Center for Neuroscience

UNIVERSITY OF CALIFORNIA AT DAVIS

Long-term (episodic) memory: Functional and neuroanatomical considerations

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Visit us on the web at: http://DynamicMemoryLab.org

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Why assess long-term memory?

- LTM is one of the most severely impaired cognitive functions in schizophrenia
- LTM impairments are not explained by
  - education or gender
  - medication status
  - duration or severity of illness
- Traditional neuroleptic medications do not ameliorate LTM impairment
- Degree of LTM impairment strongly predicts functional outcome
- Relates directly to other cognitive functions:
  - Planning for the future
  - Prospective memory (e.g., remember to take your medicine)

Courtesy Dan Ragland

CNTRICS Survey: Candidate constructs in long-term memory

- Encoding (including item and relational, binding, or associative encoding)
- Retrieval (item specific or associative/relational)
- Source Memory
- Strategy Generation and Application
- Recollection
- Familiarity
- Semantic Memory/Representations
- Semantic Priming
- Reinforcement based learning

Overview

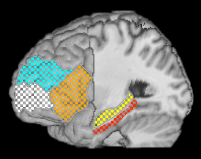
Clarification of CNTRICS constructs

Part I:

- Theoretical foundations
- Interrelationships

Part II:

- Potential neural substrates
  - Lateral Prefrontal Cortex (PFC)
  - Medial Temporal Lobes (MTL)



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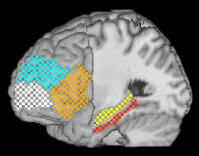


Life cycle of a memory

Forgetting

The BIG picture

- Long-term memory encoding and retrieval are not analagous to a camcorder or a computer hard disk
- What you remember depends collectively on
  - what happens during encoding processing
  - the available cues and processes that are engaged during retrieval

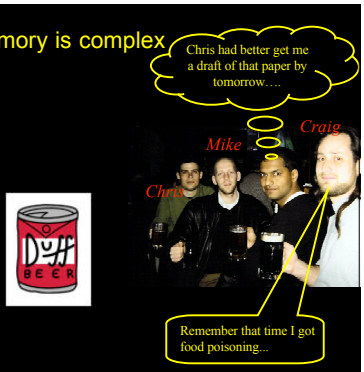
The BIG picture

- Transfer appropriate processing:
  - relationship between type of processing at encoding, and the type of retrieval test
- Encoding specificity
  - relationship between the information that is encoded and the nature of retrieval cues.
- Context dependency
  - even the study context can act as a retrieval cue.

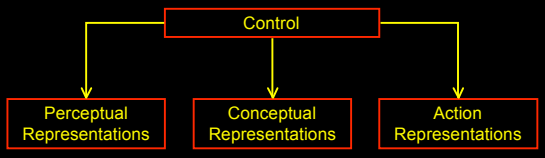
Long-term memory encoding

- The relationship between how information is processed and the degree to which this processing impacts learning is called encoding

Memory is complex



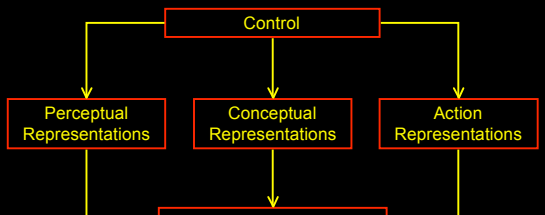
Memory is the outcome of multiple cognitive operations



Working memory/Long-term memory "Encoding"

- Partly determines the "content" and subsequent accessibility of memories
- Thus, impairments to other aspects of cognition (e.g., WM, attention, etc.) will affect LTM performance

Memory encoding is the outcome of multiple cognitive operations



Binding the disparate aspects of an event makes it a coherent **episodic memory**

Memory Retrieval

- The set of processes involved in recovering/reconstructing a memory for a prior event
- Retrieval Cue: a piece of information that can guide retrieval of a memory of a prior event
- Different types of tests offer different types of retrieval cues

Free Recall, Cued Recall & Recognition

Free Recall	What items were on the list?
Cued Recall	What item was paired with *window*? (or)
	What item began with *rea*____?
Yes/No Recognition	Was *reason* on the list?
Forced-choice Recognition	Which was on the list, *reason* or *tree*?
Remember/Know	*reason* Remember, Know or Not studied?

Test	Cues
Free Recall	Context
Cued Recall	Context + part of list item
Y/N Recognition	Context + entire list item
F-c Recognition	Context + entire list item + entire nonlist item

Slide courtesy of Craig Stark

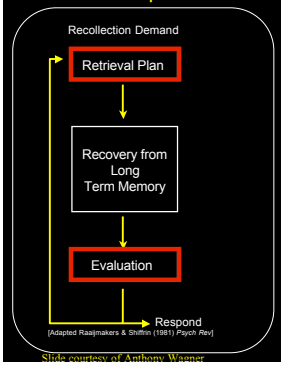
Retrieval Cues

- A piece of information that elicits retrieval of a memory of a prior event
- Different types of tests offer different types of retrieval cues

Free Recall:	Cued Recall:	Recognition Memory
???	"C____"	"Cabin?"

Fewer Cues ⟷ More Cues

Component Processes of Episodic Retrieval

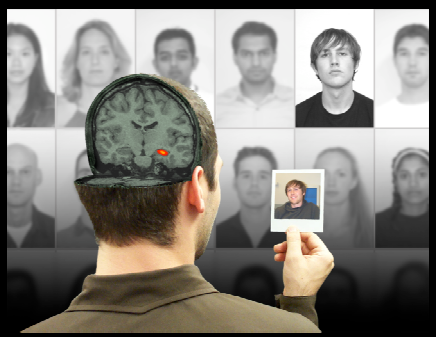


Pre-Retrieval Processes
- Use goals to constrain retrieval
- Maintain cues in WM

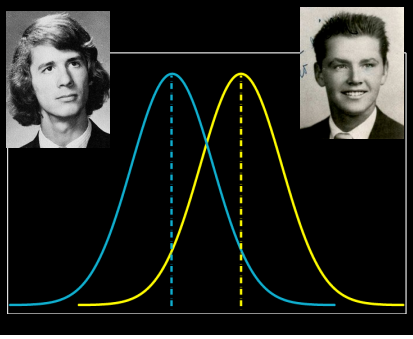
Post-Retrieval Processes
- Selection of relevant retrieved details
- Constructive inferences
- Attributional processes (systematic ←→ heuristic)

Slide courtesy of Anthony Wagner

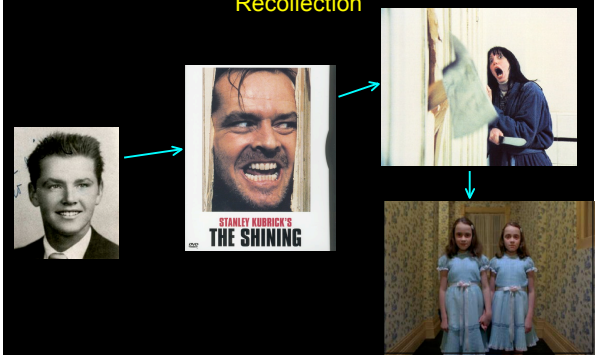
Recognition memory



Familiarity



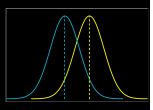
Recollection



Dual-process models of recognition

Two processes are used to recognize items

- Familiarity
  - A graded change in the "strength" of an item with repetition
  - Similar to SDT or "Global Matching" models
  - Does not specify context of an event
  - Influence is relatively fast
- Recollection
  - "Pattern completion" process
  - Supports source memory
  - Also supports recall and accurate associative memory
  - Influence requires more time



See Diana et al. PBR (2006) Yonelinas (2002) JML; Norman & O'Reilly (2003) Psych Rev.

Evidence for dual process models

1. Differences between recall and recognition
2. Remember-Know Method
3. Item vs. Source Memory
4. Process-Dissociation Procedure
5. Differential electrophysiological correlates

Source Monitoring Framework (SMF)

Johnson et al. (1993)

"…people do not typically directly retrieve an abstract tag or label that specifies a memory's source…rather, activated memory records are evaluated and attributed to particular sources through decision processes performed during remembering"

- Different memories have different characteristics
  - Records of thoughts, feelings, actions, sensations
- Accurate memory attributions depend on:
  - Availability of specific information about previous event
  - Monitoring processes to weight specific information when making a decision

Source Monitoring Framework (SMF)

Johnson et al. (1993)

Familiarity vs. Recollection

- Recollecting an event relies on the availability of specific information (sights, sounds, etc.)
- Familiarity is a nonspecific kind of information that generally does not specify source
- Thus, familiarity is more susceptible to misattribution errors ("false fame effect")…

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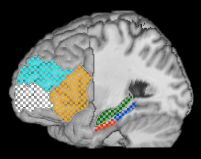
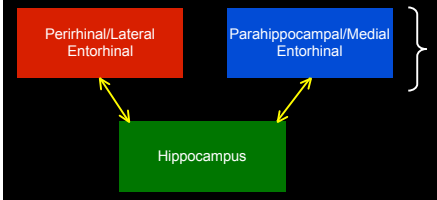
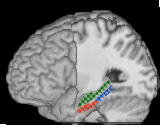


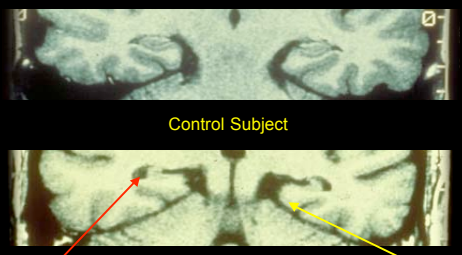
Medial Temporal Lobes & Memory



- MTL damage causes severe anterograde amnesia
- Involved in forming representations that help bind episodic memories

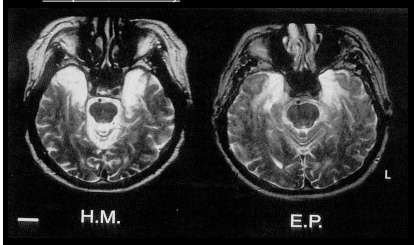


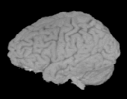
Hippocampal Damage as Seen Using MRI



H.M.: Temporal Lobectomy

E.P.: Viral Encephalitis





These types of conditions affect the hippocampus and the cortex of the parahippocampal gyrus (entorhinal, perirhinal, parahippocampal cortex)

Stefanacci et al. (2000), *J Neurosci*

Slide courtesy of Craig Stark

Theories/Models/Ideas about MTL function

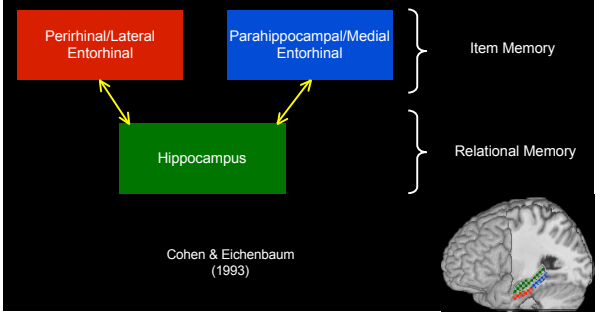
Animal models:

- Spatial memory (O'Keefe & Nadel)

Models for human amnesia:

- Declarative memory (Squire)
- Relational Memory (Cohen and Eichenbaum)
- Episodic memory (Tulving)
- Recollective Memory (Aggleton & Brown)
- Rapid, complex associations (McClelland, McNaughton & O'Reilly)

Medial Temporal Lobes & Recognition Memory

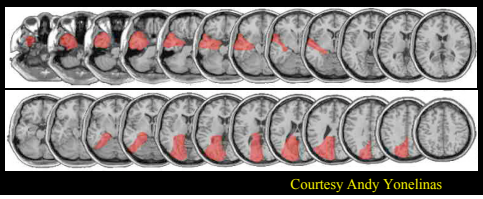


Cohen & Eichenbaum (1993)

Yonelinas et al. (2002): H vs. H+ Lesions

Patients (3-5/group + age-matched controls)

- **Hippocampal Lesions (H)**: hypoxic-ischemic (cardiac arrest)
- **Hippocampal and parahippocampal Lesions (H+)**: Left temporal lobectomy, and left posterior cerebral artery infarct (stroke) patients

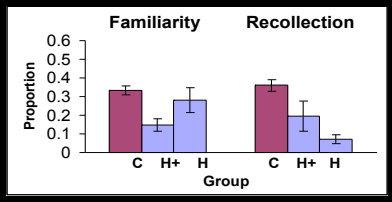


Courtesy Andy Yonelinas

Remember/Know

Study: word1, word2…

Test: word2, word7…"R / K / N"

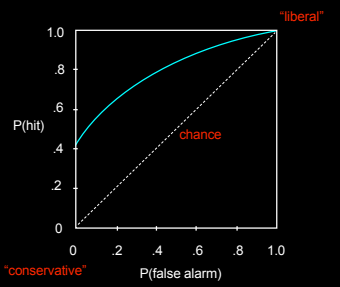


- *Patients with focal hippocampal damage show specific recollection deficits*
- *Patients with hippocampal + perirhinal damage show deficits in familiarity and recollection*

Courtesy Andy Yonelinas

Two-processes revealed in human recognition by ROC

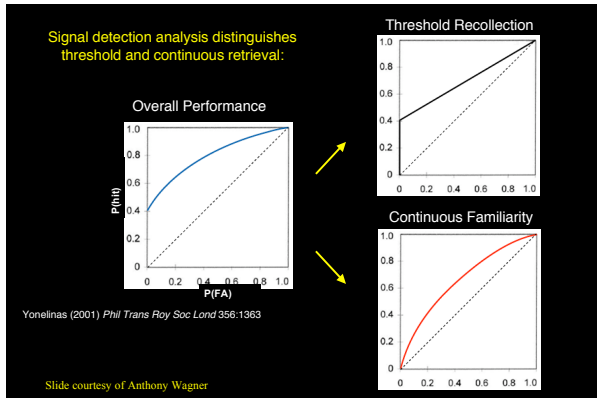
ROC: Overall Performance



Slide courtesy of Anthony Wagner

Yonelinas (2001) Phil Trans R Soc Lond 356:1363

Signal detection analysis distinguishes threshold and continuous retrieval:



Yonelinas (2001) *Phil Trans Roy Soc Lond* 356:1363

Slide courtesy of Anthony Wagner

Neuropsychological studies

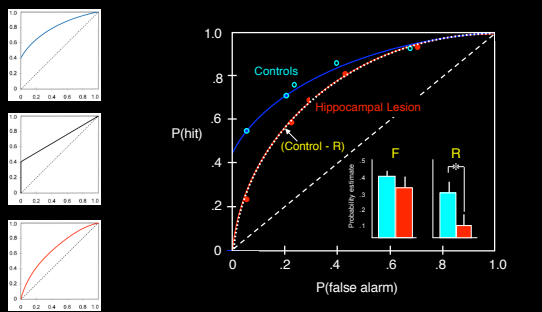
Amnesia literature

- Hippocampal amnesic patients (e.g., mild hypoxia) can show impaired recollection with normal familiarity
  - e.g., Yonelinas et al. (2000), Aggleton et al. (2005), Holdstock et al. (2005)
- ...but some studies report impaired familiarity and recollection
  - e.g., Manns & Squire (2000), Cipolotti et al. (2006), Wais et al. (2006)

Animal neuropsychology

- Mixed results, but mapping b/w tasks and processes is unclear
- Fortin et al. (2004):
  - Analysis of recognition ROC curves in rats using dual-process model
  - Focal hippocampal lesions in rats impaired recollection but not familiarity

Recollection depends on the hippocampus

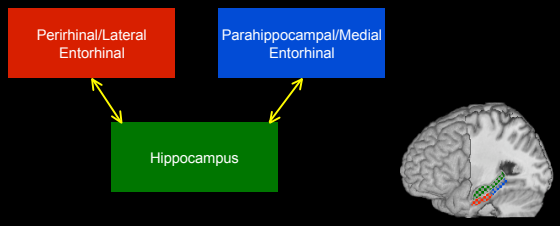


Slide courtesy of Anthony Wagner

Fortin et al., *Nature* 431:188, 2004

Recollection and Familiarity: FMRI studies

Is there evidence for differentiation within the MTL?

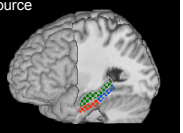


Recollection and Familiarity: FMRI studies

Is there evidence for differentiation within the MTL?

Eichenbaum, Yonelinas, & Ranganath (in press) Ann. Rev. Neurosci.

- Reviewed results from contrasts that reported neural correlates of Recollection and/or Familiarity in the MTL
- Recollection:
  - Remember > Know
  - Recognized items w/ source > Recognized w/o source
- Familiarity:
  - Know > Forgotten
  - Recognized w/o source > Forgotten
  - Correlations with recognition confidence

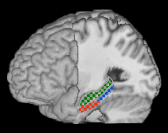


Recollection and Familiarity: FMRI studies

Is there evidence for differentiation within the MTL?

Eichenbaum, Yonelinas, & Ranganath (in press) Ann. Rev. Neurosci.

- Compared frequency of activations reported in
  - Hippocampus (Hipp)
  - Posterior Parahippocampal Gyrus (PPHG)
  - Anterior Parahippocampal Gyrus (APHG)



FMRI Studies: Familiarity

Study	*Method*	*Materials*	*Stage*	*Contrast*	*HIPP*	*PPHG*	*APHG*
Davachi et al., 2003	SC/SI/Miss	words	Encoding	SC=SI > Miss	None	None	L
Gold et al., 2006	SC/SI/Miss	words	Encoding	SC=SI > Miss	L	B	R
Henson et al., 1999	RKN	words	Encoding	K > R	None	None	R
Kensinger & Schacter, 2006	SC/SI/Miss	emotional pictures	Encoding	SI > Miss	None	None	L
Kensinger & Schacter, 2006	SC/SI/Miss	emotional words	Encoding	SI > Miss	None	None	L
Kirwan & Stark, 2004	Assoc. rec.	face-name	Encoding	intact recognized > intact called new	None	R	R
Ranganath et al., 2003	SC/SI/1-6	words	Encoding	1-4 linear increase	None	None	L
Uncapher & Rugg, 2005	RKN	words	Encoding	K > Miss	None	None	R
Uncapher et al., 2006	SC/SI/Miss	words + 2 sources	Encoding	All recognized > forgotten	None	None	L
Daselaar et al., 2006	1-6 conf	words	Retrieval	1-6 linear decrease	L	None	L
Eldridge et al., 2005	RKN	picture-word	Retrieval	RK>Miss=CR	R	R	None
Gonsalves et al., 2005	RKN	faces	Retrieval	R>K>Miss=CR	None	L	B
Montaldi et al., 2006	1-4R	scenes	Retrieval	1-4 linear decrease	None	None	B
Weis et al., 2004	SC/SI/Miss	scenes	Retrieval	SI>Miss	None	None	R
Yonelinas et al., 2005	1-4R	words	Retrieval	1-4 linear decrease	B	None	None
				Reported Activations	**4**	**4**	**13**
				Total contrasts	**15**	**15**	**15**
				%	**27%**	**27%**	**87%**

FMRI Studies: Recollection of items

List does not include studies in which items are associated with other items

Study	*Method*	*Materials*	*Stage*	*Contrast*	*HIPP*	*PPHG*	*APHG*
Davachi et al., 2003	SC/SI/Miss	words	Eneeding	SC > SI	B	L	None
Gold et al., 2006	SC/SI/Miss	words	Eneeding	SC > SI	None	None	L
Kensinger & Schacter, 2006	SC/SI/Miss	emotional pictures	Eneeding	SC > SI	L	R	None
Kensinger & Schacter, 2006	SC/SI/Miss	emotional words	Eneeding	SC > SI	L	None	None
Ranganath et al., 2003	SC/SI/1-6	words	Eneeding	SC > SI	R	R	None
Uncapher & Rugg, 2005	RKN	words	Eneeding	R > K	L	None	None
Uncapher et al., 2006	SC/SI/Miss	Words + 2 sources	Eneeding	Both SC > 1 or 2 SI	R	None	None
Staresina & Davachi, 2006	Recall+Source	Words + colors	Eneeding	Recall > SC > SI > Miss	B	None	L*
Cansino et al., 2002	SC/SI/Miss	words	Retrieval	SC > SI	R	L	None
Daselaar et al., 2006	1-6 conf	words	Retrieval	6 > 1-5	L	None	None
Dolcos et al., 2005	RKN	neutral pictures	Re	R > K	B	R	None
Dolcos et al., 2005	RKN	emotional pictures	Re	R > K	B	B	B
Eldridge et al., 2000	RKN	words	Retrieval	R > K	B	R	None
Kahn et al., 2004	SC/SI/Miss	words	Retrieval	SC > SI	None	B	None
Montaldi et al., 2006	1-4R	scenes	Retrieval	R > all else	B	None	None
Sharot et al., 2004	RKN	scenes	Retrieval	R > K	None	R	None
Weis et al., 2004	SC/SI/Miss	scenes	Retrieval	SC > SI	B	None	None
Wheeler & Buckner, 2004	RKN	words	Retrieval	R > K	B	None	None
Woodruff et al., 2005	RKN	words	Retrieval	R > K	R	R	None
Yonelinas et al., 2005	1-4R	words	Retrieval	R > 4	B	L	None
				Activations	**17/20**	**11/20**	**3/20**
				%	**85%**	**55%**	**15%**

FMRI Studies: Recollection of associations between items

Study	*Method*	*Materials*	*Stage*
Jackson & Schacter, 2004	Assoc. rec.	word pairs	Encoding
Kirwan & Stark, 2004	Assoc. rec.	face-name	Encoding
Eldridge et al., 2005*	RKN	picture-word	Retrieval
Fenker et al., 2005	RKN	word-fearful face	Retrieval
Fenker et al., 2005	RKN	word-neutral face	Retrieval
Kirwan & Stark, 2004	Assoc. rec.	face-name	Retrieval

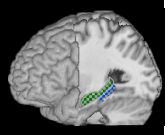
FMRI Studies: Recollection of associations between items

Study	*Method*	*Materials*	*Stage*	*Contrast*	*HIPP*	*PPHG*	*APHG*
Jackson & Schacter, 2004	Assoc. rec.	word pairs	Encoding	Intact hit > intact called recombined	L	None	L
Kirwan & Stark, 2004	Assoc. rec.	face-name	Encoding	Intact hit> intact called recombined	R	R	None
Eldridge et al., 2005*	RKN	picture-word	Retrieval	R > K	L*	None	B
Fenker et al., 2005	RKN	word-fearful face	Retrieval	R > K	R	None	R
Fenker et al., 2005	RKN	word-neutral face	Retrieval	R > K	B	L	None
Kirwan & Stark, 2004	Assoc. rec.	face-name	Retrieval	Intact hit > intact called recombined	R	R	B
				Reported Activations	**6**	**3**	**4**
				Total contrasts	**6**	**6**	**6**
				%	**100%**	**50%**	**67%**

Recollection and Familiarity: FMRI studies

Is there evidence for differentiation within the MTL? **Yes**

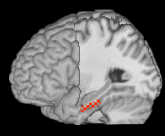
- Hippocampal activation is
  - Consistently higher for recollected than non-recollected items
  - Generally insensitive to changes in familiarity strength.
- Similar results in the PPHG
- Results consistent across
  - Encoding and retrieval
  - Different measurement techniques
  - Different stimulus types.

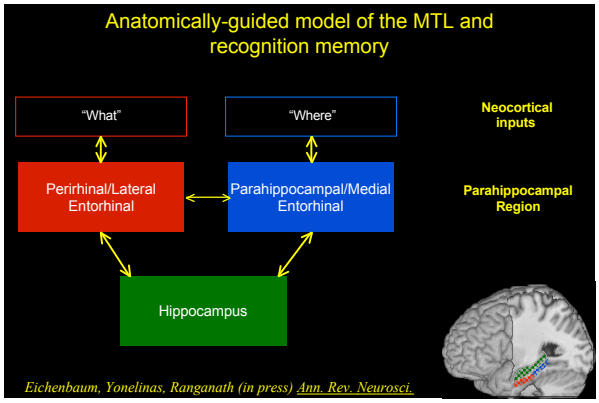


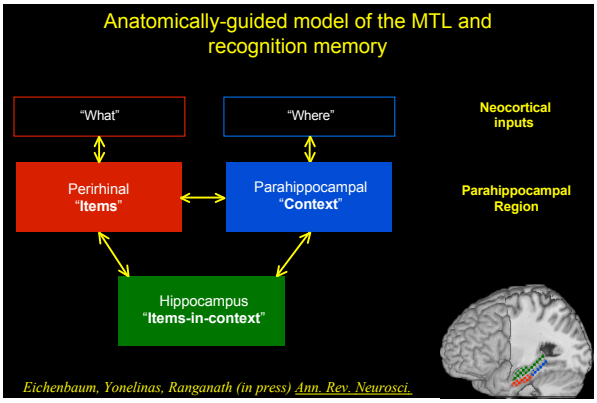
Recollection and Familiarity: FMRI studies

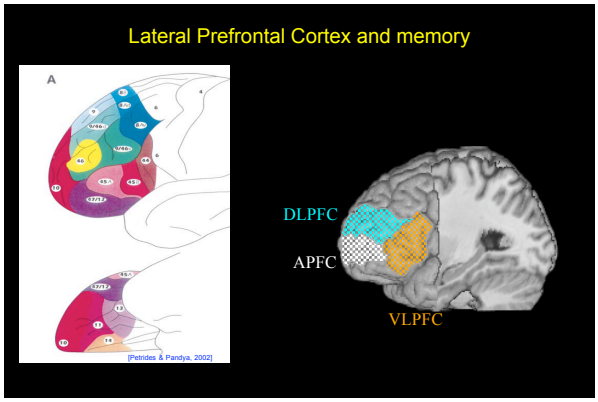
Is there evidence for differentiation within the MTL? **Yes**

- APHG activation is
  - Consistently correlated with familiarity
  - Rarely correlated with recollection of items
  - May be correlated with recollection when items are associated with other items
- Results consistent across different measurement techniques and different stimulus types.









PFC and Memory: Lesion Studies

- Patients with PFC Lesions—most common complaint is "memory problems"
- In fact, research suggest memory impairment depends on how material is studied and tested.
- Orbital prefrontal patients may have specific memory deficits

Summary of Lesion Results

PFC patients show…

- Near-normal memory...
  - ...when given structured encoding tasks
  - ...when given retrieval tests that place minimal demands on effortful processing (e.g., forced choice recognition)
- Impaired memory...
  - ...when forced to initiate strategies during encoding
  - ...when given retrieval tests that require more effortful processing (e.g., free recall, source memory)

Improving memory in PFC patients

- If patients with PFC patients have problems initiating strategies to encode and retrieve information, can these deficits be addressed?
- Effects of
  - Organization of material
  - Constrained encoding tasks
  - Specific retrieval cues

PFC lesions and memory

Theories generally fall into 2 classes:

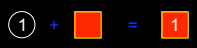
1. Selection accounts
   - Distractibility
   - Poor ability to resolve interference
2. Organizational accounts
   - Poor use of strategies
   - Little evidence for organizational structure in memory performance

Imaging results suggest that both accounts have some validity

Blumenfeld & Ranganath (in press) The Neuroscientist

Levels of organization in episodic memory

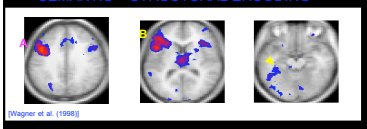
1. Events are composed of items in context.

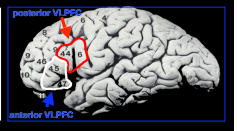


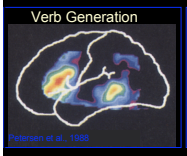
2. Binding associations between events.

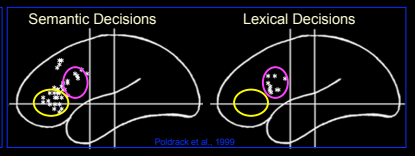
VLPFC: Depth of Processing at Encoding

SEMANTIC > STRUCTURAL ENCODING



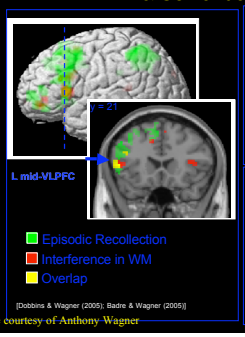


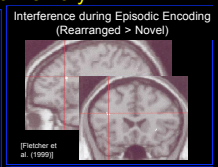


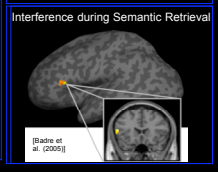


Slide courtesy of Anthony Wagner

Interference Resolution in Episodic Memory, Working Memory, & Semantic Memory

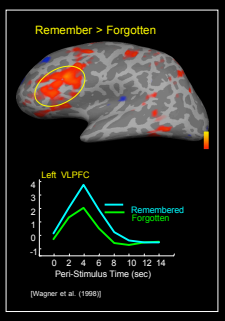


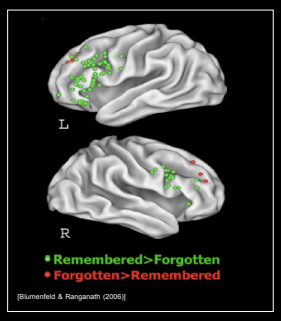




Slide courtesy of Anthony Wagner

VLPFC: Encoding Predictors of Subsequent Memory

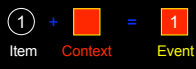




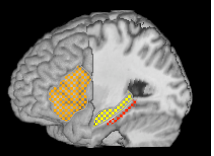
Slide courtesy of Anthony Wagner

VLPFC and Memory

1. Binding items to a particular context.

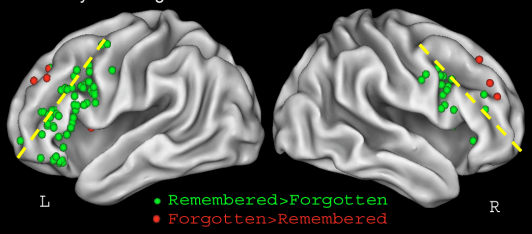


VLPFC may contribute to long-term memory by specifying features of items during encoding and resolve competition during retrieval



FMRI studies of memory formation

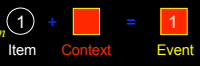
Activation peaks in PFC reported in >30 FMRI studies of memory encoding:



Blumenfeld & Ranganath, (2006) J. Neuroscience

FMRI studies of memory formation

- Consistent subsequent memory effects in VLPFC, but not in DLPFC
- Most of these studies focused on encoding of item-specific information (i.e., *"Was this item on the study list?"*)



Blumenfeld & Ranganath, (2006) J. Neuroscience

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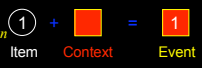
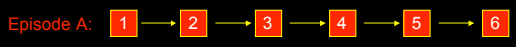


- Few studies have looked at memory for associations *between* items



Blumenfeld & Ranganath, (2006) J. Neuroscience

How are episodes bound in long-term memory (LTM)?

- Working memory (WM) control processes implemented by dorsolateral prefrontal cortex (DLPFC) may solve this binding problem

DLPFC and relational binding in WM

- DLPFC activation tends to be relatively weak in tasks that primarily involve
  - Selection/inhibition of stimuli or responses
  - Short-term maintenance of items or locations
- DLPFC activation tends to be seen in tasks that involve processing of relationships between items
  - "Chunking" (Bor et al., 2004, 2005)
  - "Manipulation" (e.g., D'Esposito et al., 1999, 2000; Postle et al., 1999)
  - Mathematical operations (Prabhakaran et al., 2001)
  - Extraction and integration of relationships during reasoning (Christoff et al., 2001, Kroger et al., 2002)

Hypothesis

- DLPFC encodes relations between items in list
- Most FMRI studies focus on item-specific encoding conditions and retrieval tests
  - Encoding inter-item relations is often irrelevant and possibly detrimental to performance
- DLPFC activity should be related to successful memory formation specifically when relational encoding processes are emphasized

DLPFC and relational binding in WM and LTM

- Several studies have now shown that DLPFC activity is correlated with successful LTM formation specifically when
  - relational processing is engaged during encoding…
  - and/or when retrieval test is sensitive to organization/relational binding
  - Examples:
    - Blumenfeld & Ranganath (2006), J. Neuroscience
    - Murray & Ranganath (in press), J. Neuroscience
    - Staresina & Davachi (2006), J. Neuroscience
    - Summerfield et al. (2006), PLoS Biology

PFC and relational binding in WM and LTM

Question:

How do we bind associations between items in memory?

Hypotheses:

1. DLPFC supports relational processing during memory encoding
2. DLPFC activity during encoding supports successful encoding of associations between items

Linda Murray

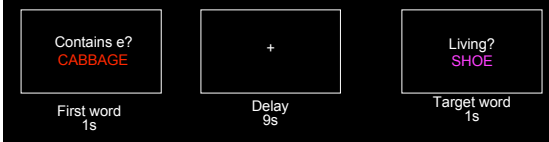
The experiment:

Examine DLPFC activation during encoding of word pairs using tasks that focus on item-specific or relational processing

Murray & Ranganath (in press…almost)

Item-specific vs. relational encoding

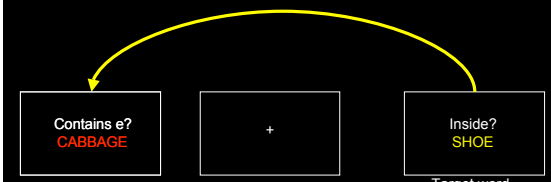
- **Item-Specific Encoding Trials:**



First word 1s | Delay 9s | Target word 1s

Item-specific vs. relational encoding

- **Relational Encoding Trials:**

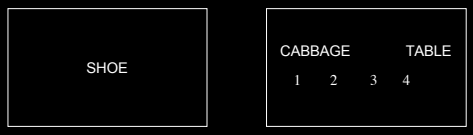


First word 1s | Delay 9s | Target word 1s

Subsequent LTM tests

- Item memory: Remember-Know test

- Associative memory: Associative Recognition

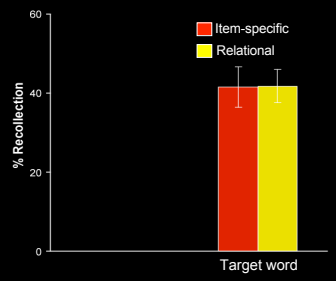


Activity during WM trials averaged as a function of performance on subsequent LTM test

Overview

- On item-specific encoding trials, participants deeply process target word in isolation
- On relational encoding trials, participants build a relationship between first word and target word

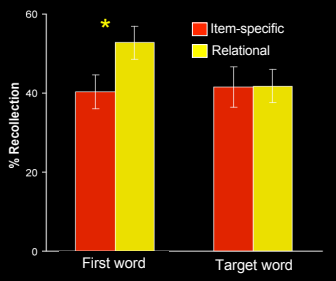
Subsequent LTM performance: Item Memory



- Target word Memory: Relational = Item-Specific
- *Both tasks **equally** effective for encoding item information*

Murray & Ranganath (in press…almost)

Subsequent LTM performance: Item Memory

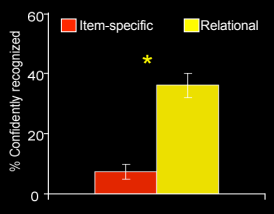


- First word memory: Relational > Item-Specific
- *Relational task involves association b/w first and target words*

Murray & Ranganath (in press…almost)

Subsequent LTM performance

Associative memory increased for relational encoding trials



Murray & Ranganath (in press…almost)

Predictions

WM

- *DLPFC activation during target word encoding should be ___ on relational than on item-specific trials*

LTM

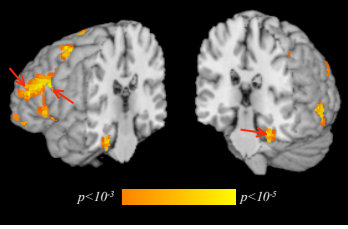
- *DLPFC activity during target word should specifically predict subsequent memory for inter-item associations*

FMRI Results

- Relational > Item-specific during target word processing:

FMRI Results

- Relational > Item-specific during target word processing:
- L. DLPFC (BA 46)
- L. VLPFC (BA 44, 45/47)
- L. Parahippocampal cortex



Predictions

WM

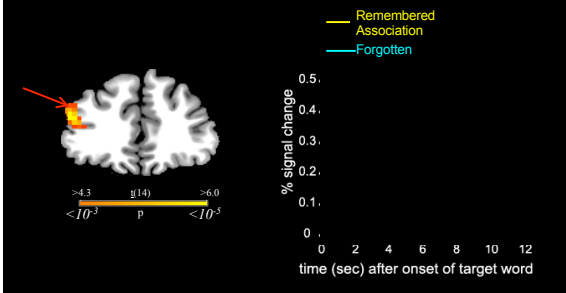
✓ *DLPFC activation during target word higher on relational than on item-specific trials*

LTM

❑ *DLPFC activity during target word should specifically predict subsequent memory for inter-item associations*

FMRI results: DLPFC (BA 46)

• DLPFC activation predicts associative memory formation



Murray & Ranganath (in press…almost)

FMRI results: DLPFC (BA 46)

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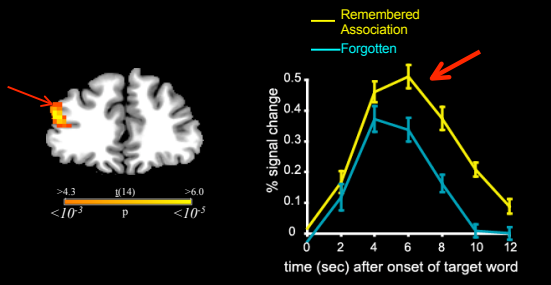
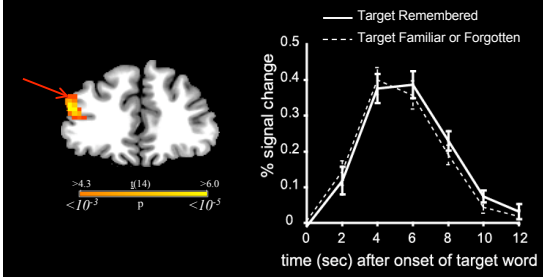


Murray & Ranganath (in press…almost)

FMRI results: DLPFC (BA 46)

•Activation does not predict subsequent memory for target word



Murray & Ranganath (in press…almost)

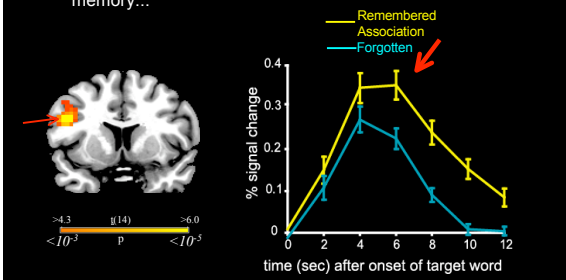
Hypotheses

- ✓ *DLPFC activity during target word higher on relational than on item-specific trials*
- ✓ *DLPFC activity during target word specifically predicts subsequent memory for inter-item associations*

What about VLPFC?

FMRI results: VLPFC (BA 44)

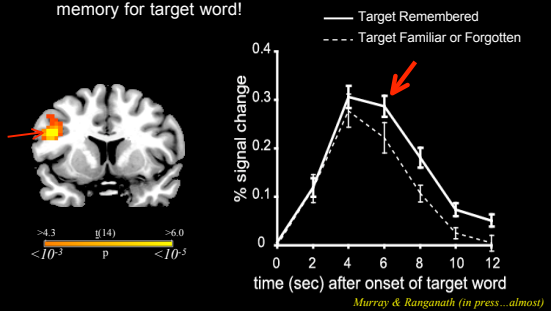
• Target word activation predicts subsequent associative memory...



Murray & Ranganath (in press…almost)

FMRI results: VLPFC (BA 44)

- ...and subsequent item memory for target word!

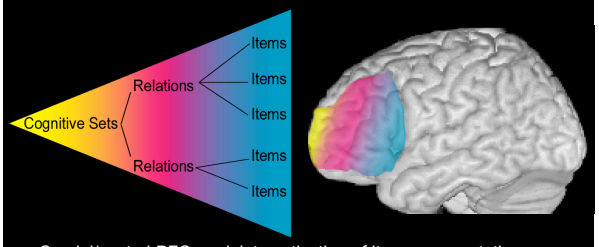


Murray & Ranganath (in press...almost)

Overall summary

1. DLPFC activation is increased during active processing of relationships between items in WM
   - Semantic
   - Temporal
2. DLPFC activation specifically predicts subsequent LTM when processing of relational information is critical
3. VLPFC (BA 44) activation predicts item and relational memory under a broader range of conditions

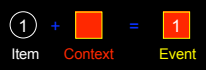
Rampant speculation: Hierarchical organization of PFC

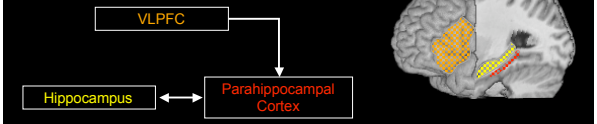


- Caudal/ventral PFC modulate activation of item representations
- More rostral/dorsal regions modulate activation of rules that support organization and relational memory

Rampant speculation: Levels of binding

1. Binding items to a particular context.

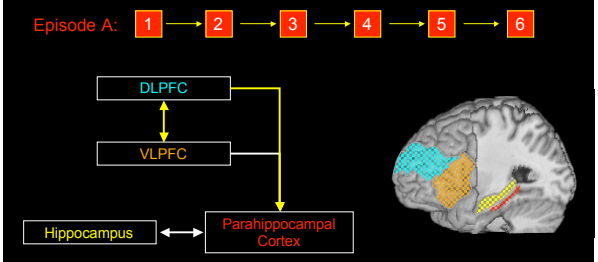




Hypothesis: VLPFC intact/compensating in Schizophrenia

Rampant speculation: Levels of binding

2. Binding associations between events.



Hypothesis: DLPFC impaired in Schizophrenia

Open questions

- Relationships between individual difference variables and experimentally-studied processes
  - Often assumed to be the same…
  - …but individual differences may be driven by genetic and environmental factors that diffusely affect multiple neurocognitive systems
  - Examples:
    - Autoimmune response during pregnancy can affect brain development
    - Genetic polymorphisms that affect efficiency of GABA-ergic transmission

Open questions

- Relationships between individual difference variables and experimentally-studied processes
- Mapping measures to processes
  - Memory measures aren't process-pure

Open questions

- Relationships between individual difference variables and experimentally-studied processes
- Mapping measures to processes
- Relationships between LTM and other CNTRICS content areas:
  - Perception, WM, attention, executive control, social cognition

Open questions

- Relationships between individual difference variables and experimentally-studied processes
- Mapping measures to processes
- Relationships between LTM and other CNTRICS content areas
- Potential solution:
  - Look for patterns of convergence/divergence across memory and "non-memory" measures
  - Identify **theory-guided** factors

Acknowledgements

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Visit us at: http://DynamicMemoryLab.Org



Rob

Linda

Craig

Rachel

Debbie

Mike

Logan


Andy Yonelinas


Howard Eichenbaum

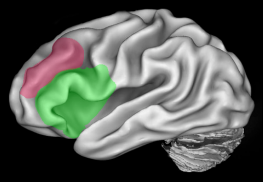
Extra slides

A role for DLPFC in WM and LTM

DLPFC: BA 9 & 46

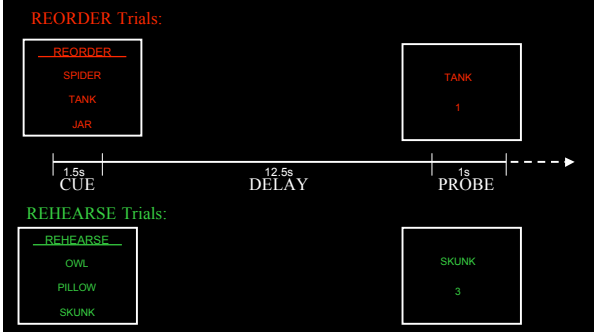
WM: Active Manipulation & Organization

LTM: *Enhancing inter-item associations?*




Rob Blumenfeld

Experimental Design: WM task



Blumenfeld & Ranganath, (2006) J. Neuroscience

Experimental Design: LTM task

REMEMBER: studied details?

KNOW: recog. w/o details?

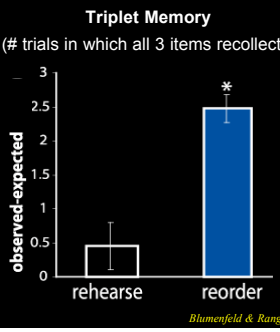
NEW: new item?

fMRI Activity during WM trials averaged as a function of performance on subsequent LTM test

LTM Performance

- WM maintenance on rehearse trials should support LTM by building item strength
- Relational processing on reorder trials should support LTM by building associations between the items in each triplet

Increased relational memory on reorder trials

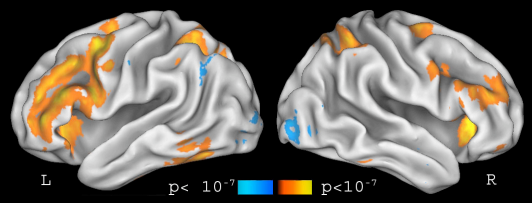


Blumenfeld & Ranganath, (2006) J. Neuroscience

Predictions

- WM
- *DLPFC activity during memory delay should be higher on reorder than on rehearse trials*
- LTM
- *DLPFC activity during delay period will be related to subsequent LTM specifically on reorder trials*

REORDER - REHEARSE



DLPFC and VLPFC: Reorder > Rehearse during delay period

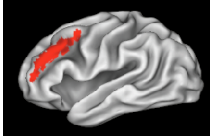
Blumenfeld & Ranganath, (2006) J. Neuroscience

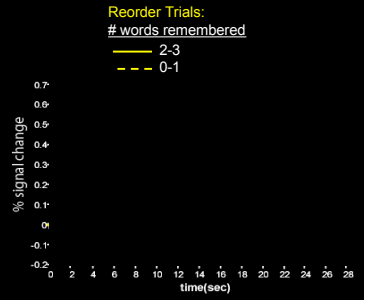
Predictions

- ✓ WM
- ✓ *DLPFC activity during memory delay higher on reorder than on rehearse trials*
- LTM
- *DLPFC activity during delay period will be related to subsequent LTM specifically on reorder trials*

FMRI Subsequent Memory Effects:

DLPFC: Left BA 46/9

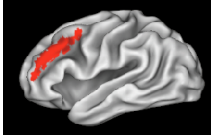


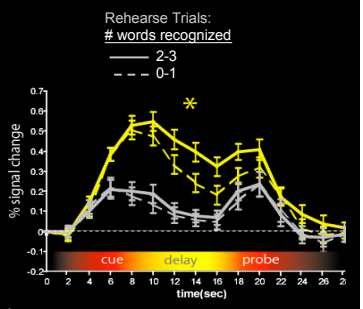


- Significant subsequent memory effect on reorder…

FMRI Subsequent Memory Effects:

DLPFC: Left BA 46/9





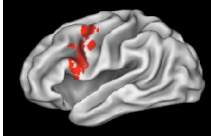
- …but not on rehearse trials

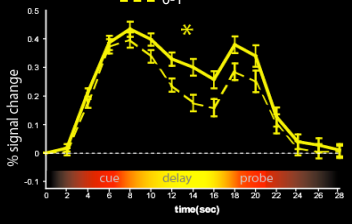
Results in DLPFC

- ✓ WM
- ✓ *DLPFC activity during memory delay higher on reorder than on rehearse trials*
- ✓ LTM
- ✓ *DLPFC activity during memory delay specifically correlated with subsequent LTM on reorder trials*

FMRI Subsequent Memory Effects:

VLPFC: Left BA 6/44

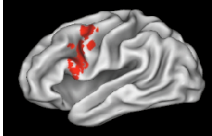


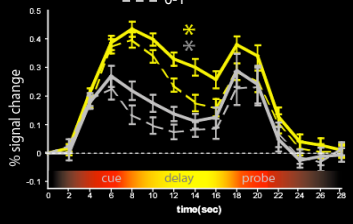


- Significant subsequent memory effect on reorder…

FMRI Subsequent Memory Effects:

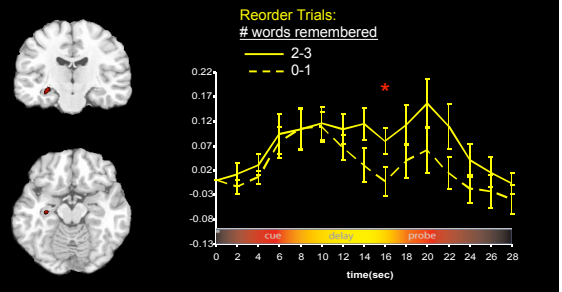
VLPFC: Left BA 6/44





- …and on rehearse trials

Hippocampal subsequent memory effect during late delay period



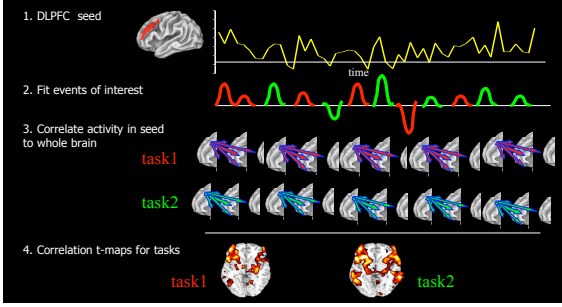
p<.05

Functional connectivity in prefrontal cortex

- Do different PFC subregions act as independent modules?
- No. More likely that relational processing in WM depends on interaction b/w DLPFC and VLPFC
- If so, then connectivity between DLPFC and VLPFC should be increased during reorder trials, as compared with rehearse trials.

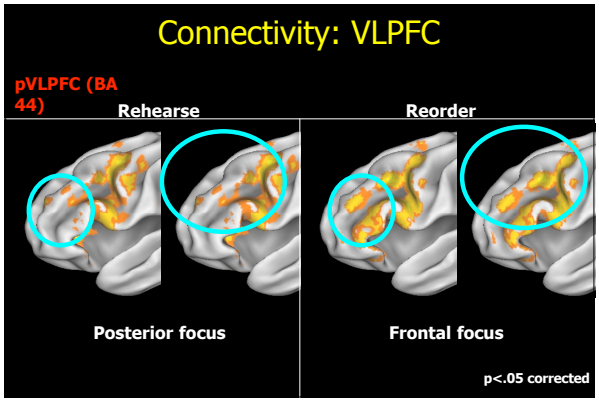
Functional Connectivity

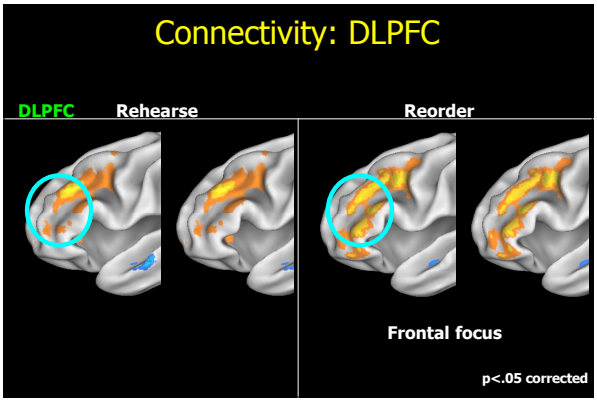
Seed Correlation method: (Rissman et al 2004)



Maintenance vs. Manipulation

- **Predictions**:
- **Rehearse Trials**: Increased connectivity b/w PFC and posterior cortex during delay period
- **Reorder Trials**: Increased connectivity between DLPFC and VLPFC during delay period


Connectivity: VLPFC
pVLPFC (BA 44)
Rehearse
Reorder
Posterior focus
Frontal focus
p<.05 corrected


Connectivity: DLPFC
DLPFC
Rehearse
Reorder
Frontal focus
p<.05 corrected