A basic control condition (LOW) required subjects to remember the same number of letters (4) without organization, while a difficulty-matched control condition (HIGH) required subjects to remember seven letters without organization. Regions of interest, based on previous experimentation and computational modeling work, were dorsolateral PFC (BA 9, BA 46, and lateral BA 10) and superior parietal cortex (BA 7 and BA 40). Examination of average BOLD timeseries in these regions revealed significant delay-period activation in BA 7 and left lateral BA 10 for the ORG condition, relative to both LOW and HIGH, and significant delay-period activity for both the ORG and HIGH conditions, relative to the LOW condition, in BA 46 and right lateral BA 10. Timecourses for the three different conditions were similar in all other tested regions. These results suggest that parietal cortex, specifically BA 7, is involved whenever items in working memory need to be maintained in an organized or structured manner. The current results fail to distinguish organization demand from load in mid-DLPFC, although enhanced activation for organization was seen in a more anterior region (left lateral BA 10), suggesting that this area might play an important role in the organization of content in working memory.

TALK SESSION III

Roshan Cools

Dopaminergic modulation of stability and flexibility of representations in visual working memory

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The mesocorticolimbic dopamine (DA) system is known to be implicated in the cognitive processes of working memory and cognitive flexibility. Recent theorizing suggests that dopaminergic drugs may have contrasting effects on cognitive function depending on task demands. Moreover, there is large individual variability in the direction and extent of drug effects: Some individuals benefit from dopamine (DA)-enhancing drugs while the performance of others is impaired. We investigated the neural effects of DA receptor stimulation in human volunteers on the flexibility and stability of representations in visual working memory as a function of personality trait impulsivity. A large sample ($n > 1000$) of young psychology undergraduates were prescreened on the Barratt Impulsiveness Scale (BIS-11, Patton et al., 1995). We selected two groups of 10 participants from the tail ends of the resulting normal distribution of total BIS scores. These two groups were scanned with functional Magnetic Resonance Imaging on two occasions, once following administration of an oral dose of the DA D2 receptor agonist bromocriptine (1.25mg) and once following placebo. During scanning, participants performed a visual, delayed match-to-sample paradigm which allowed the separate assessment of (i) the flexible adaptation to changes in currently relevant information and (ii) the stable maintenance of relevant information in the face of distraction. Preliminary data analysis revealed that bromocriptine increased or decreased BOLD activity in fronto-striatal circuitry depending on task demands and trait impulsivity.

Susan Landau

Aging and compensation: What is the relationship between individual variability in dopamine function and working memory processing?

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Individual variability in dopamine (DA) function has important consequences for working memory (WM) function. The healthy older population shows a great deal of variability in DA function, since DA levels decline with age but these declines may be compensated for via upregulation of DA synthesis and/or functional activation during WM performance. Psychopharmacological studies in young subjects have suggested that WM span as measured by the Listening Span Test (Daneman & Carpenter 1980), in particular, may correlate with DA levels. Additionally, functional neuroimaging studies have suggested that prefrontal cortex activation during performance of a delayed WM task may depend on DA levels and WM span. To address these hypotheses regarding the relationship between DA levels and WM function in normal aging, we conducted PET and fMRI scanning in the same group of healthy older adults and obtained the following measurements: (1) DA measurements in caudate and putamen using the tracer 6-[18F]Fluoro-L-m-tyrosine (FMT), (2) fMRI activation in prefrontal and basal ganglia regions during the Sternberg delayed recognition task, and (3) neuropsychological tests of motor and WM function, including the Listening Span Test. Preliminary analyses have revealed that WM span, as measured by the LST, does correlate positively with caudate DA synthesis levels as predicted, such that higher span individuals have higher levels of DA. Performance on the Sternberg task also correlates with caudate DA levels such that faster and more accurate subjects have higher caudate DA. Finally, a negative correlation was observed between caudate DA levels and activation in ventrolateral prefrontal cortex during the encoding phase of the Sternberg task. Subjects with higher caudate DA had less ventrolateral prefrontal activation during encoding than subjects with low caudate DA. These findings suggest that upregulation of DA synthesis and ventrolateral prefrontal activation may serve as compensatory mechanisms for maintaining working memory function in the high-performing older population.

Brice Kuhl

Forgetting and remembering during competitive memory retrieval: Prefrontal and parietal mechanisms impact episodic memory suppression and recovery

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Episodic retrieval often involves selection of a target amidst interference from competing memories. To explore the neurobiological mechanisms recruited during retrieval in the face of competition and the mechanisms that contribute to the suppression of selected-against competitors, we used fMRI to study retrieval-induced forgetting (Anderson, Bjork, & Bjork, 1994). Participants (n=13) initially studied cue-associate word pairs, learning multiple associates for each cue. Subsequently, participants performed retrieval practice for some of the associates of some of the cues. Finally, a cued recall test was administered for all items. Behavioral data replicated the retrieval-induced forgetting effect: unpracticed associates of a practiced cue (competitors) were less likely to be recalled than unpracticed associates of an unpracticed cue (baseline items)-behavioral evidence for suppression of competing memories. Initial fMRI analyses targeting the neural processes associated with suppression and the recovery of selected-against memories revealed two main findings. First, fMRI data collected during retrieval practice revealed a correlation between the magnitude of activation in intraparietal sulcus (IPS) and the extent of forgetting (suppression) of competing memories, suggesting a role of IPS in internally guiding selective attention to target memory representations. Second, successful recall of previously selected-against competitors on the final test was associated with increased activity in dorsolateral prefrontal cortex (DLPFC), suggesting that DLPFC is involved in overcoming suppression such that competitors can be successfully recovered. Taken together, these data provide evidence for a consequence of IPS selective attention mechanisms for memory suppression during competitive retrieval, and of DLPFC in overcoming interference in service of remembering.

Scott Frein

Effects of valence and arousal on spatial context memory for unpleasant stimuli

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Previously, the authors demonstrated that emotional words impact contextual memory in different ways. Specifically, in a series of four studies, the authors demonstrated that spatial and temporal memory does not differ between pleasant and neutral words. However, there is a significant decrease in both spatial and temporal memory for unpleasant words compared to both pleasant and neutral words. These differences were consistently found even though unpleasant words enhanced free recall memory compared to the neutral words. This study builds on those previous findings by examining the role that arousal plays in the impairment of spatial memory for negative words and examines whether or not participantsí spatial memory scores are correlated with specific assessment instruments. Using one of two lists of 96 words, forty-eight participants individually identified the spatial location and rated the valence of each word. The lists contained 48 neutral and 48 unpleasant words. The two groups of words were matched on the dimensions of imageability, frequency, part of speech and semantic relatedness. In one set of words, the unpleasant words were subdivided into high and low arousal groups while still being matched on valence. Results indicated that spatial memory performance for the unpleasant words was significantly lower than for the neutral words. When the unpleasant words were subdivided into high and low arousal groups, the spatial memory scores for the high arousal words were significantly lower than for the low arousal words and accounted for virtually all of the difference in spatial memory scores between the neutral and unpleasant words. We had previously balanced for arousal in a third study in which we included pleasant words matched to the unpleasant words on arousal as well as all of the other previously listed dimensions. Results from that study indicated that there was no difference in spatial memory scores between the pleasant and neutral words and that there was a significant impairment in spatial memory scores for the unpleasant words. Taken together, these studies suggest that negative valence alone leads to a deficit in spatial context memory, but that highly arousing unpleasant words create more of a deficit than do low arousal unpleasant words. At the end of each study, participants completed multiple behavioral and mood assessment instruments. Spatial memory scores for unpleasant words correlated significantly with participantsí scores on the Dissociative Experiences Scale (DES) such that as a participant scored higher on the DES, he scored lower on the spatial memory test for unpleasant words. DES scores were not significantly correlated with overall spatial memory scores. These findings suggest that both arousal and valence play a role in the disruption of spatial context memory for unpleasant words and that individuals who more frequently dissociate in their day to day lives may be more likely to show evidence of this disruption.

TALK SESSION IV

Mike Cohen

Reinforcement learning signals predict future decisions

Mike Cohen
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The ability to use the outcomes of ones actions to dynamically adapt ongoing reward-seeking behavior is critical to biological and social survival. Reinforcement learning theory provides a mathematical framework for understanding learning and decision-making processes, and although neuroscience research is beginning to uncover how the brain identifies reinforcements as being better or worse than expected (i.e., reward prediction error), little is known about how reinforcements are used to guide future decisions, and further, how individual differences might influence this process. I will present evidence that neural responses as early as 300 milliseconds following negative reinforcements predicts human decision-making behavior in subsequent trials. This predictive activity can be observed in several different decision-making situations, and is encoded in a network of anatomically and functionally interconnected regions including the anterior cingulate and ventral striatum. A computational reinforcement learning model suggests that this predictive brain activity reflects ongoing errors in reward prediction, because (1) the models calculated reward prediction errors following each trial during the experiment closely resemble changes in human brain activity, and (2) when the model is given each subjects unique history of decisions and reinforcements, the models reward prediction error signal generated after each trial predicts both choice behavior and neural activity during those choices. Further, the model that incorporates individual differences in learning rates predicts behavior and brain activity significantly better than a model in which these learning rates are fixed, as they have been in previous studies. These and other recent findings suggest that human decision-making processes are well characterized by simple equations derived from reinforcement learning theory, and that ongoing assessments of errors in reward prediction mediate the use of reinforcements to guide future decisions.

Alison Adcock

Reward-motivated learning: Proactive mesolimbic influences on encoding

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We examined the effects of reward anticipation on memory. Using event-related functional MRI, mesolimbic regions reflecting reward anticipation were independently localized, then investigated along with medial temporal lobe memory regions during a novel reward-motivated memory encoding task. Cues signaled a high- or low-value reward for memorizing an upcoming scene. High-confidence scene recognition was tested 24 hours later. We found that dopamine-rich regions (ventral tegmental area, nucleus accumbens and anterior hippocampus,) were selectively activated during high-value cues that preceded later-remembered scenes. Activations were correlated in these regions and predicted individuals' memory scores. In contrast to hippocampus, reward-driven activation in dopamine-poor parahippocampal cortex was not specific to remembered trials during either cues or scenes. These novel results demonstrate first, that transient antecedent activation (mesolimbic and hippocampal) predicts long-term memory for an upcoming experience, and second, that memory-related functional coupling of hippocampus and mesolimbic regions occurs during reward anticipation.

Daniel Krawczyk

Influences of reward motivation on encoding and delay in human working memory

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Reward motivation generally tends to enhance performance in working memory tasks; however, there has been some degree of controversy about which brain regions support this enhancement. It is generally accepted that the prefrontal cortex (PFC) supports both working memory and reward processing, but the regional specificity has been unclear. The majority of investigations into this process come from single-neuron electrophysiology, which is limited in providing information about broad cortical organization. The possible role of posterior regions has also received little investigation. We tested working memory for faces or scenes with fMRI in a task in which participants were required to attend to one picture type and ignore the other. Information about the attended pictures was consistent for each block of 16 trials. Four pictures were presented serially followed by an 8-12s delay and probe picture. Participants made match non-match judgments about the probe responding within 1s. Points were given for correct probe responses at high, medium, and no reward levels across the trials. Points were exchangeable for money at the end of the session and reward values were presented prior to each encoding period. Thus reward motivation and working memory trials were compared along with passive viewing trials that did not require picture maintenance or probe judgments. Behavioral results indicated response time decreases with higher reward levels, while accuracy levels remained high across all reward levels. This finding indicates that subjects were able to emphasize both speed and accuracy in responding and that reward aids performance as measured by response time. At the encoding period BOLD contrasts indicated that a PFC exhibited greater activity at higher levels for highly rewarded compared to non-rewarded trials. Further analysis of a scene-specific visual association temporal cortical area indicated that this region showed enhancement of the BOLD signal for remember scene trials and suppression of signal for ignore scene trials at encoding. This pattern of results was enhanced for non-rewarded over non-rewarded trials. At delay, a left PFC region showed reward-related suppression, while face-responsive visual regions showed reward enhancement of signal. This result indicates that the PFC may suppress inappropriate stimuli during delay and that face-stimuli show reward-related effects later in the task compared to scenes. Overall these results are consistent with the hypothesis that reward motivation can enhance performance through modulation of the network of brain regions supporting working memory function.