

Presentation 5 – Michael Motes

Testing Hypotheses of Changes in Prefrontal Function Related to Gulf War Syndrome

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Purpose

- Summarize previous work on neuroimaging age-related cognitive deficits
- Propose model for understanding Gulf War Syndrome-related cognitive deficits

Gulf War Symptoms

Syndrome: "Impaired Cognition"

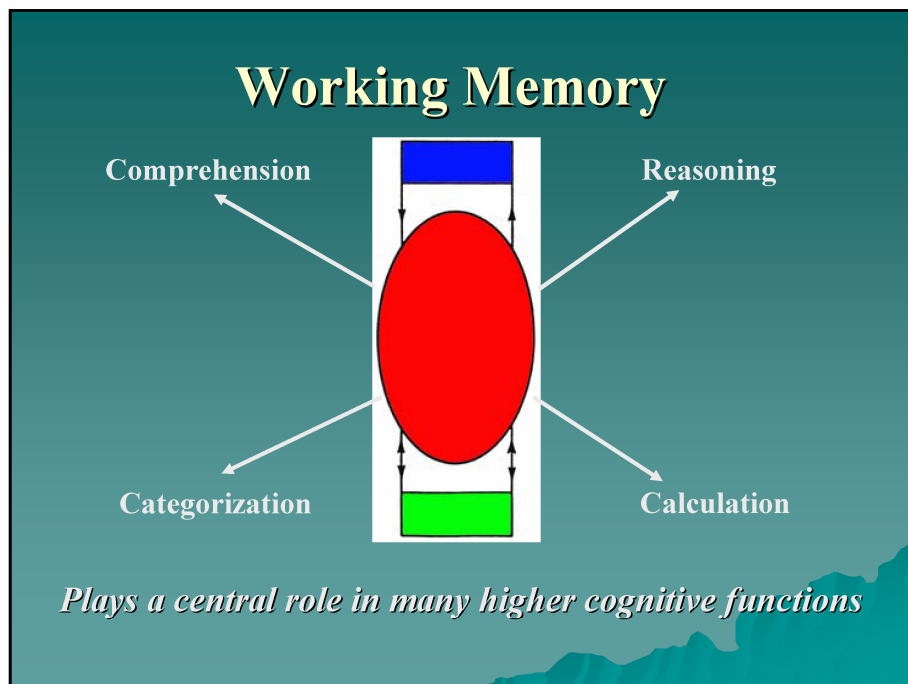
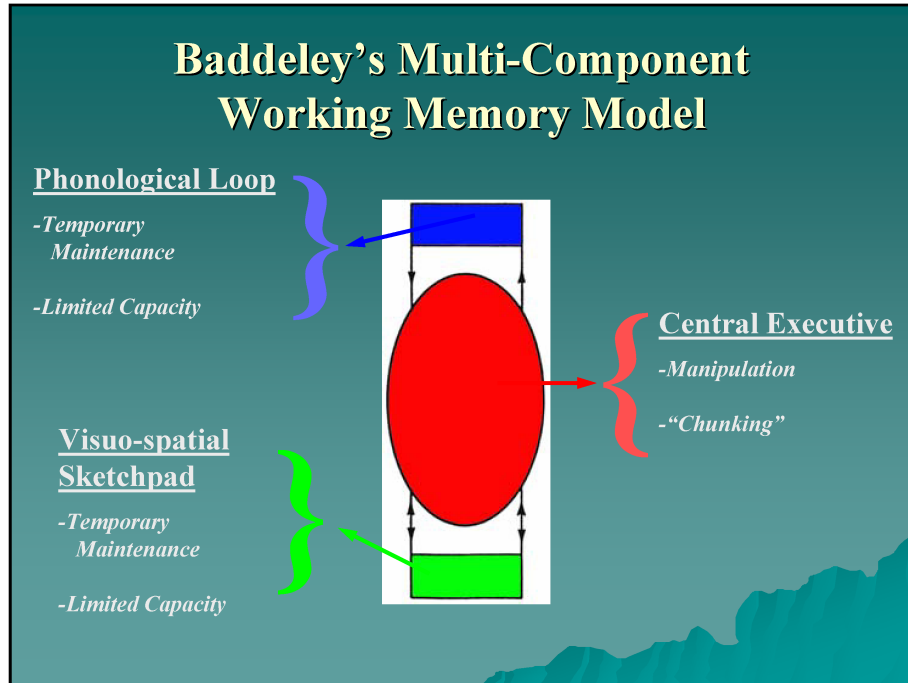
- Memory
 - Impaired short-term memory
- Executive Control
 - Impaired attention/concentration
- Reasoning

Haley, Kurt, & Hom, 1997

What is Working Memory?

Processes that support:

- *short-term retention of information*
- *manipulation of that information*



Neural Underpinnings of Working Memory

Working memory task

Associative memory task

Cue

Cue and response

Delay

Response

PFC Lesion

Working Memory

Long-term Memory

Impaired

Unimpaired

Goldman-Rakic et al., 1992

Used fMRI to Examine Functional Subsystems of Prefrontal Cortex

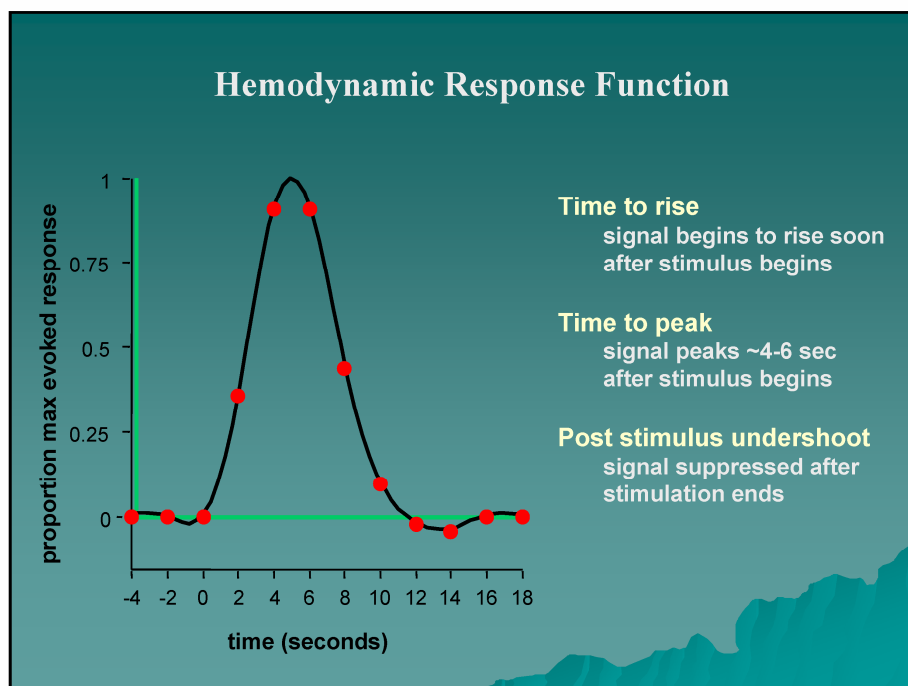
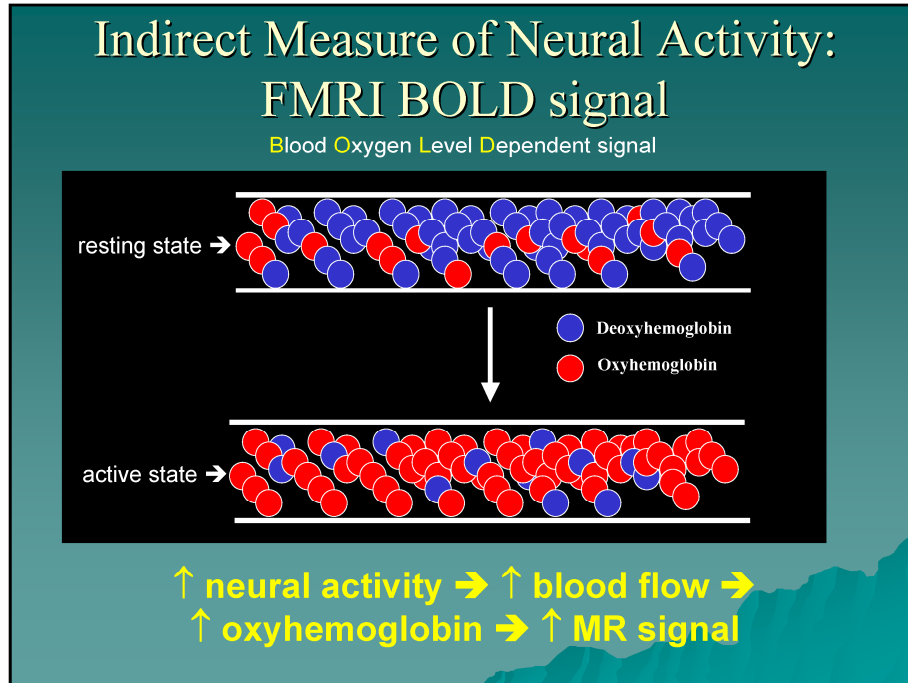
Dorsolateral Prefrontal Cortex

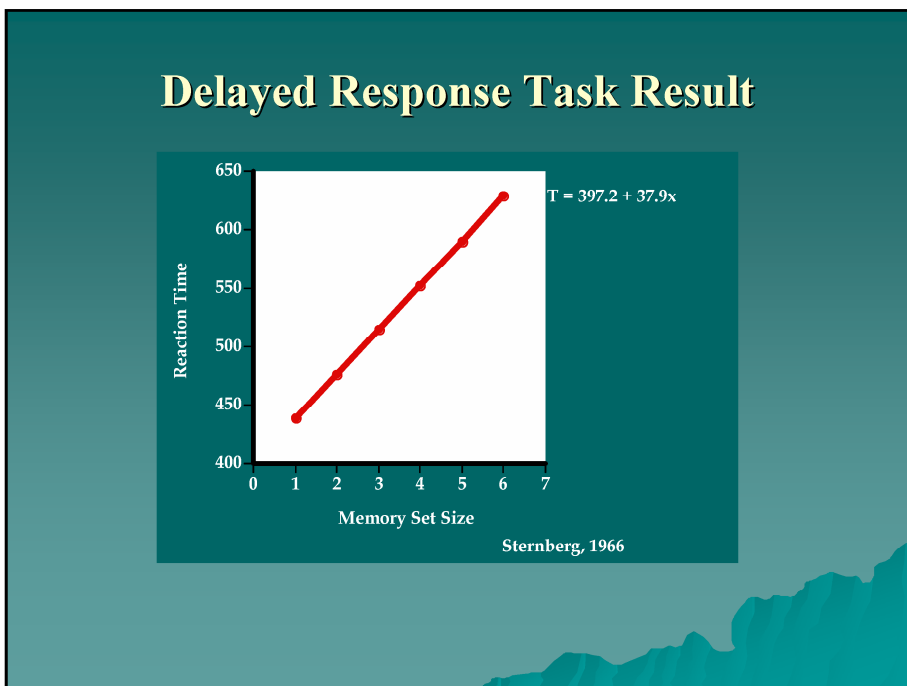
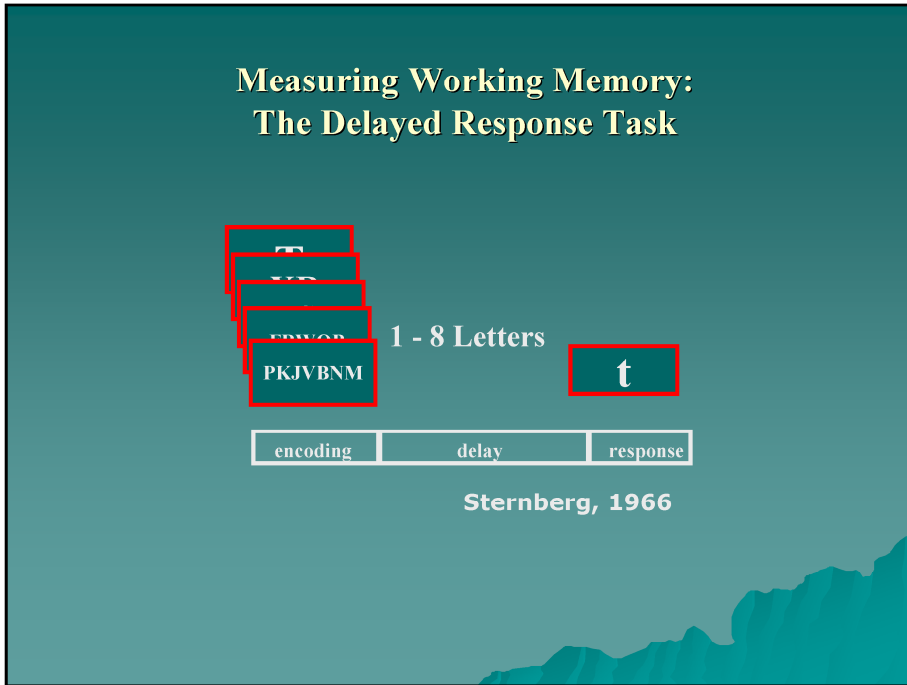
- Manipulation Working Memory Processes
- Chunking*

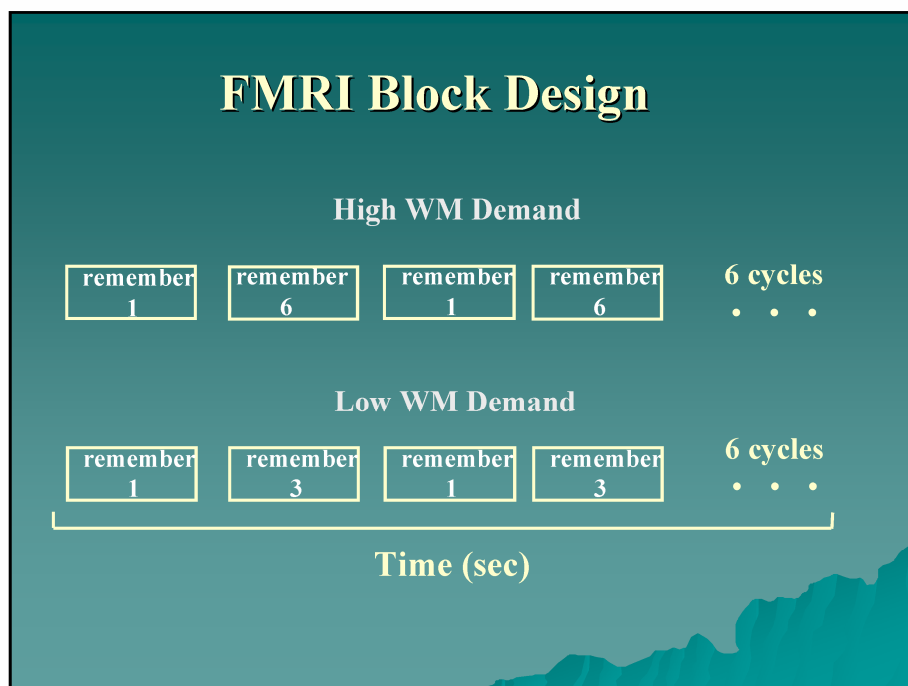
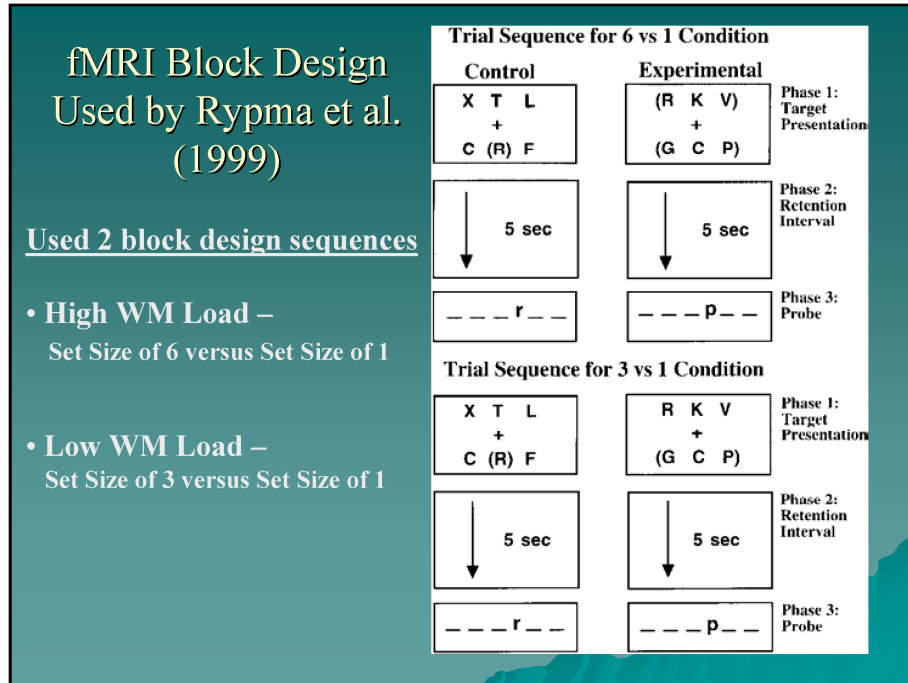
Ventrolateral Prefrontal Cortex

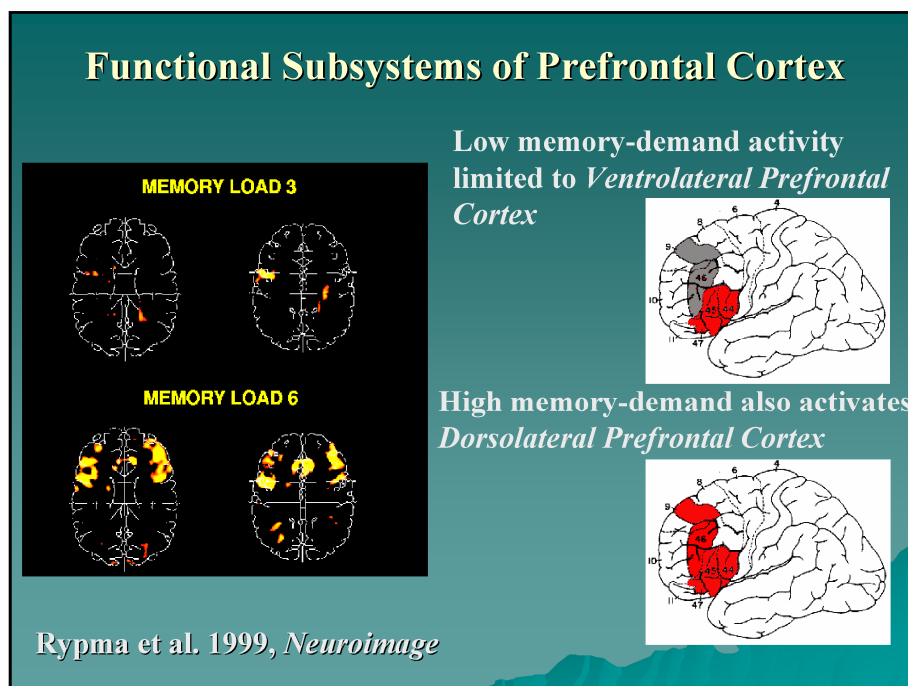
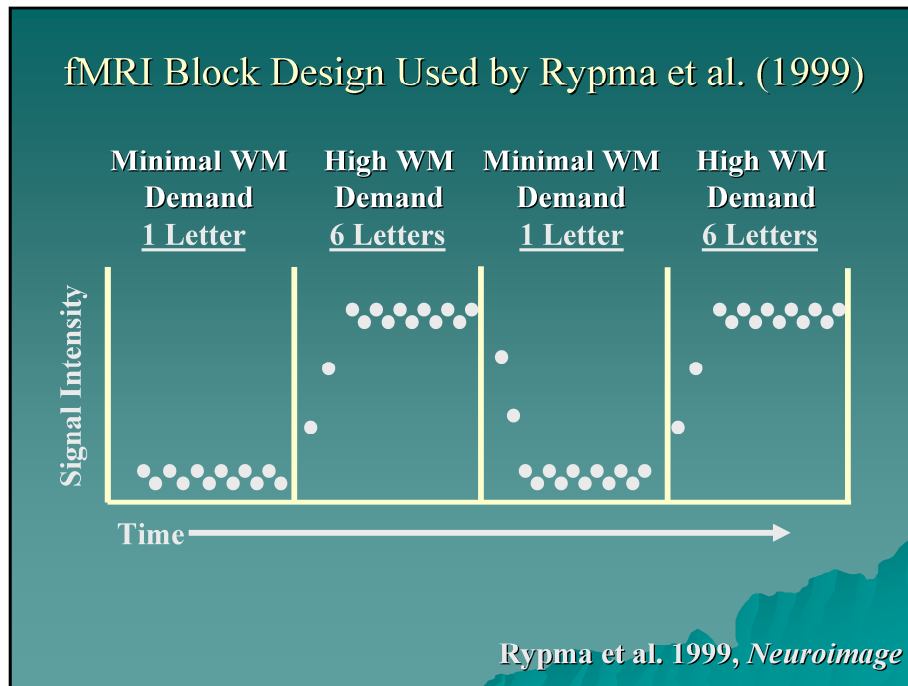
- Maintenance Working Memory Processes
- Rehearsal*

(Rypma et al. 1999, *Neuroimage*)



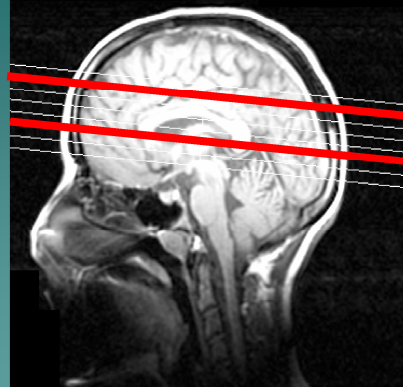






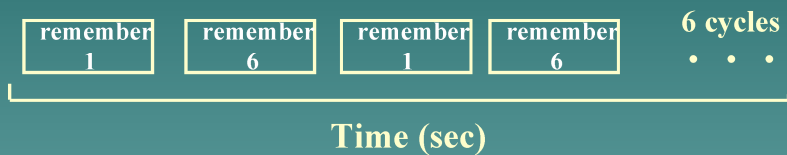
Relationship between PFC Function & Age-Related WM Deficits

- ❖ 6 younger subjects, 6 older subjects
- ❖ Delayed Response WM Task

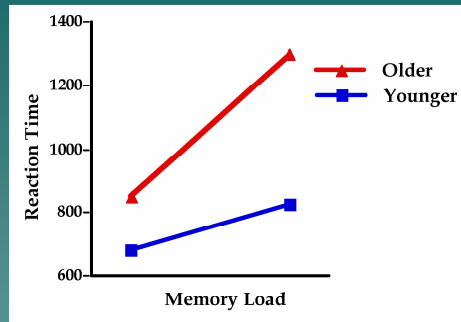


Rypma, Prabhakaran, Desmond, & Gabrieli, 2001
Psychology and Aging

FMRI Block Design



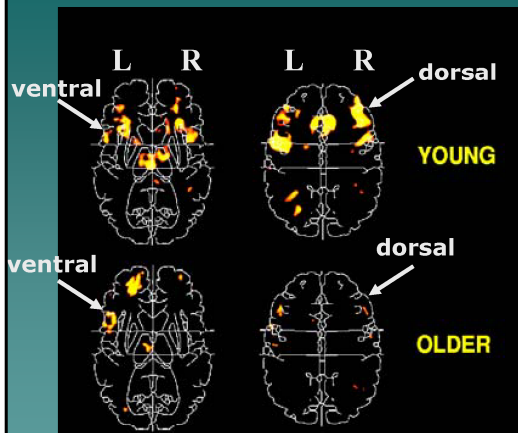
Age Differences in Memory Search Time



(Anders, Fozard & Lillyquist, 1972)

Age differences increase with increasing memory set size

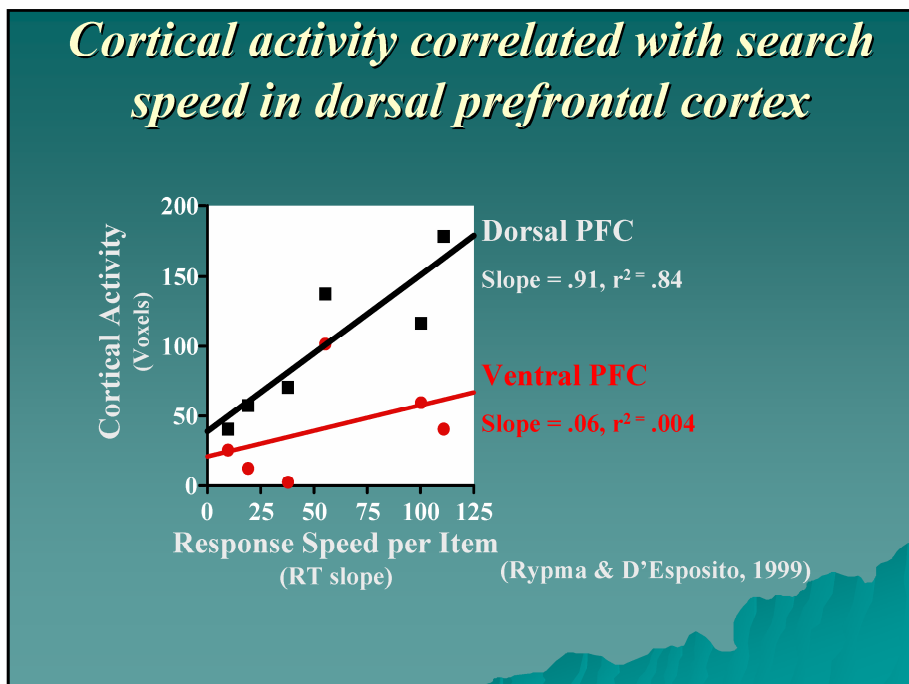
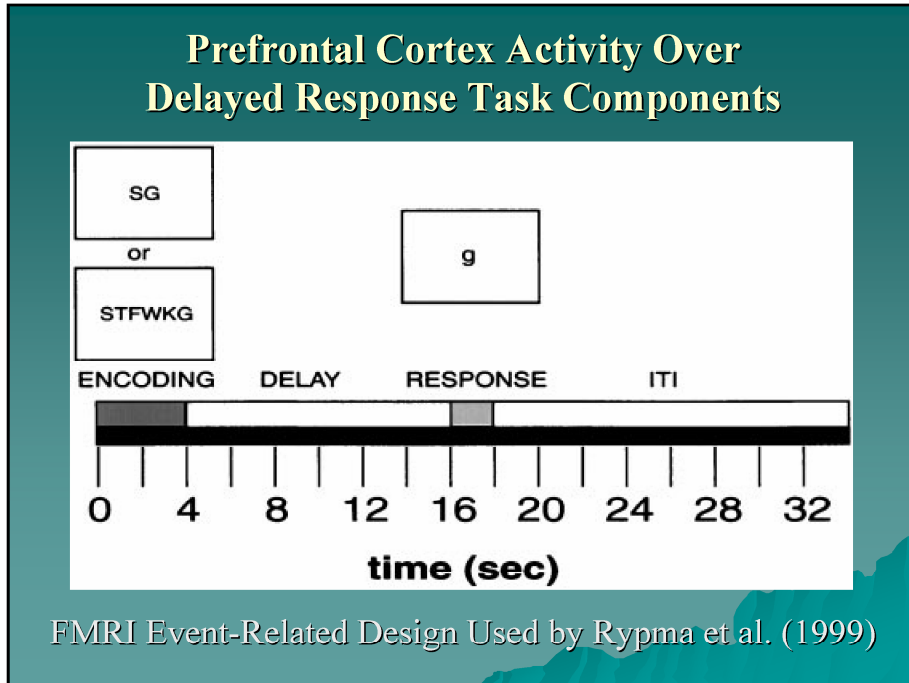
FMRI Results



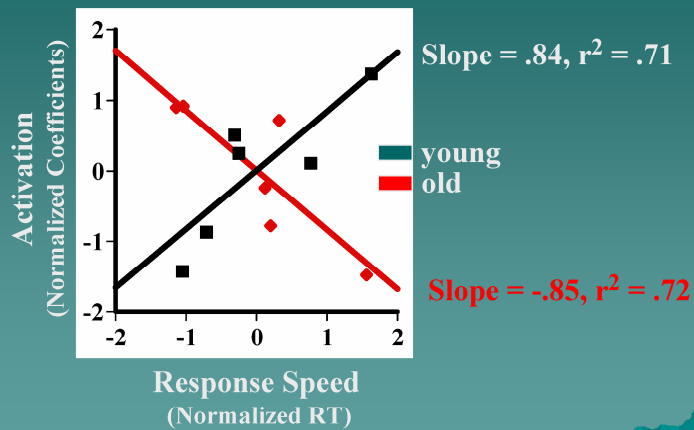
-Decreases in dorsal PFC activation with age

-Equivalent ventral PFC activation with age

Rypma, Prabhakaran, Desmond, & Gabrieli, 2001
Psychology and Aging



Dorsolateral PFC Activity Differentially Related to Search Speed for Young and Old



(Rypma & D'Esposito, 2000
Nature-Neuroscience)

Processing Speed

Digit Symbol Substitution Test

10. DIGIT SYMBOL	1	2	3	4	5	6	7	8	9	SCORE															
	1	2	3	4	5	6	7	8	9																
	-	J	□	L	U	O	△	X	=																
SAMPLES																									
	2	1	3	7	2	4	8	2	1	3	2	1	4	2	3	5	2	3	1	4	5	6	3	1	4
	1	5	4	2	7	6	3	5	7	2	8	5	4	6	3	7	2	8	1	9	5	8	4	7	3
	6	2	5	1	9	2	8	3	7	4	6	5	9	4	8	3	7	2	6	1	5	4	6	3	7
	9	2	8	1	7	9	4	6	8	5	9	7	1	8	5	2	9	4	8	6	3	7	9	8	6

... (90sec)

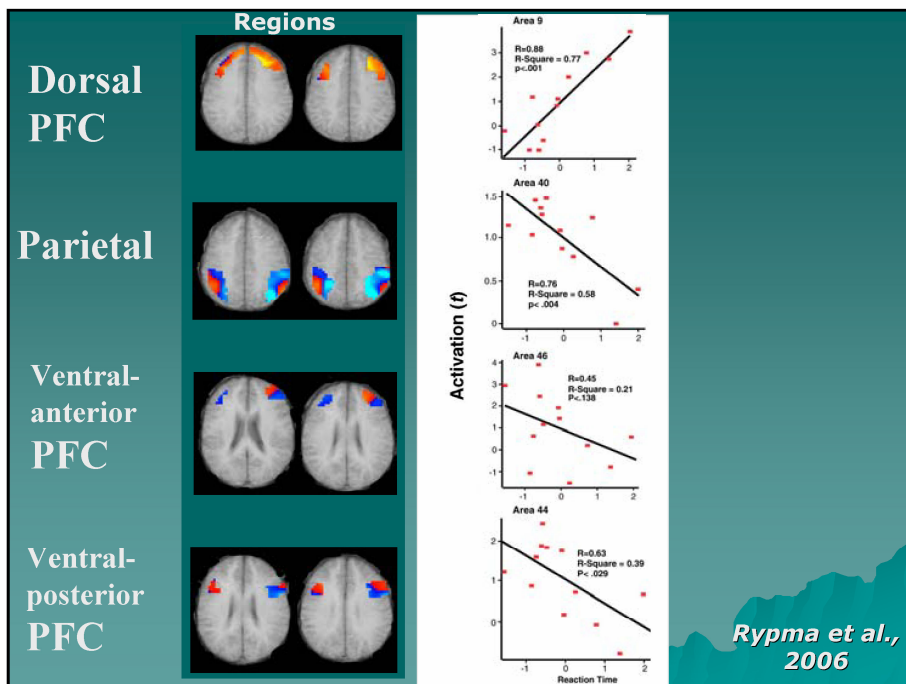
- *Psychometric research identified processing speed as basic cognitive ability*
- *Age-related variability in processing speed predicts variability in other cognitive tasks*

A Symbol-Digit Test for fMRI

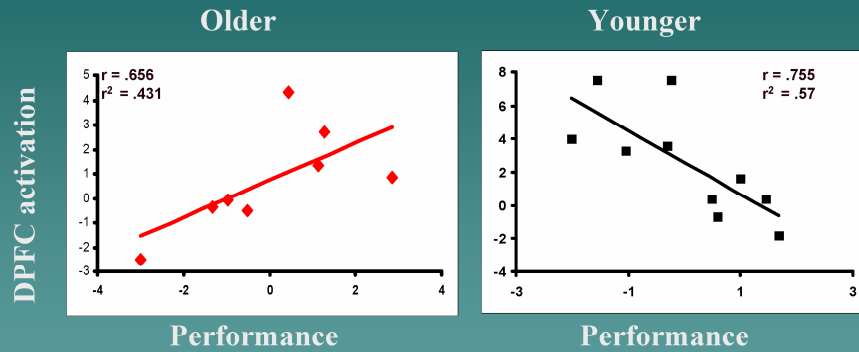
□	◦	┌	┐	└	>	+	□	◦
1	2	3	4	5	6	7	8	9



The "Symbol-Digit Verification Task"
Rypma et al., 2006

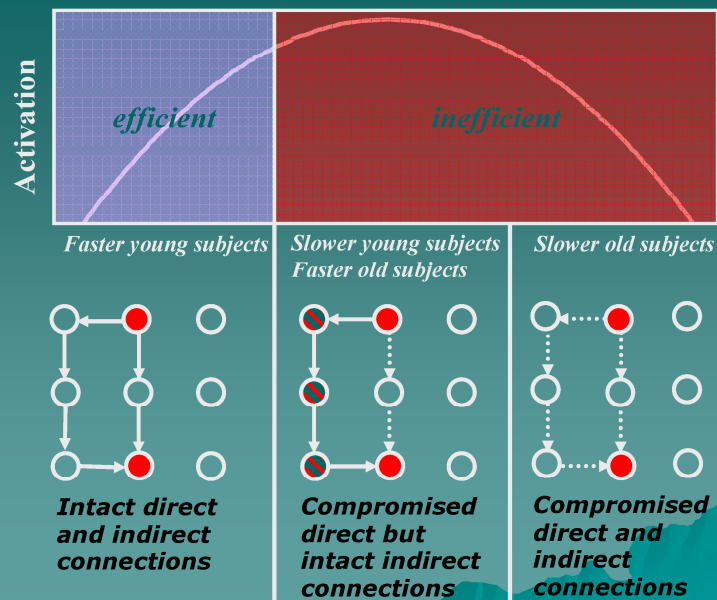


Dorsal PFC Activation-DSST Performance



*Age differential activation in dorsal PFC.
Replicates previous working memory study.*

Neural Efficiency Hypothesis



Symbol Verification Task: Granger Causality Analysis

- ◆ *Connectivity maps while performing the Digit-Symbol Verification task*

Slower

Faster

left

right

caudal

rostral

■ $P < .05$

■ $P < .10$

- ◆ *Reduced task-related connectivity in faster young subjects*

Symbol Verification Task: Granger Causality Analysis

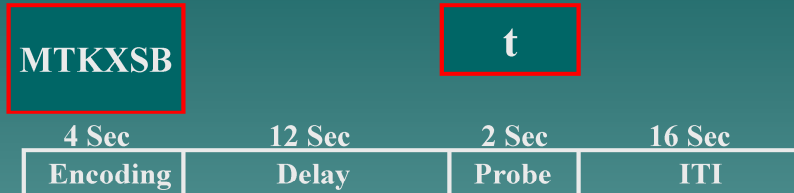
Reaction Time	Number of PFC Influences
1050	3
1150	5
1200	4
1250	5
1300	3
1350	6
1400	7
1450	5
1500	9
1600	8
1700	7

Faster young subjects

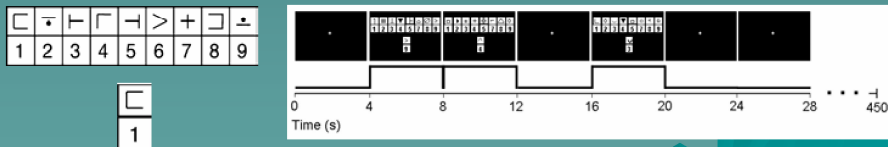
Slower young subjects

◆ *Question: Are Gulf-War Syndrome working memory changes related to neural efficiency?*

Working Memory Measure: Delayed Response Task



Processing Speed Measure: Digit-Symbol Verification Task



Hierarchical Regression

- ◆ Test Syndrome-Related Differences on WM and Processing Speed Tasks
 - Neural activity differences
 - Activity-Performance relationship differences
 - Task-related functional connectivity differences
- ◆ Test Syndrome-Related Differences in Neural Activity Relationships Between Tasks

