TALK SESSION I

Rob Blumenfeld

Dorsolateral prefrontal cortex contributes to relational memory encoding

R.S. Blumenfeld, S. Trefethen, & C. Ranganath
UC Davis Center for Neuroscience and the Department of Psychology

Evidence from neuropsychological and transcranial magnetic stimulation studies suggest that the dorsolateral prefrontal cortex (DLPFC) plays an important role in long-term memory encoding. In contrast, event-related functional magnetic resonance imaging (fMRI) studies have yielded little evidence to support this notion. Most previous fMRI studies examined prefrontal activity during the encoding of single items, leaving open the possibility that DLPFC may contribute to long-term memory encoding by forming relations amongst multiple items in working memory. We conducted an event-related fMRI study to test this hypothesis by investigating prefrontal activity during performance of two different working memory tasks: On REHEARSE trials, participants actively maintained sequences of three words across a twelve second delay. On REORDER 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. Both REHEARSE and REORDER trials required active maintenance of each item, but REORDER trials additionally required processing of inter-item relations. After scanning, subjects received a surprise long-term memory test for words presented in both REHEARSE and REORDER conditions. Behavioral results showed that subjects were significantly more likely to remember multiple items presented during REORDER trials than during REHEARSE trials. Preliminary analyses of fMRI results showed that DLPFC, along with ventrolateral prefrontal and hippocampal regions showed sustained activity increases during the delay period for REORDER trials relative to REHEARSE trials. Furthermore the magnitude of delay period activity during REORDER trials was related to subsequent long-term memory for multiple items in the memory set. These findings suggest that DLPFC contributes to long-term memory encoding through its role in actively forming relations amongst items held in working memory.

Brian Gonsalves

Spatiotemporal predictors of later face recollection:
Prefrontal cortex mediates top-down modulation of encoding

B. Gonsalves [1], I. Kahn [1,2], T. Curran [3], K. Norman [4], & A.D.Wagner [1,5]
[1] Dept. Psychology & Neurosciences Program, Stanford University, [2] Brain & Cognitive Sciences, MIT, [3] Psychology, Univ. of Colorado, Boulder, [4] Psychology, Princeton, [5] Martinos Center for Biomedical Imaging, MGH/MIT/HMS

Functional MRI evidence suggests that memory encoding depends on prefrontal and posterior cortical mechanisms, with dissociable encoding processes supporting later recollection of event-specific details and later stimulus familiarity. Such findings suggest that prefrontal cortex plays a top-down modulatory role at encoding, although the relative timing of prefrontal and posterior neural events that predict subsequent recollection remains unclear. Using fMRI and anatomically-constrained magneto-encephalography (aMEG), we sought to delineate the spatiotemporal dynamics of encoding events leading to later recollection and familiarity. Faces were incidentally encoded during a target detection task. A subsequent recognition memory test included studied faces, unstudied faces that were perceptually similar to studied faces, and dissimilar unstudied faces. Subjects responded "remember", "know", or "new" to each test face. MEG data were submitted to source localization, using each subject's cortical surface reconstructed from MRI. MEG analyses focused on regions of interest identified by fMRI to predict subsequent face recollection (remember > know and new), including L. frontal operculum and anterior inferior prefrontal cortex, R. orbital frontal, and bilateral fusiform. MEG activity showed a temporal lag between frontal and posterior encoding responses. Specifically, recollection-selective encoding effects onset between 150-250 ms in frontal regions and between 350-450 ms in fusiform. Prefrontal top-down modulation of face-processing regions during encoding appears important for later face recollection.

Bong Walsh

Novelty & encoding: The neural basis of the von Restorff effect

B.J. Walsh [1,2], G. Rainer [3], A.P. Yonelinas [1,2], & C. Ranganath [1]
[1] UC Davis, Center for Neuroscience, [2] UC Davis, Center for Mind & Brain,
[3] Max Planck Institute, Tubingen, Germany

The occurrence of a contextually novel event elicits a cascade of neural responses that results in orienting of attention and enhanced memory encoding (the "von Restorff effect"). Here we used functional magnetic resonance imaging (fMRI) to identify the neural mechanisms of the von Restorff effect during encoding and retrieval. During the encoding phase, subjects made pleasantness judgments on pictures of faces and houses. In each encoding block, the majority of items were of one stimulus type (standard; e.g. house), and a minority of items were of the other stimulus type (novel; e.g. face). Across blocks, an equivalent number of faces and houses were shown as novels and as standards. Each encoding block was followed by a test block in which subjects were shown studied pictures from the novel and standard categories, as well as previously unseen houses and faces. Subjects were required to decide whether each item was old or new, and for items judged old, to additionally decide whether it was recollected or it was recognized on the basis of familiarity. Behavioral results showed a robust von Restorff effect, as evidenced by increased recollection of novels relative to standards. Analyses of fMRI responses during encoding showed that, relative to standards, contextually novel items elicited enhanced activation in a distributed cortical network including anterior and posterior cingulate, retrosplenial, ventrolateral and dorsolateral prefrontal, and medial and lateral parietal cortices. For novel items, encoding activation in the amygdala, hippocampus, anterior cingulate, and ventrolateral prefrontal cortex was predictive of subsequent recollection. In contrast, for standard items, encoding activation in ventrolateral and dorsolateral prefrontal and inferior temporal cortex was predictive of subsequent recollection. These results suggest that processing within a limbic network including the amygdala, hippocampus, and anterior cingulate cortex mediates enhanced encoding of contextually novel events.

Itamar Kahn

Functional neurobiology of episodic recollection:
Identifying the temporal dynamics of retrieval

I. Kahn [1,2] & A.D. Wagner [1]
[1] Psychology & Neurosciences Program, Stanford University, [2] Department of Brain & Cognitive Sciences, MIT

Neural processes supporting recognition memory can be identified by comparing activation during correctly recognized old items (Hits) to that during correctly rejected new items (CR). Prior fMRI and electrophysiological (EEG) studies have revealed old/new effects in prefrontal and parietal cortices, suggesting that these regions support (1) control processes that subserve retrieval attempts and/or (2) processes that are sensitive to successful retrieval. At present, the relation between retrieval-related responses observed with hemodynamic vs. electrophysiological based measures (e.g. fMRI vs. EEG/MEG) remains unclear. Using anatomically-constrained magnetoencephalography (aMEG) we sought to further identify the temporal dynamics of the circuitry and cortical sources supporting retrieval attempt and success. During encoding, subjects were engaged in two orienting tasks intermixed on a trial-by-trial basis. On the following day, MEG scans accompanied a one-step recognition test that probed for item and source memory. A companion fMRI study, conducted prior to MEG, revealed that left PFC subregions, and to a lesser extent left parietal cortex, were sensitive to familiarity-based retrieval success but were insensitive to recollection-based success. Accordingly, engagement of these neural processes appeared to depend on perceived familiarity, suggesting that these regions have early access to familiarity signals and are gated depending on the expected utility of attempts to recollect. Analyses of the MEG data, using an fMRI-driven region-of-interest approach, revealed multiple generators contributing to MEG differences between Hits and CR. These responses included (a) an early (300ms) and late (800-1200ms) left inferior parietal source, (b) a left inferior frontal/frontopolar source (350-400 ms), and (c) a left ventrolateral/dorsolateral PFC source (350-400ms; 550-600ms; and 750-800ms). Subsequent analyses, comparing recollection-based (Item plus Source) and familiarity-based (Item only) Hits, revealed differential correlates of these two recognition states. Collectively, the MEG data lend further support to the role of left parietal and PFC in guiding attempts to recollect details about past experience.

Craig Brozinsky

Recognition-related activity in rhinal cortex:
Evidence for repetition suppression across different repetition intervals

Craig J. Brozinsky, Andrew P. Yonelinas, Neal E.A. Kroll, & Charan Ranganath
Psychology Department, University of California, Davis

Single-unit recording studies of monkeys have shown that neurons in rhinal (perirhinal and entorhinal) cortex exhibit activity reductions following stimulus repetition. These "repetition suppression" effects have been proposed as a signal that may support recognition memory decisions. However, human neuroimaging studies have not revealed strong evidence to support the idea that human rhinal cortex exhibits repetition suppression during recognition memory. Here, using event-related fMRI, we examined medial temporal lobe activity during a continuous recognition memory task in which the interval between item repetitions was parametrically varied from 2 to 32 intervening items. This procedure allowed us to measure recognition-related activity at short repetition intervals, when it is likely to be most robust, and additionally determine whether responses in medial temporal regions vary with study-test interval. We found that, evidence of repetition suppression in rhinal cortex, but only when the repetition interval was relatively short. Bilateral hippocampal regions also showed time-sensitive repetition effects, but recovery functions in these regions were distinct from those seen in rhinal cortex. Our findings indicate that repetition suppression can be observed in the human rhinal cortex and support the notion that this region may support familiarity-based recognition.

TALK SESSION II

Nadine Gaab

Neural correlates of auditory learning - an fMRI training study

Nadine Gaab [1,2], Christian Gaser [2,3], & Gottfried Schlaug [2]
[1] Department of Psychology, Stanford University, [2] Department of Neurology, Music and Neuroimaging Laboratory, Beth Israel Deaconess Medical Center, Harvard Medical School, [3] Department of Psychiatry, University of Jena, Germany

The neural effects of learning a pitch memory task are described using functional MR imaging. A group of 14 subjects underwent daily training (1hr/day for 5 days) in a pitch memory experiment. Functional MR imaging data while performing this pitch memory task were obtained before and after the training period. The training group was compared to a control group (n=10) that was scanned twice (7 days apart) without any intervening training. Based on a Cluster-Analysis of the improvement scores, the training group was divided into a Strong-Learners (L+) and a Weak-Learners (L-) group. Pre- and post-training session contrasts showed for L+ a left-sided positive change in the posterior superior temporal and supramarginal gyrus while L- activated the lingual, inferior frontal and parahippocampal gyrus. By contrasting the post >pre images for L+ and L-, the supramarginal gyrus (SMG) became significant in the contrast L+ > L-. Our results indicate that besides typical auditory association areas (left > right), the SMG seems also to be of critical importance in the short- term retention of non-verbal auditory information.

Scott Frein

Valence-specific effects of emotional words on memory for spatial and temporal context

Scott T. Frein & Richard J. Maddock
Departments of Psychiatry and Psychology, University of California Davis

Emotionally arousing stimuli have multiple effects on memory. Enhanced free recall is consistently observed with emotional words, but similar enhancement is not seen on recognition testing. This suggests that factors leading to improved item retrieval rather than item encoding underlie the free recall effect. Possible mechanisms include 1) stronger inter-item associations; and 2) stronger item-context associations. In addition, asymmetrical effects of valence on free recall (pleasant recalled better than unpleasant) are sometimes observed, suggesting the possibility that valence may interact with the effect of emotional arousal on memory. This study investigated the effect of pleasant and unpleasant emotional words on memory for spatial and temporal context. Ninety-six subjects entered one of two lists of 36 words into a spatial grid, and rated their valences. The 12 pleasant, 12 unpleasant and 12 neutral words were fully matched on dimensions affecting memory. At test, subjects were shown each word and instructed to enter it into the same cell as at study. Accuracy was quantified as a proximity score. Free recall was assessed following spatial memory testing. Free recall was significantly better for both pleasant and unpleasant compared to neutral words, and for pleasant compared to unpleasant words. In addition, memory for spatial context was significantly worse for unpleasant than pleasant or neutral words. Similar effects were seen in 48 additional subjects tested on memory for temporal context. The results fail to support the model of enhanced item-context associations for emotional words. Impaired free recall of unpleasant compared to pleasant words and impaired spatial and temporal context memory for unpleasant words compared to both pleasant and neutral words suggest a disruptive effect of emotion on context memory that is specific to negatively valenced stimuli. The findings may have relevance to the "fragmentation" of traumatic memories observed in patients with post-traumatic stress disorder.

Christine Wu Nordahl

White matter changes compromise prefrontal cortex function in healthy elderly individuals

Christine Wu Nordahl [1], Charan Ranganath [1], Andrew Yonelinas [1],
Evan Fletcher [1], Charles DeCarli [1], & William J. Jagust [2]
[1] Center for Neuroscience, University of California, Davis, [2] Helen Wills Neuroscience Institute, University of California, Berkeley

Changes in memory function in elderly individuals are often attributed to dysfunction of the prefrontal cortex (PFC). One mechanism for this dysfunction may be disruption of white matter tracts that connect PFC with its anatomical targets. White matter hyperintensities (WMH), an MRI finding associated with cerebrovascular disease, are commonly seen in healthy elderly individuals and are indicative of white matter pathology. Here, we use WMH as a marker for white matter abnormalities to test the hypothesis that disruption of white matter tracts reduces prefrontal function in the elderly. Specifically, we used structural magnetic resonance imaging (MRI) to quantify the extent of WMH in a group of cognitively normal elderly individuals and tested whether these measures were predictive of the magnitude of prefrontal activity observed during performance of an episodic retrieval task and a verbal working memory task. Results showed that an increase in WMH severity was associated with decreases in PFC activity during both tasks. These results suggest that disruption of white matter tracts may be a mechanism for age-related changes in prefrontal functioning.

Norbert Schuff

Brain arterial spin labeled MRI in Alzheimer's disease, mild cognitive impairment, and normal aging

N. Schuff [1], N. Johnson [5], G.H. Jahng [1], X. Zhu [1], K.L. Li [1], B.L. Miller [2],
H.C. Chui [3], W.L. Jagust [4], & M.W. Weiner [1]
[1] VAMC and UCSF Department of Radiology, [2] UCSF Department of Neurology, [3] University of Southern California, Los Angeles, [4] Lawrence Livermoore Laboratories, Berkeley, [5] U Penn, Department of Radiology

Arterial spin labeled (ASL) MRI is an attractive imaging technique for measuring CBF, because it is entirely non-invasive, it can be rapidly repeated and acquired in the same session as MRI. Here, we present results from ongoing ASL-MRI studies of patients with Alzheimer's disease (AD), mild cognitive impaired (MCI) subjects, a non-demented group with isolated memory impairment who are at high risk for development of AD, and cognitively normal elderly. Our specific goal was to demonstrate that ASL-MRI detects a stereotypical regional pattern of hypoperfusion in AD and MCI patients that might aid diagnosis and prediction of cognitive decline. Another goal was to improve quantification of ASL-MRI measurements by measuring the kinetics of ASL perfusion in the aging brain. In a study that included 22 AD patients, 18 MCI, and 20 cognitive normal subjects, we found in AD significant hypoperfusion in the posterior cingulate gyri and parietal association cortices compared to controls. MCI subjects showed also hypoperfusion in posterior cingulate, similar to AD, despite absence of clinical symptoms of dementia. Evaluation of perfusion kinetics in 10 subjects between 30 and 80 years old showed transit time and filling time of the capillary bed with the spin label tracer increased markedly with age ($r = 0.71$, $p<0.02$), while cerebral blood flow declined. In summary, these results demonstrate that ASL-MRI can detect abnormally perfused brain regions in AD patients and also in MCI subjects, potentially prior to the onset of dementia. Furthermore, the finding of age-related changes in perfusion kinetics is consistent with pathological studies that brain microvasculature is altered with normal aging. Taken together, these findings suggest ASL-MRI is a useful tool for the functional characterization of normal aging and AD and may be useful for early detection of dementia.

POSTER SESSION

Silvia Bunge

Task rule retrieval and task-switching: Separable neural processes

Silvia A. Bunge* & Eveline A. Crone
Department of Psychology & Center for Mind and Brain, UC Davis
*presenter, on behalf of student

The ability to flexibly switch between tasks is considered an important component of cognitive control. It is often assumed that lateral prefrontal cortex (LatPFC) is necessary for flexibly switching between tasks, both because patients with LatPFC damage perseverate on previously relevant task rules and because this region is often recruited during imaging studies of task-switching. A review of the brain imaging literature suggests, however, that activations related to task-switching are less reliably observed in LatPFC than in medial PFC or posterior parietal cortex, and that LatPFC is engaged on both switch and repeat trials. Moreover, transcranial magnetic stimulation of these latter regions in healthy adults disrupts task-switching; no such findings have been reported with stimulation of LatPFC. In contrast, a growing body of evidence, including work from our laboratory, points to the role of LatPFC, in particular ventrolateral PFC (VLPFC), in learning, retrieving, and maintaining task rules online. These findings, together with the long- term memory literature implicating VLPFC in the controlled retrieval of semantic associations, suggest that VLPFC may not be critical for switching between tasks, per se, but rather for the controlled retrieval of cue-rule associations.

In a related vein, recent developmental psychology studies by Crone et al. suggest that rule representation and task-switching have different maturational timecourses during childhood. These studies suggest that the ability to retrieve complex rules is still maturing during adolescence, whereas the ability to flexibly switch between rules is mature by the age of twelve. Putting these findings together with the cognitive neuroscience findings discussed above, Dr. Crone and I have hypothesized that 1) LatPFC activation in task-switching studies is related to rule retrieval, 2) the development of task-switching over childhood is correlated with the recruitment of medial PFC and parietal cortex during this time-period, and 3) the development of rule retrieval is correlated with the recruitment of LatPFC and, in particular, VLPFC. To test this hypothesis, we have designed a child-friendly task in which subjects are cued to switch between simple task rules. Using this task, we have collected fMRI data for over 50 subjects aged 8-25. The focus is on fMRI data from 20 adults, which convincingly support our first hypothesis; that is, that rule retrieval and task-switching are separable cognitive processes with different underlying neural substrates.

Trey Hedden

Neural correlates of inhibitory and switching component processes of attentional control

T. Hedden, A. Bernstein, & J.D. Gabrieli
Psychology Department, Stanford University

The nature of the component processes underlying attentional control (also known as executive function), such as the inhibition of distracting information and switching between relevant task goals, has been a topic of much debate in cognitive psychology and cognitive neuroscience. A network of frontal and parietal regions is thought to be involved in attentional control, but specific associations between control operations and activation in particular regions within this network have been difficult to identify, in part due to differences between tasks thought to tap separate component processes. In this study, participants performed an attention-orienting task in the global-local paradigm while undergoing functional magnetic resonance imaging in a 1.5 Tesla GE scanner. The global-local paradigm presents participants with a large letter made up of smaller letters, with participants being cued on each trial to respond to the global or local levels. In a blocked design, participants responded to stimuli in which they had to both inhibit distracting material and switch between the global and local levels on subsequent trials, inhibit only, switch only, or neither inhibit nor switch. Both inhibition and switching activated a set of regions in the frontal-parietal network, including dorsolateral prefrontal cortex, inferior frontal gyrus, anterior cingulate cortex, and superior and posterior parietal cortex. These regions of interest were investigated to identify activations that were similarly and differentially modulated by component processes of inhibition and switching within a single task domain.

Ching Kao

Subjective versus neural predictors of long-term memory performance: an fMRI study on metamemory and the subsequent memory paradigm

Y.C. Kao, E.S. Davis, & J.D.E. Gabrieli
Department of Psychology, Stanford University

Effective learning depends on one's judgments as to whether information has been successfully or unsuccessfully learned at the onset. This evaluation of encoding performance is the basis of judgments-of-learning (JOLs) where participants predict whether studied information will be later remembered. Actual encoding success can be objectively measured by performance on memory tests. Neural activities in medial temporal lobe (MTL) and prefrontal cortex (PFC) regions during encoding predict whether experiences will be subsequently remembered. This study investigated whether JOLs rely on the same neural processes as those underlying successful encoding. In this rapid event-related fMRI study, subjects were scanned while viewing 350 scenes, during which they made predictions about whether they would later remember or forget the scenes when tested. Outside the scanner, an old/new recognition test was administered. MTL and PFC activations predicting encoding success were found when comparing scenes that were later remembered to scenes that were later forgotten, replicating previous studies on subsequent memory. The neural correlates of JOLs were assessed by comparing "will-remember" predictions with "will-forget" predictions. This contrast yielded significant activations in bilateral inferior frontal gyrus (BA 11/47). Interestingly, the JOL contrast did not reveal any MTL activations, suggesting that subjective evaluations of encoding success do not rely on processes critical to memory encoding. A second-level conjunction analysis revealed a region in left middle frontal gyrus (BA 9) that was activated in both the subsequent memory and the JOL contrasts. This area is likely to be involved in JOL accuracy (when JOL predictions match retrieval outcomes) by tracking both memory encoding and subjective evaluations. Further analyses were conducted to correlate individual differences in JOL accuracy with brain activations.

Mark Kishiyama

Novelty processing and amnesia

Mark M. Kishiyama [1], Andrew P. Yonelinas [1], & Michele M. Lazzara [2]
[1] Department of Psychology, University of California, Davis, [2] SAM Technology, Inc., San Francisco, CA

The ability to detect and encode novel information is an essential component of the biological memory system. Neuroimaging studies have identified widely distributed "novelty-processing networks" in the human brain. Investigations attempting to more precisely delineate the neural substrates of these networks have implicated a number of critical structures including regions in the medial temporal lobes (MTL) and the thalamus. In the current study, we investigated novelty processing in amnesic patients with damage to regions in the MTL and thalamus using pictorial materials and a modified von Restorff paradigm. The memory performance of amnesic patients and age-matched controls was compared on a remember/familiar recognition test. Novelty effects were reduced in amnesic patients relative to age-matched controls on overall recognition performance and in estimates of recollection and familiarity. The current findings support prior evidence suggesting that these neural regions are important for processing and encoding novel information.

Marisa Knight

The impact of emotional goals on age differences in memory

Marisa Knight & Mara Mather
Cognitive Psychology, UC Santa Cruz

While aging is associated with a general decline in many domains, recent work examining emotional memory across the lifespan has highlighted emotional functioning as an area of resiliency and even improvement across the lifespan (see Mather, 2001). The purpose of the current study was to examine the contribution of executive processes to age differences in emotional memory. The results revealed that older adults with high performance on tasks associated with frontal lobe function had a significantly larger recall proportion of positive images and a significantly smaller recall proportion of negative images compared with younger adults. Older adults with lower performance on the frontal measures showed a strikingly different pattern compared to high performing older adults, recalling a significantly smaller proportion of positive images. These findings demonstrate that older adults who are better able to implement their emotional goals and exert internal control over the contents of working memory are more successful at having emotionally gratifying memories.

Jary Larsen

Prefrontal regions supporting verbal learning strategies

Jary Larsen [1,2], Juliana Baldo [2,3], & Diane Swick [1,2]
[1] University of California, Davis, [2] VA Northern California Health Care System, Martinez, CA, [3] Scripps College, Claremont, CA

Previous research has shown that orbitofrontal cortex (OFC) plays an important role in strategic memory by enabling spontaneous mobilization of effective behavioral strategies in early, unstructured learning conditions (Savage et al., 2001). Lateral prefrontal cortex (LPFC), on the other hand, has been shown to mediate semantic organizational strategies (Savage et al., 2001; Gershberg & Shimamura, 1995, Baldo et al, 2001). The current study is a behavioral replication of a PET study in young control subjects (conducted by Savage et al., 2001). We compared free recall list learning performance in OFC and LPFC patients under three conditions: 1) spontaneous and undirected with semantic categories; 2) directed with semantic categories; and 3) undirected and unrelated without semantic categories. Based on their PET results, which found that blood flow in the OFC during memory encoding predicted which young control subjects (n=8) would initiate effective strategies spontaneously during free recall, Savage et al. suggested that the OFC supports early and effective behavioral strategies in novel and ambiguous situations. Although the OFC initiates mobilizing strategies during ambiguous tasks, Savage et al. suggested that the LPFC actually mediates the strategic semantic organization. Therefore, on a 24-item list-learning task, once provided strategies, OFC patients with intact LPFC should be able to implement the use of semantic clustering to improve their overall performance. LPFC patients, on the other hand, would not spontaneously make use of an organizational strategy.

The results of the present behavioral study with a patient population did not support these assertions, however. Overall free recall in OFC patients (n=6) did not differ from age-matched controls, and there was no interaction with list condition. LPFC patients (n=8) were not impaired relative to controls, either for overall recall across the three lists or for an interaction with list condition. In contrast, semantic clustering did reveal some differences amongst the groups. Although the OFC patients displayed reduced semantic clustering relative to age-matched controls, they were not differentially impaired in the spontaneous condition, as would be predicted from the PET results. The semantic clustering of the LPFC group did not differ from either controls or the OFC patients. The current behavioral findings may reflect a paucity of patients due to strict selection criteria. It may also represent a difference in mean age for the two studies amongst the subject groups: Savage et al. mean age of 28 (sd=6.8 yrs), OFC mean age of 53 (sd=9.9 yrs), and LPFC mean age of 68 (sd=11.2). The lack of positive findings in this study suggests that further investigation is needed to clarify the role of the OFC and the LPFC. Alternatively, it could indicate that the patients have shown some recovery of function to compensate for their lesions.

Diane E. Marian

Effects of emotional facial expression on memory for faces and associated expressions

Diane E. Marian & Arthur P. Shimamura
University of California, Berkeley

Past research has suggested that memory is better for faces with happy expressions compared to faces with other emotional expressions. However, it is unclear whether this happy face advantage, extends to memory for the face itself or is limited to memory for the emotional expression. Our results indicate that the memory benefit does extend to recognition of the face, however, the effect is not as robust as memory for the associated emotional expression. Furthermore, our findings suggest that recognition memory is reduced for angry faces compared with other facial expressions – a reduction not evident when testing recall for emotional expressions. Finally, the effects of emotional facial expression on later memory appear to be automatic, consistent with other studies demonstrating that detection of facial expressions is an automatic process.

Mara Mather

Retrieving a positive memory inhibits other positive memories:
Part-set cueing inhibition for emotional material

Jo Ann Sison & Mara Mather*
University of California, Santa Cruz
*presenter, on behalf of student

Inhibition as a result of partial-set cueing is typically demonstrated with semantically-associated word lists. The typical experimental paradigm uses a list composed of words from several semantic categories. After study of the word list, a subset of items from one of those categories is re-presented to the participant, and somewhat surprisingly, the re-presentation of this partial list decreases the recall of the remaining items from that category. This impairment in recall results from competition that occurs when the re-presentation or retrieval of some list items strengthens those items relative to non-cued items, which are in turn inhibited. The goal of this set of experiments was to see if part-set cueing inhibition would be observed for emotional materials. Two experiments were conducted using pictures from the International Affective Picture System (IAPS, 1995). In the first experiment, participants viewed a randomly ordered slide show of 60 pictures that included 20 pictures of each valence (positive, negative, and neutral). Half of each valence set was comprised of pictures of people and half was comprised of pictures without people in them.

In the second experiment, participants viewed a randomly ordered slide show of 64 pictures from specific emotion categories (16 each from amusement, awe, disgust, and fear). Participants were randomly assigned to either a cue condition or a control (no-cue) condition. In both experiments, participants who were cued to recall a partial set of pictures from either a valence type or an emotion category experienced inhibited recall of non-cued pictures of that type relative to control participants' recall for those same pictures. For example, when cued to retrieve half of the positive pictures, participants recalled fewer of the remaining positive pictures relative to control participants who saw no cues. These positively cued participants had no decrement in recall of either negative or neutral picture items. The finding that part-set cueing inhibition can be triggered by emotional categories supports the notion that emotions serve as a basis for conceptual organization, as is proposed in network theories of emotion (e.g., Bower, 1981). However, our results suggest that mechanisms of memory inhibition need to be added to such models. In addition, our findings may help explain puzzling findings of mood incongruent recall (e.g., Parrott & Sabini, 1990).

Angie Morey

High-altitude hypoxia and the hippocampus

Angie Morey [1], Rich Ivry [1], & Philip Lieberman [1,2]
[1] Department of Psychology, University of California – Berkeley, [2] Department of Cognitive and Linguistic Science, Brown University

This work is part of an ongoing project aimed at assessing the cognitive and linguistic deficits that result from exposure to an oxygen-poor environment at extreme altitudes. Various lines of evidence suggest that the hippocampus is disproportionately affected under such conditions. To investigate this issue, we used an implicit, contextual learning task previously found to be sensitive to medial temporal lobe damage. In this task, participants perform a visual search in stimulus displays that are either novel or repeat across trials. Contextual learning is observed by a reduction in RT on trials with the repeating context, although participants are unaware of this manipulation. Mount Everest Climber subjects performed this task at Base Camp (5400m) and again at Camp Two (6300m) and Camp Three (7300m). The subjects' performance at Base Camp was comparable to that of normal participants: they exhibited a response time benefit when searching repeating displays compared to those that were novel. In contrast, when these subjects were tested higher up on the mountain, their performance was similar to that of patients with hippocampal damage: the response time benefit on the repeated arrays was absent. These results are consistent with the hypothesis that hippocampal function is compromised in an environment of reduced oxygen.

Alison Preston

Stimulus-specific novelty responses in human medial temporal lobe

Alison R. Preston [1], Meghan E. Gaare [1], & Anthony D. Wagner [1,2]
[1] Department of Psychology and [2] Neurosciences Program, Stanford University

A central question in memory research regards the distinct contribution of medial temporal lobe (MTL) subregions to long term memory processing. Substructures within human MTL may be functionally homogenous and interchangeable with respect to memory encoding, or may support encoding depending on the nature of the to-be-learned information. Using a combination of high-resolution functional magnetic resonance imaging (fMRI) and cortical flattening techniques, the present experiment examined stimulus-specific, novelty-related encoding responses to investigate the topographic organization of encoding processes in human MTL and to determine whether different MTL subregions demonstrate stimulus-specific encoding responses consistent with known anatomical connectivity. Subjects performed a novelty encoding task on five classes of stimuli that differed according to perceptual domain (visual-object, visuo-spatial, and auditory): Scenes, Non-Nameable Sounds, Visually-presented Words, Aurally-presented Words, and Unfamiliar Faces. These stimulus categories take advantage of distinct neural pathways that underlie the processing of visual-object, visuo-spatial, and auditory information. These distinct pathways maintain their segregation within MTL subregions, allowing for investigation of domain-sensitive MTL encoding processes. Novelty responses along the anterior-posterior axis of MTL differentiated by stimulus class. Parahippocampal cortex demonstrated novelty-related encoding responses during the presentation of scenes, whereas anterior temporal regions, including perirhinal and inferior temporal cortices, demonstrated novelty-related encoding responses during the presentation of unfamiliar faces. These results suggest that encoding processes in MTL are not homogenous, but rather, are specialized, with certain classes of stimuli being differentially processed by specific MTL subregions.

Joe Sala

Investigating effective connectivity of prefrontal cortex and cognitive control using dynamic causal modeling

Joseph B. Sala [1], David Badre [1,2], & Anthony D. Wagner [1,3]
[1] Department of Psychology, Stanford University, [2] Department of Brain and Cognitive Sciences, MIT, [3] Neurosciences Program, Stanford University

Cognitive control guides the flow of information within multiple processing regions in line with a behavioral goal. Neuroimaging and neuropsychological investigations have implicated a distributed system of prefrontal and neocortical regions in tasks engaging cognitive control processes. Analyses of effective connectivity, such as dynamic causal modeling (DCM), are designed to characterize the influence of one local neural system over others. DCM uses a non-linear multiple-input multiple-output system to parameterize the coupling between brain regions and the impact experimental factors have on this coupling. As control demands arising in a given task are likely to be mediated by multiple interacting component neural processes, DCM has the potential to uniquely characterize the functional integration of these signals and so further constrain models of cognitive control. Presently, we outline an approach for applying DCM to test three specific classes of alternate predictions from established models of cognitive control: 1) the relationship between ACC monitoring functions and the up regulation of PFC control mechanisms in resolving response and non-response forms of conflict; 2) the processing architecture of lateral PFC, particularly focusing on the relationship among ventrolateral PFC (VLPFC), dorsolateral PFC (DLPFC), and lateral frontal polar cortex (FPC); and 3) the interactions that PFC has with posterior neocortical regions such as parietal cortex. Preliminary results highlight critical issues both in theoretical approaches to cognitive control as well as the application of effective connectivity analyses in higher-order cognition.

Daphna Shohamy

Hippocampal vs. basal ganglia contributions to probabilistic learning and reversal: Evidence from Parkinson's disease and MTL amnesia

D. Shohamy [1], C. E. Myers [2], R.O. Hopkins [3], J. DeLuca [4], J. Sage [5], K. Geghman [6] & M. Gluck [6]
[1] Department of Psychology, Stanford University, [2] Department of Psychology, Rutgers University, [3] Brigham Young University, [4] Kessler Medical Research Rehab Corp, [5] UMDNJ, [6] Center for Neuroscience, Rutgers University

Converging evidence suggests that the hippocampus and the basal ganglia make distinct contributions to learning and memory function. For example, patients with Parkinson's disease (PD) and amnesic patients show distinct patterns of impairment on probabilistic category learning tasks. The purpose of this study was to examine the contribution of each of these structures to both learning and reversal. PD and amnesic patients were tested on a novel probabilistic category learning task. In this task, subjects learn to predict a category outcome based on the presentation of three visual cues. Each cue is independently and probabilistically associated with a category outcome (.8 probability for each of the 3 cues); however, the 3-cue configuration is 100% predictive of category outcome. Thus, a subject can learn to categorize based on any of the individual three cues, or (optimally) based on the configuration of all 3 cues. Performance on this task was assessed for a group of PD patients, a group of hypoxic amnesic patients, and healthy controls. We found that all groups were able to learn the task at similar levels, and all groups appeared to learn single cue-outcome associations, rather than the 3-cue configuration. However, when challenged with a reversal, we found that amnesic patients were impaired and were not able to reverse, while the PD subjects were not. Interestingly, however, performance during the reversal phase appeared to be based upon different strategies in each of the groups: controls continued to rely upon the same cue that they used during acquisition (but reversed the outcome), PD patients used a different cue during reversal than they used during acquisition (learning a new cue-outcome association), while amnesic patients continued to use the same cue and respond with the same outcome (not reversing). These results suggest dissociated contributions of the basal ganglia vs. the MTL during learning, consistent with prior findings in animal and human studies: while the basal ganglia may be critical for incremental stimulus-response associations, the MTL appear to be involved in setting up flexible stimulus-stimulus representations.

DATA BLITZ

Susan Ravizza

The locus of selective verbal working memory deficits

Susan M. Ravizza [1,3], Stefanie L. Griffin [4], Julie A. Fiez [1,2,3], & Daniel Tranel [4]
[1] Department of Psychology, U. Pittsburgh, [2] Department of Neuroscience, U. Pittsburgh, [3] Center for the Neural Basis of Cognition, [4] Dept. of Neurology, U. Iowa

Neuropsychological case reports have documented that selective impairments of verbal working memory (VWM) can be caused by focal brain damage, with the most likely site of common damage located in the left inferior parietal cortex adjacent to the temporal-parietal junction (Shallice & Vallar, 1990). However, this finding stands in contrast to the majority of results from functional imaging studies, which have pointed to more dorsal and bilateral inferior parietal regions as being involved in VWM. To further examine contributions of parietal cortex to VWM, we conducted a retrospective review of the Iowa Patient Registry. All subjects who met the following criteria were included in the study: 1) presence of unilateral damage to inferior parietal and/or superior temporal cortices, 2) availability of digit span data obtained from the Wechsler Adult Intelligence Scale (R or III), 3) availability of spatial working memory data obtained from the Benton Visual Retention Test (BVRT), and 4) absence of damage to the prefrontal cortex. Twenty left-hemisphere (LH) and twenty (RH) patients met these criteria. RH patients were more likely to exhibit a selective deficit in spatial memory than LH patients, whereas a selective deficit of VWM was more associated with LH damage than RH damage. Of the LH patients with VWM deficits, all had damage that included portions of the temporoparietal junction, and none had damage restricted to the dorsal inferior parietal cortex. Our findings, obtained from a lesion approach, suggest that impaired VWM (as indexed by reduced digit span) is associated with ventral, but not dorsal, left parietal lesions. Moreover, the common area of overlap resided in the white matter tracts underlying the Sylvian fissure, suggesting that short-term memory deficits may be characterized best as a failure to integrate acoustic and articulatory information rather than as an impairment in phonological storage.

Audrey Duarte

Prefrontal cortex supports recollection and familiarity-based recognition: Evidence from patients with unilateral prefrontal lesions

Audrey Duarte [1], Charan Ranganath [2], Celina Trujillo [1], & Robert T. Knight [1]
[1] Helen Wills Neuroscience Institute, UC Berkeley, [2] Center for Neuroscience, UC Davis

Results from studies of patients with prefrontal lesions have generally supported the idea that the prefrontal cortex (PFC) is not necessary for recognition memory. However, recent functional neuroimaging evidence implicates this region in both recollection and familiarity-based recognition. Because typical neuropsychological studies examine memory in patients with unilateral lesions, the possibility remains that recognition processes may be supported by the intact hemisphere. In the present study, we examined recollection and familiarity in a group of patients with lateral PFC lesions (5 left, 2 right) and matched controls during the retrieval of pictures. Critically, during encoding, stimuli were presented either to the left or the right visual field (i.e., contra- and ipsilateral to the lesion) in order to specifically tax encoding processing within either the intact or lesioned hemisphere. Results from remember-know testing indicated that patients were significantly impaired in recollection for all pictures and familiarity for contralesionally-presented pictures. These results suggest that the prefrontal cortex is necessary for both familiarity and recollection.

Rich Ivry

Is sleep-related learning dependent on the hippocampus?

Michelle Sunm, Rebecca Spencer, & Richard Ivry
UC, Berkeley

Is sleep-related learning dependent on the hippocampus? To date, studies showing that sleep has a beneficial effect on memory consolidation have used explicit learning tasks. We compared sequence learning under explicit and implicit learning conditions, using the serial reaction time task. Consistent with previous reports, sleep led to a significant improvement in performance when participants were told of the presence of a sequence (explicit learning). In contrast, we failed to observe sleep-specific improvements under implicit learning conditions. The question that remains to be answered is whether the implicit/explicit distinction accounts for the differential impact of sleep, or whether is specific to implicit learning tasks that do not require the hippocampal learning system. We are conducting a second experiment in which implicit learning is thought to be mediated by hippocampal processing.

Michael Weiner

The purpose of this abstract is to inform scientists in the Bay Area about the overall activities of our Center.

The Center for Imaging of Neurodegenerative Disease at the VA Medical Center/UCSF is an interdisciplinary group of about 75 scientists focusing on use of MRI/MRS to investigate neurodegenerative diseases, especially Alzheimer's disease. Our group is composed of scientists involved in MRI/MRS technique development (including structural MRI, perfusion, diffusion, spectroscopic imaging, fMRI, image reconstruction and image processing) and medical applications (Alzheimer's disease, frontotemporal dementia, lewy body dementia, mild cognitive impairment, normal aging, ALS, Parkinson's disease, HIV, alcohol etc). Our major goals are to develop improved methods for diagnosis, treatment monitoring, and early detection of these disorders. We have two MRI scanners, one at 1.5 T and one at 4 T devoted full time to research. We have just begun to remodel a building that will hold about 100 scientists, and hope to move into our new quarters in about 1 year.

TALK SESSION III

Carter Wendelken

Organization in working memory: A computational model and experimental investigation of the role of lateral prefrontal cortex

Carter Wendelken [1] & Silvia Bunge [2]
[1] UC-Davis, Center for Mind and Brain, [2] UC-Davis, Department of Psychology and Center for Mind and Brain

It is well established that lateral prefrontal cortex (PFC) plays an important role in the short-term maintenance of information, or working memory. Obtaining a better understanding of the implementation of working memory in this region is a key goal in the study of memory and cognitive control. In this talk I will describe an implemented connectionist computational model of working memory and lateral PFC. This model is an elaboration and extension of the process-specific theory of lateral PFC, wherein the ventral subdivision (VLPFC) subserves working memory maintenance while the dorsal subdivision (DLPFC) subserves manipulation (Petrides 1991, D'Esposito et. Al 1999). The model is also aimed at reconciling this process-specific theory with evidence that suggests an important link between DLPFC and spatial representations in parietal cortex (Goldman-Rakic 1987). Specifically, the model demonstrates how working memory maintenance can be accomplished via interaction between dedicated maintainer cells in VLPFC and semantic representations in inferotemporal and parietal cortices. Most importantly, it demonstrates how the organization of maintained items can be achieved by DLPFC, as cells in this region mediate dynamic bindings between VLPFC maintainer cells and spatial representations in parietal cortex. An fMRI investigation of this model is currently being conducted. Subjects in the scanner view sets of six letters (verbal task) or grid locations (spatial task) presented in one, two, or three groups (denoted by color), and are asked to indicate, after a delay, if two probe letters or locations were in the same group. The model predicts that greater organizational demands, here assumed to correlate with number of memorized groups, will produce greater activation of DLPFC. Preliminary results of this experiment will be discussed.

Christian Fiebach

Stimulus-specific modulation of verbal working memory maintenance activity in cortical language areas

C.J. Fiebach & M. D'Esposito
Dept. of Psychology, Henry H. Wheeler, Jr. Brain Imaging Center,
Helen Wills Neuroscience Inst., UC Berkeley

Cognitive theories of verbal working memory (WM) debate whether maintenance of verbal information relies exclusively on phonological codes, or whether other codes such as orthographic, lexical or semantic representations are also activated. We used event-related fMRI during a WM task to explore the dependency of activity in cortical language areas on the availability of distinct verbal codes during verbal maintenance. Left hemispheric temporal, parietal and frontal language regions were identified in independent localizer experiments. Participants retained sets of two or five visually presented words or pseudowords over a 10 sec delay in a delayed recall task. Inferior parietal cortex, generally implicated in phonological short-term storage, is not modulated by the presence or absence of lexical-semantic representations or by WM load. However, several other language-relevant regions show stimulus-specific modulations. The left fusiform word recognition area shows a lexicality-by-load interaction, with increased activity for the maintenance of five words compared to all other conditions. Posterior temporal and anterior inferior prefrontal regions implicated in semantic processing, differentially contribute to word and pseudoword maintenance. Finally, the posterior inferior frontal lobe, associated with phonological processing, shows increased activity for pseudoword maintenance and for high vs. low WM load. Our results extend previous neurophysiological and neuroimaging studies showing top-down modulation of inferotemporal regions during visual WM. They indicate that temporary maintenance of verbal information reflects top-down modulation of cortical language areas. Furthermore, our results suggest that persistent activity during verbal WM is not restricted to areas coding phonology, but is also detectable in brain regions representing lexical-semantic information.

Brian Miller

Characterizing the dynamic interplay of bottom-up and top-down mechanisms across subcomponent processes in working memory

Brian T. Miller & Mark D'Esposito
Helen Wills Neuroscience Institute, Dept. of Psychology, University of California, Berkeley

While fMRI has revealed a number of brain regions critical for working memory (WM), it has confronted significant challenges in explaining the temporal dynamics of this distributed network. One reason for this is that neural mechanisms underpinning the encoding, maintenance, and retrieval of mnemonic representations are inherently confounded in fMRI signals due to the temporal overlap of the slowly evolving hemodynamic responses. This feature of the fMRI signal poses a major obstacle for teasing apart subtle latency differences across brain regions that could reflect differential involvement in critical processing stages. In this study, we apply a design and analysis technique (Ollinger et al., 2001) capable of estimating robust stage-specific timecourses without assuming a predicted shape of the response. Subjects performed typical "full" delayed-recognition WM trials in which a face is encoded (500ms), maintained over a brief delay (1500ms) and then retrieved. By also including an equal proportion of "cue-only" and "cue+delay" partial trials we were able to obtain unique estimates of the fMRI responses to the encoding and retrieval stages. These waveforms offer a unique opportunity to explore the relative temporal relationships of task-critical regions during discrete stages of WM. At encoding, the response in the fusiform face area (FFA) peaks before the response in both the prefrontal cortex (PFC) and the intraparietal sulcus (IPS). This timing pattern is consistent with a bottom-up flow of sensory information from visual association regions to the PFC and IPS during memory encoding. At retrieval, the left PFC becomes involved earlier than the FFA indicating a potential top-down contribution to guide the mnemonic decision. These findings highlight a role for fMRI latency analysis in detecting context-dependent timing differences across regions during subcomponent WM processes.

Jesse Rissman

Functional connectivity during working memory maintenance

Jesse Rissman, Adam Gazzaley, & Mark D'Esposito
Department of Psychology, Henry H. Wheeler, Jr. Brain Imaging Center, University of California, Berkeley

Many theories of visual working memory postulate that the prefrontal and parietal cortices provide top-down input to posterior visual association areas in order to keep behaviorally relevant sensory information activated when it is no longer present in the environment. To characterize the nature of these interactions, we applied a recently developed functional connectivity analysis method to two similar event-related fMRI datasets in which subjects performed delayed face recognition tasks. This multivariate method's principle advantage over existing analytical techniques is its ability to model the functional connectivity between brain regions during distinct stages of a cognitive task. The method is implemented by using separate covariates to model the activity evoked during the cue, delay, and probe stages of each individual trial in the context of the general linear model (GLM). The resulting parameter estimates (beta values) are sorted according to the stage from which they were derived to form a set of stage-specific beta series. Regions whose beta series are correlated during a given stage are inferred to be functionally interacting during that stage. To identify the neural network mediating the active maintenance of the face stimuli, the fusiform face area (FFA) was defined as a seed and used to generate whole brain correlation maps. Random effects analysis of correlation data (pooled across datasets) revealed a network of brain regions exhibiting significant correlations with the FFA seed during the delay period of the working memory tasks. This maintenance network included the dorsolateral and ventrolateral prefrontal cortex, premotor cortex, intraparietal sulcus, caudate nucleus, thalamus, hippocampus, and occipitotemporal regions. Many of these regions showed robust correlations during all stages of the task. This finding is in sharp contrast with that obtained using a standard univariate analysis approach, which revealed a dramatic decrease in BOLD signal levels throughout the brain during the delay period. The ability of the beta series correlation method to detect high correlations in the presence of low univariate activity suggests that there is more information contained in fMRI data than is typically revealed by univariate analysis methods. These findings support the idea that the coordinated functional interaction of prefrontal and parietal regions with posterior visual association areas plays an integral role working memory maintenance.

TALK SESSION IV

Adam Gazzaley

Top-down enhancement and suppression of the magnitude and speed of neural activity

Adam Gazzaley, Jeffrey W. Cooney, Kevin McEvoy, Robert T. Knight, & Mark D'Esposito
Henry H. Wheeler Jr. Brain Imaging Center, Helen Wills Neuroscience Institute & Department of Psychology,
University of California, Berkeley

Human interaction with the environment involves a fluid integration of internally-driven, goal-directed decisions concerning encountered stimuli (top-down modulation) and externally-driven, perceptual influences that demand attention based on stimulus salience (bottom-up processes). Top-down modulation thus underlies our ability to selectively focus on relevant stimuli and ignore distracting stimuli, establishing a foundation for attention and memory. Theories addressing neural mechanisms of top-down modulation are driven by studies that reveal increased magnitude of neural activity in response to directed attention, but are limited by a lack of data reporting modulation of neural processing speed, as well as comparisons with a perceptual baseline necessary to evaluate the presence of enhancement and suppression. Utilizing functional MRI (fMRI) and event-related potential recordings (ERP), we provide converging evidence that both the magnitude of neural activity and the speed of neural processing are modulated by top-down influences. Furthermore, we show that both enhancement and suppression occur relative to a perceptual baseline depending on task instruction and document neural correlates of capacity limitations in these top-down resources. Lastly, we will review preliminary data of alterations in top-down modulation with aging as well as cholinergic control of enhancement and suppression. These findings reveal the fine degree of goal-directed control individuals can exert over cortical activity, the limitations and mechanism of such control, and age-related alterations in top-down modulation.

Stefan Ursu

Dissociating outcome representation from top-down control in the human orbitofrontal cortex

Stefan Ursu [1], Kristi A. Clark [2], V. Andrew Stenger [3], & Cameron S. Carter [4]
[1] Department of Psychiatry, UC Davis, [2] Department of Neuroscience, UCLA,
[3] Department of Radiology, University of Pittsburgh, [4] Department of Psychiatry, UC Davis

The human orbitofrontal cortex (OFC) is known to play a critical role in goal-directed behavior. Research to date has not been able to clearly distinguish the effects of changes in motivational states from associated adjustments in cognitive control. Therefore, it is still unknown whether the OFC contribution to guiding behavior is through top-down control of inappropriate responses or through providing a motivational context by representing potential outcomes. In two functional magnetic resonance imaging (fMRI) studies, we simultaneously and independently manipulated demands for inhibitory control and monetary incentives for correct performance. Across experiments, demands for control only engaged the OFC when they also increased the likelihood of a negative outcome, in the form of increased error rates. Irrespective of whether the demands for control were high or low, the OFC activity was modulated by expected outcomes, and its lateral areas were maximally engaged during expectation of negative outcomes. Thus, we provide convergent evidence that the OFC is specifically involved in establishing the motivational context of behavior through representation of possible outcomes.

David Badre

Frontal lobe mechanisms that resolve proactive interference

David Badre [1,2] & Anthony Wagner [1,3]
[1] Department of Psychology, Stanford University, [2] Department of Brain & Cognitive Science, MIT, [3] Neuroscience Program, Stanford University

Past experience can interfere with processing of subsequent experience; a phenomenon termed proactive interference (PI). Neuroimaging evidence has associated resolution of such PI during short-term item recognition with activation in left mid-ventrolateral prefrontal cortex (mid-VLPFC; ~BA 45). Left mid-VLPFC control processes could resolve PI through several distinct mechanisms. In this talk, predictions from several such mechanisms of PI resolution are detailed, and results are presented from an fMRI experiment that tests these predictions under conditions of PI from both verbal and non-verbal stimuli. On alternating blocks, subjects maintained a target set of words or patterns over a short delay (3 s), and then decided if a subsequent probe stimulus was contained in the current target set (positive) or not (negative). For half of the negative and positive trials, the probe had been contained in the previous target set (recent). Relative to non-recent trials, negative recent trials produced a reliable increase in response time (RT) and error rates for both verbal and non-verbal trials. In fMRI measures, recency was associated with increased activation in left mid-VLPFC, frontal polar cortex (FPC), and right inferior frontal gyrus, during both negative and positive trials. Behavioral correlations further demonstrated that the left mid-VLPFC recency effect was positively associated with recency-derived RT slowing, whereas the recency effect in FPC correlated with recency-derived changes in target discrimination. Finally, regions sensitive to verbal PI showed little sensitivity to non-verbal PI. Considered as a whole, the results serve to specify and constrain the proposed models of PI resolution.