

Episodic Memory in Schizophrenia: Lessons From Cognitive Neuroscience

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Outline of Talk

- **What is schizophrenia and why should we care about cognitive function in this disorder?**
- **Do individuals with schizophrenia have deficits on episodic memory tasks?**
- **How are episodic memory deficits in schizophrenia related to prefrontal function?**
- **Do episodic memory deficits in schizophrenia reflect disturbances in recollection or familiarity, or both?**
- **Do episodic memory deficits in schizophrenia reflect:**
 - Failure to use strategies at encoding or retrieval that facilitate performance
 - Fundamental inability to encode and/or retrieve new information
 - Both

What is schizophrenia?

- **Extremely disabling neuropsychiatric disorder**
- **Affects approximately 1% of the population (higher in some areas)**
- **Involves symptoms such as hallucinations, delusions, thought disorder, lack of motivation, blunted affect, inability to experience pleasure**
- **Many individuals experience relatively severe cognitive deficits in a number of domains, including working memory**

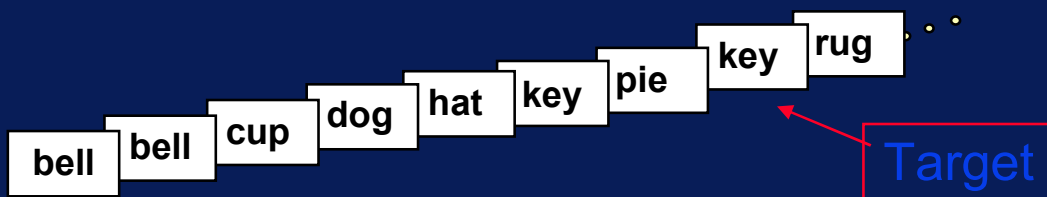
Why Pay Attention To Cognition in Schizophrenia?

- **It is an aspect of schizophrenia that is very predictive of functional outcome (Green, 1997)**
- **May be an aspect of schizophrenia directly related to neurobiological disturbances**
- **May constitute an endophenotypic marker of liability to schizophrenia**
- **Can help us understand the basic psychological and neural mechanisms that give rise to cognitive control**

Episodic Memory in Schizophrenia

Encoding

Attend to stimuli to remember for later recognition test. Press button whenever stimulus goes off the screen



Identical stimulus sequences used for both tasks, only instructions change (sequences counterbalanced across subjects)

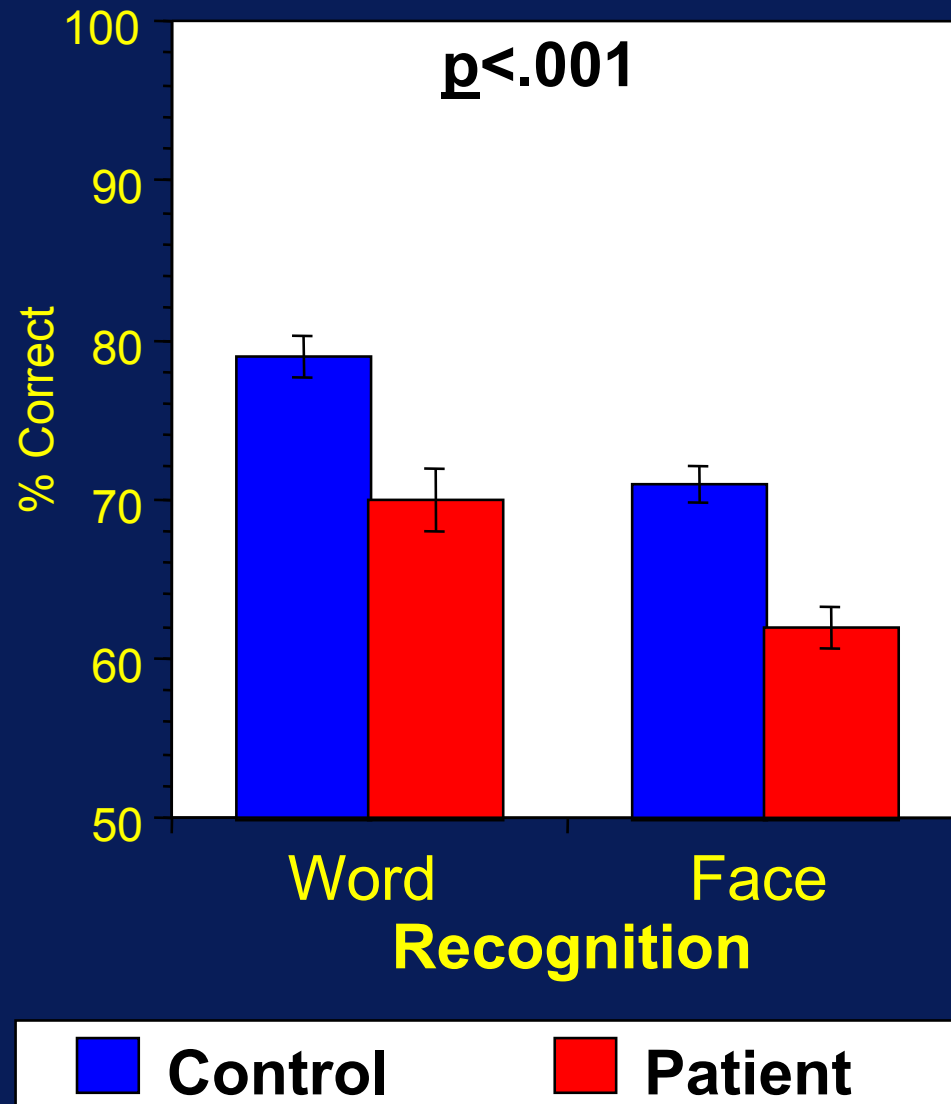
Working Memory

Forced choice response to each stimulus based on whether it is a 2back repeat or not

Retrieval:

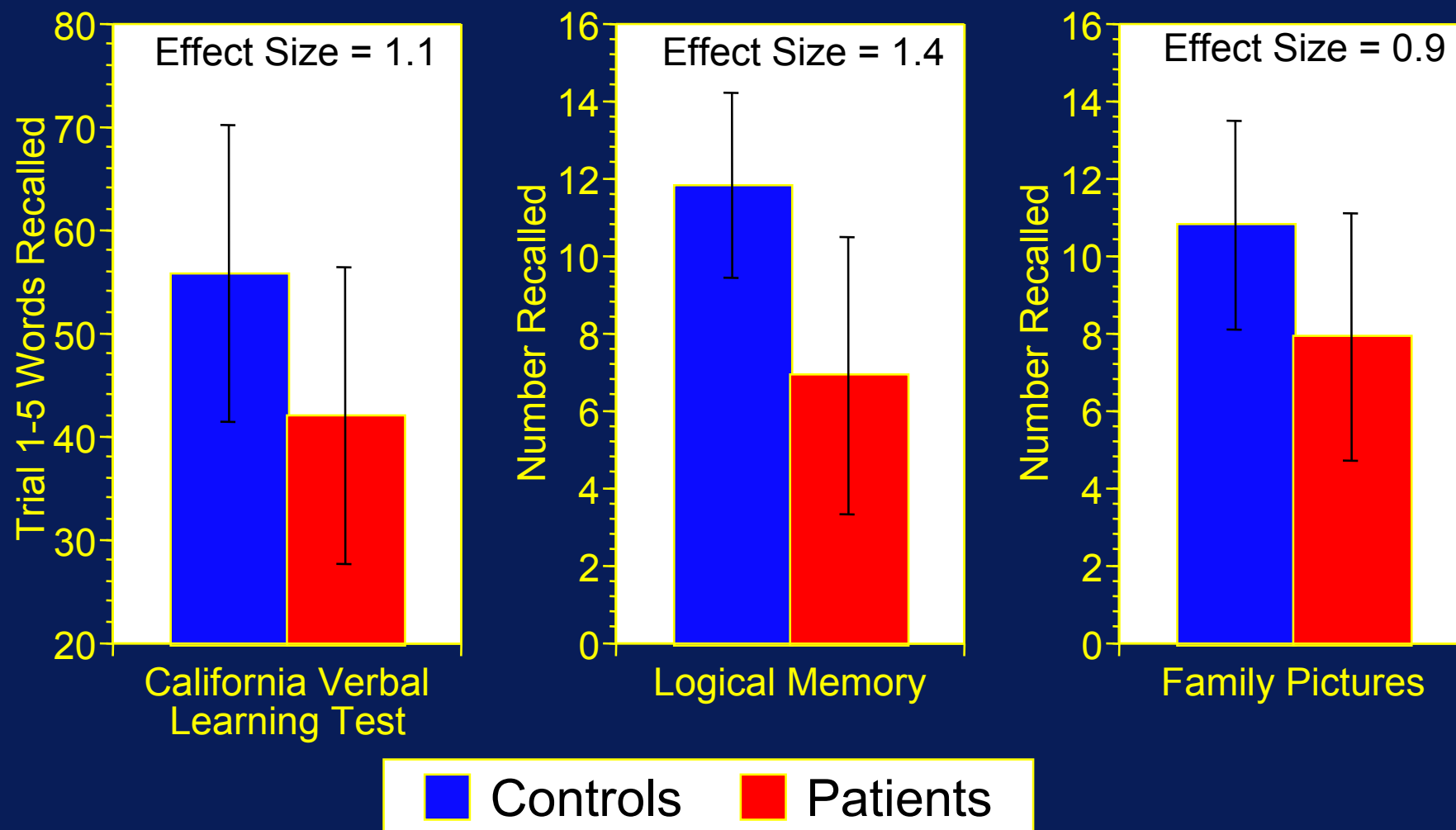
Yes/No Recognition for stimuli presented either during Encoding or during Working Memory Run

Behavioral Data



Barch et al., 2002

Episodic Memory in Schizophrenia



Barch et al., in prep

DLPFC and Episodic Memory

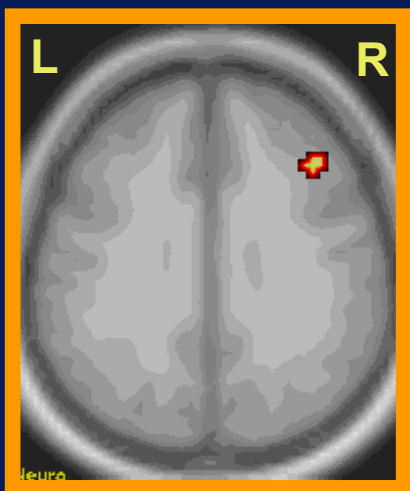
- **Among patients with Schizophrenia:**
 - Working memory deficits typically linked to DLPFC dysfunction
 - Episodic memory deficits typically linked to hippocampal dysfunction
- **Alternative Hypothesis:**
 - Both working memory and episodic memory deficits in schizophrenia reflect DLPFC cortex dysfunction
 - ◆ Lesion literature suggests that frontal lobe lesions can lead to episodic memory deficits as well as working memory deficits (e.g., Shimamura, Moscovitch)
 - ◆ Neuroimaging literature suggests that prefrontal cortex supports both working memory and episodic memory (e.g., Tulving, Buckner, Braver/Barch)

Barch et al., 2002

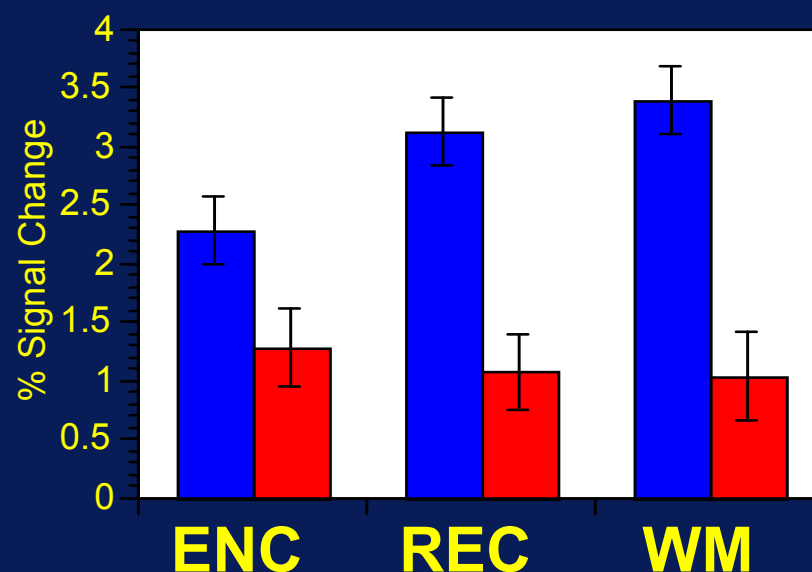
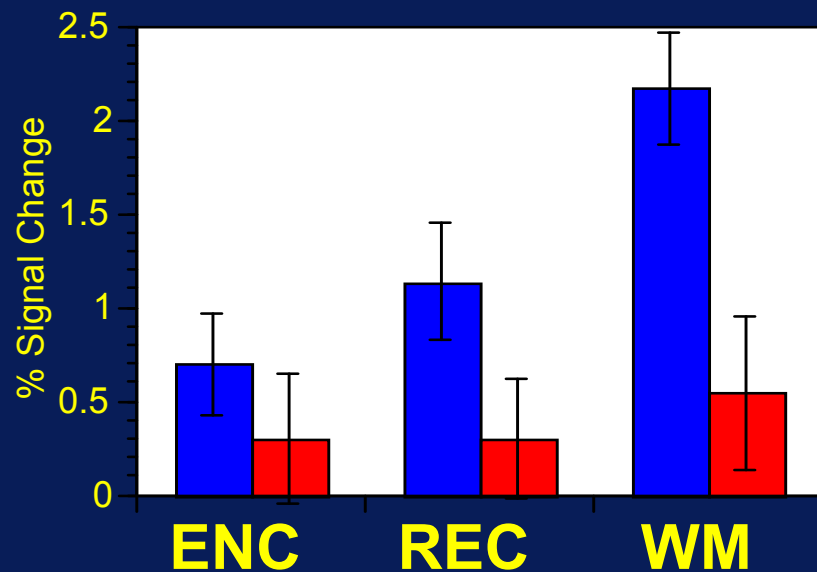
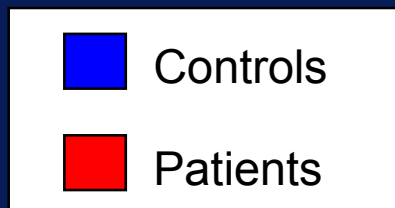
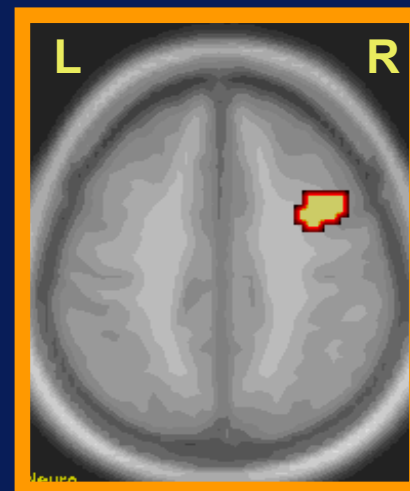
Dorsolateral PFC

Barch et al.,
2002

Z = +30

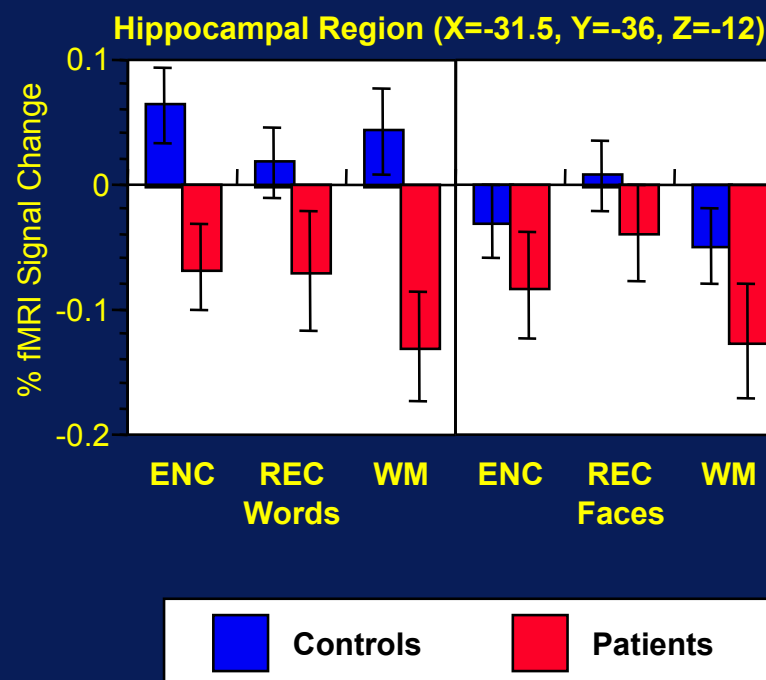
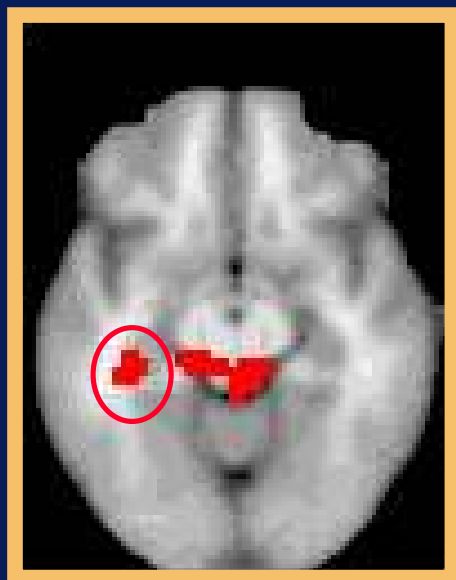


Z = +39



Hippocampus

Z = -10mm



Barch et al., 2002

What components of episodic memory?

- **If episodic memory problems in schizophrenia are related to cognitive control deficits, what aspects of episodic memory are impaired in schizophrenia?**
 - **Familiarity:**
 - ◆ Feelings of knowing, related to prior exposure to information, do not depend upon ability to access information about specific learning episodes
 - ◆ Lesion data suggest familiarity intact in individuals with DLPFC lesions, but not in individuals with hippocampal damage
 - **Recollection**
 - ◆ Ability to retrieve information associated with specific learning episode, related to ability to use contextual information to search memory
 - ◆ Impaired both in individuals with DLPFC and hippocampal deficits

Familiarity versus Recollection

- **Use opposition procedures developed by Larry Jacoby**
 - **Familiarity**
 - ◆ **Associated with accessibility bias**
 - ◆ **Are you sensitive to the frequency with which you have seen one stimulus versus another**
 - **Recollection**
 - ◆ **Associated with ability to retrieve stimulus learned at specific point in time**
 - ◆ **Can you remember what items you studied/learned in a specific session**

Jacoby Task

Pre-exposure Session

Knee Bone

Knee B_n_

Knee Bone

Knee B_n_

Knee Bend

Knee B_n_

Knee Bone

Knee B_n_

Knee Bone

Knee B_n_

Knee Bone

Knee B_n_

Knee Bend

Knee B_n_

Knee Bone

Knee B_n_

Study Session

Knee Bend

OR

Knee Bone

OR

Neither

Test Session

Knee B_n_

Jacoby Task cont

- **Trial Types**

- **Congruent**

- ◆ “Knee Bone” more frequent in Pre-exposure Phase
 - ◆ Study “Knee Bone” in Study Session
 - ◆ Familiarity and Recollection point to same response

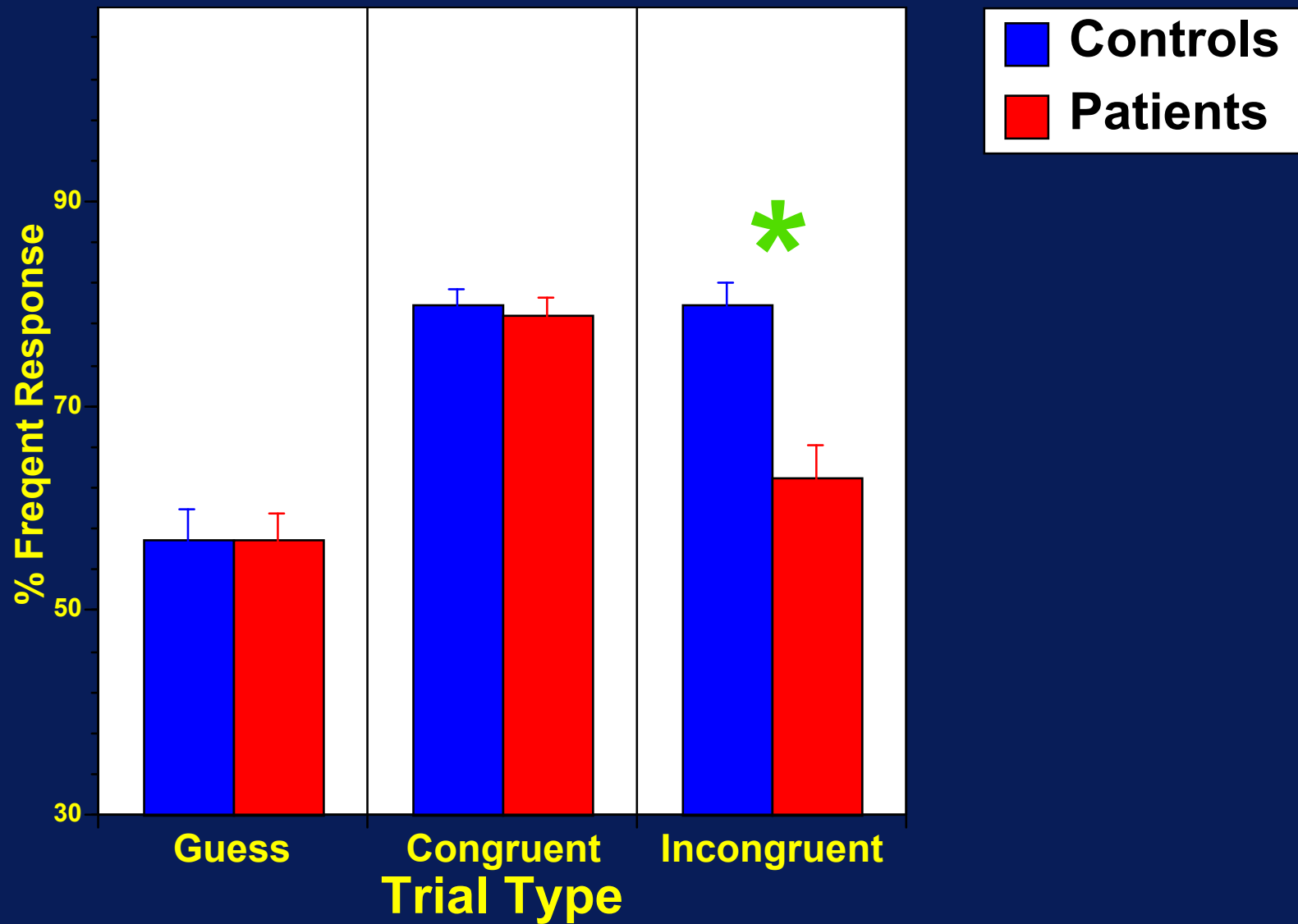
- **Incongruent**

- ◆ “Knee Bone” more frequent in Pre-exposure Phase
 - ◆ Study “Knee Bend” in Study Session
 - ◆ Familiarity and Recollection point to different responses, need Recollection to remember correct Study Item

- **Guess**

- ◆ “Knee Bone” more frequent in Pre-exposure Phase
 - ◆ Do not study either “Knee Bend” or “Knee Bone” in Study session
 - ◆ Familiarity only thing operating

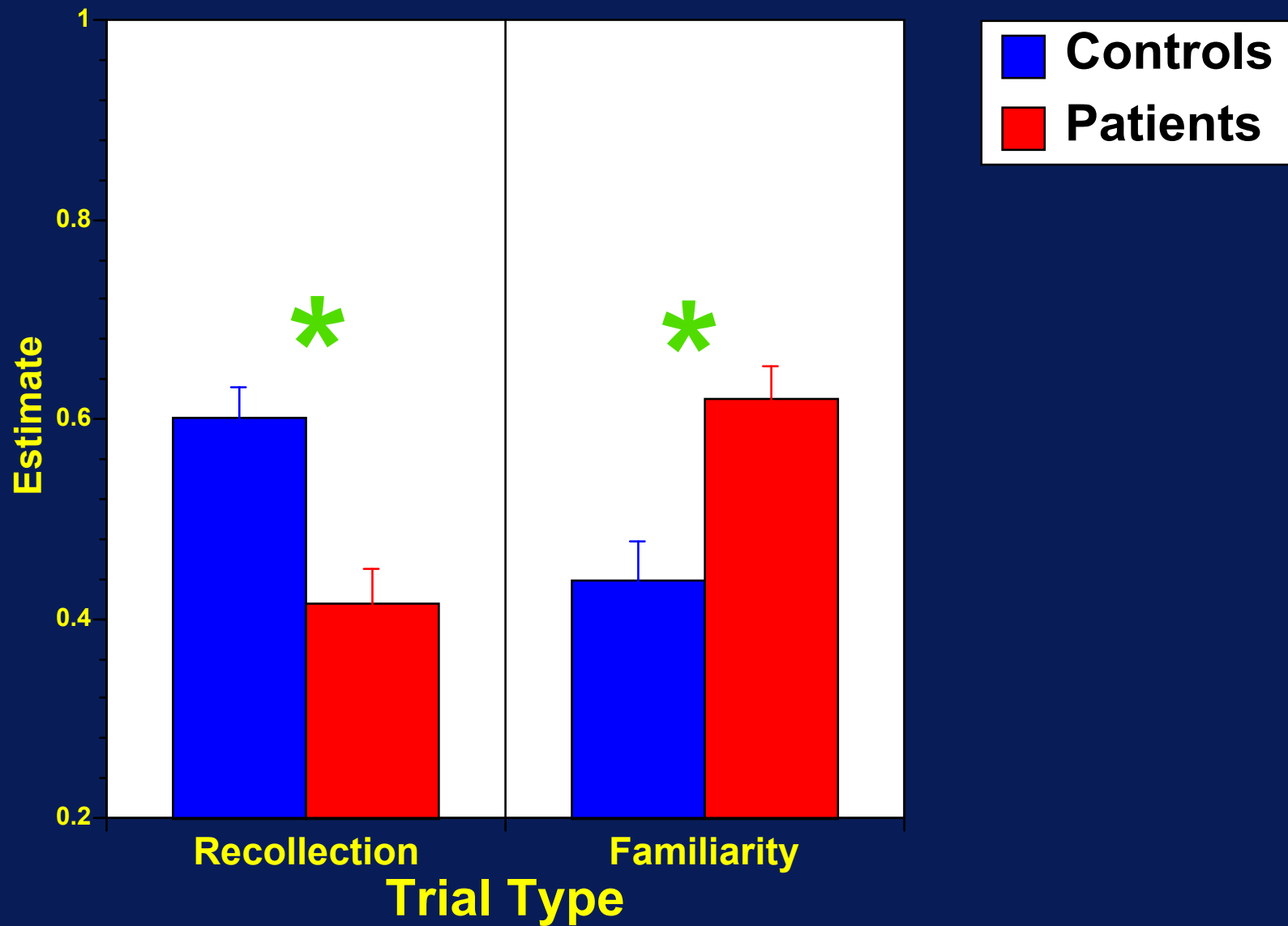
Accuracy Across Conditions



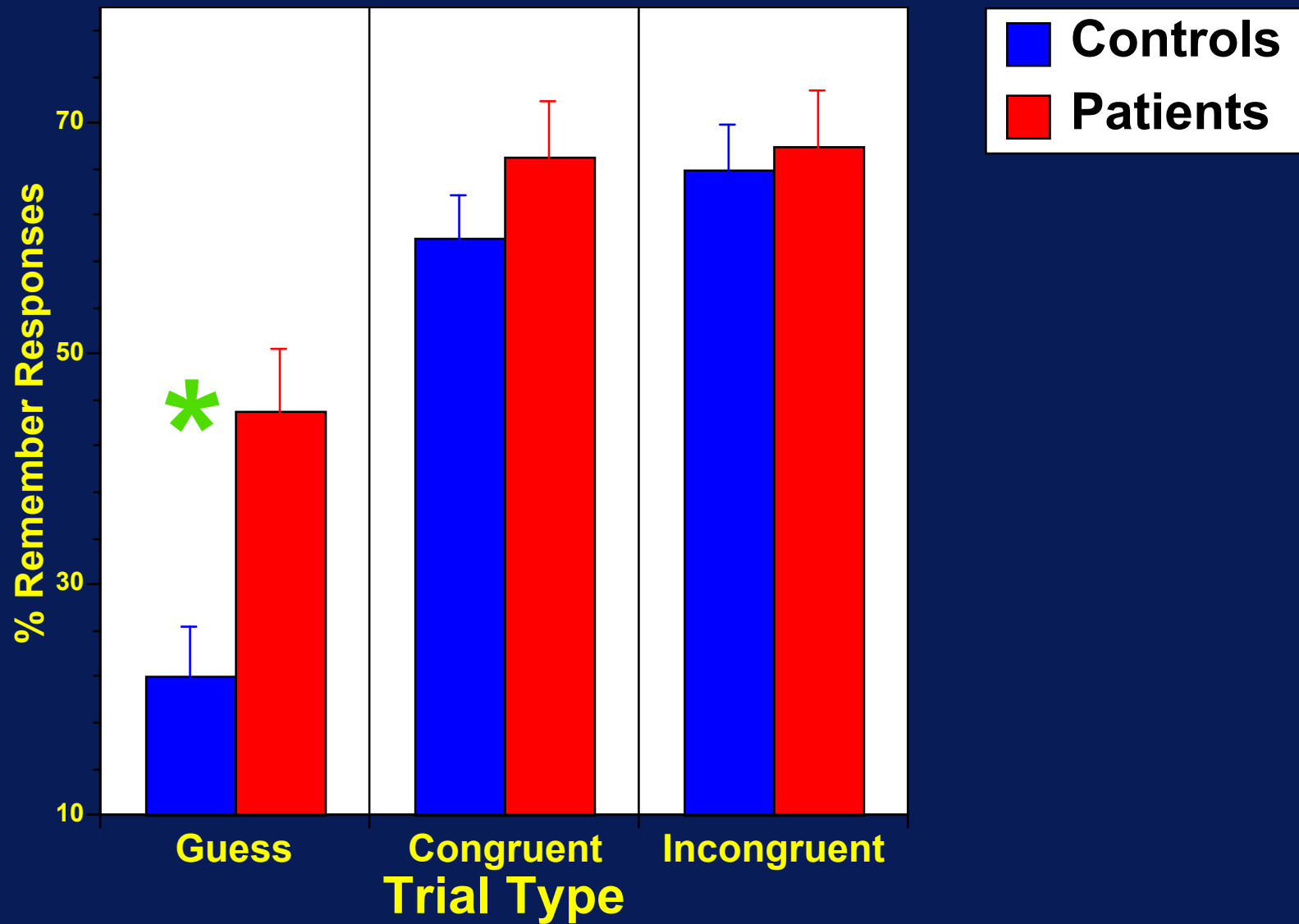
Recollection and Familiarity Estimates

- **Recollection (R)**
 - $P(\text{correct}/\text{congruent}) - p(\text{incorrect}/\text{incongruent})$
- **Familiarity (F)**
 - $P(\text{incorrect}/\text{incongruent})/1-R$

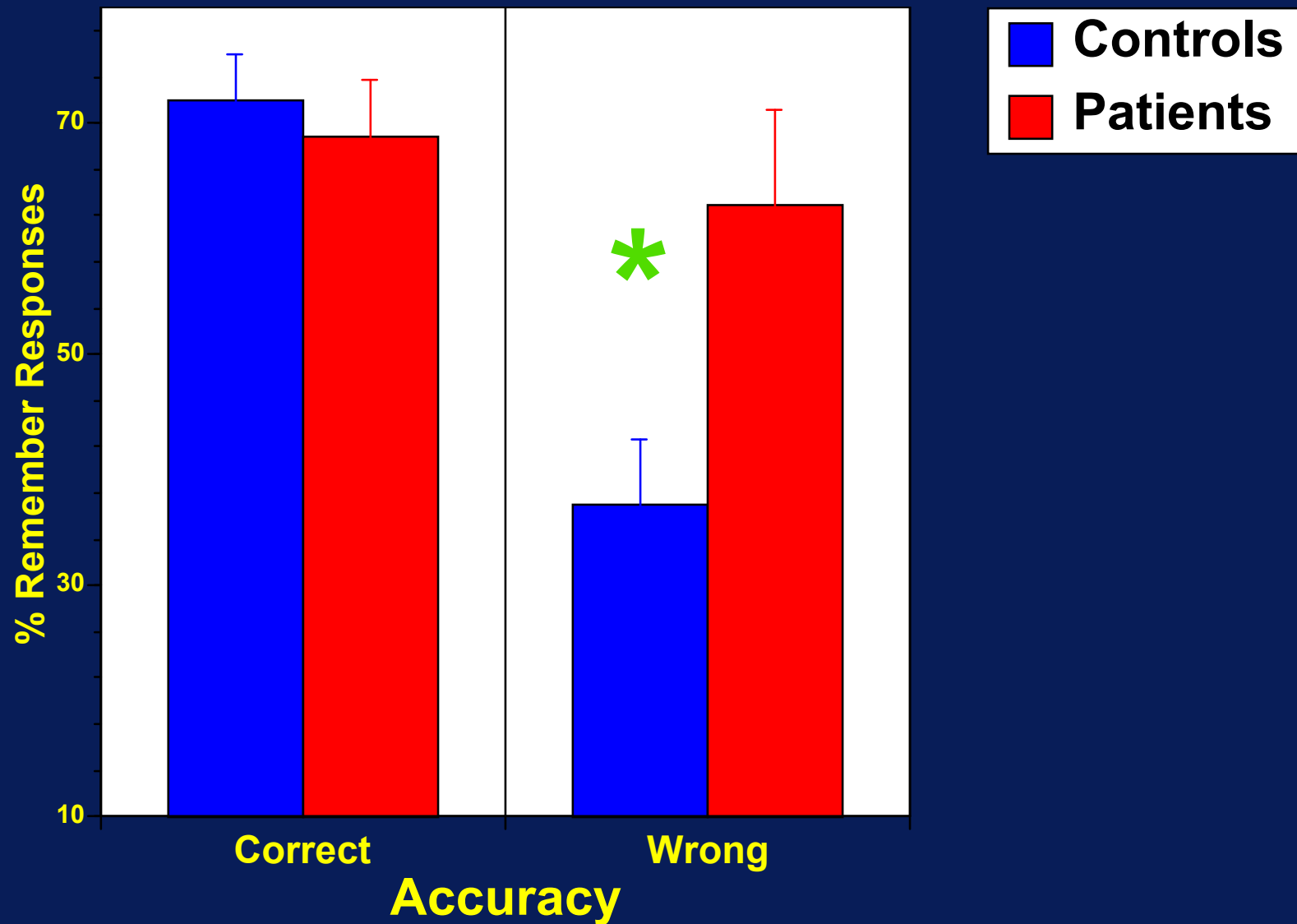
Process Dissociation Estimates



Remember Responses



Relationship to Accuracy



Why is recollection decreased?

- **Do individuals with schizophrenia have difficulties using effective encoding strategies?**
 - Perhaps individuals with schizophrenia do not spontaneously apply strategies at encoding that are effective for encoding information for later retrieval

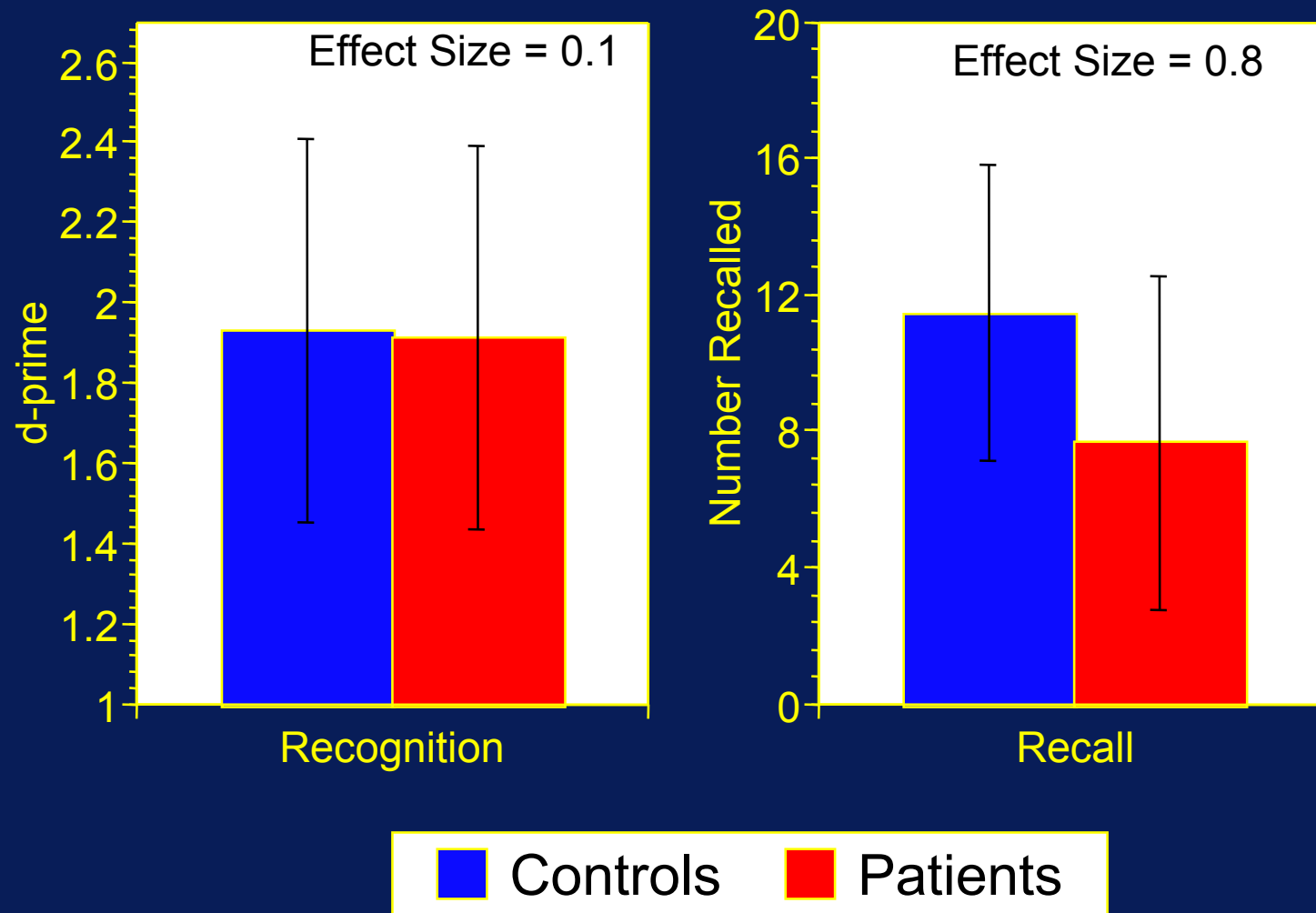
What happens when you orient people with schizophrenia to use beneficial encoding strategies?

Incidental Encoding

- **Individuals with schizophrenia and controls performed incidental encoding task**
 - Valence and arousal ratings on words that varied in valence (positive, negative, neutral) and arousal (high, low)
- **Administered surprise recognition and recall tasks**

Mathews & Barch, in press

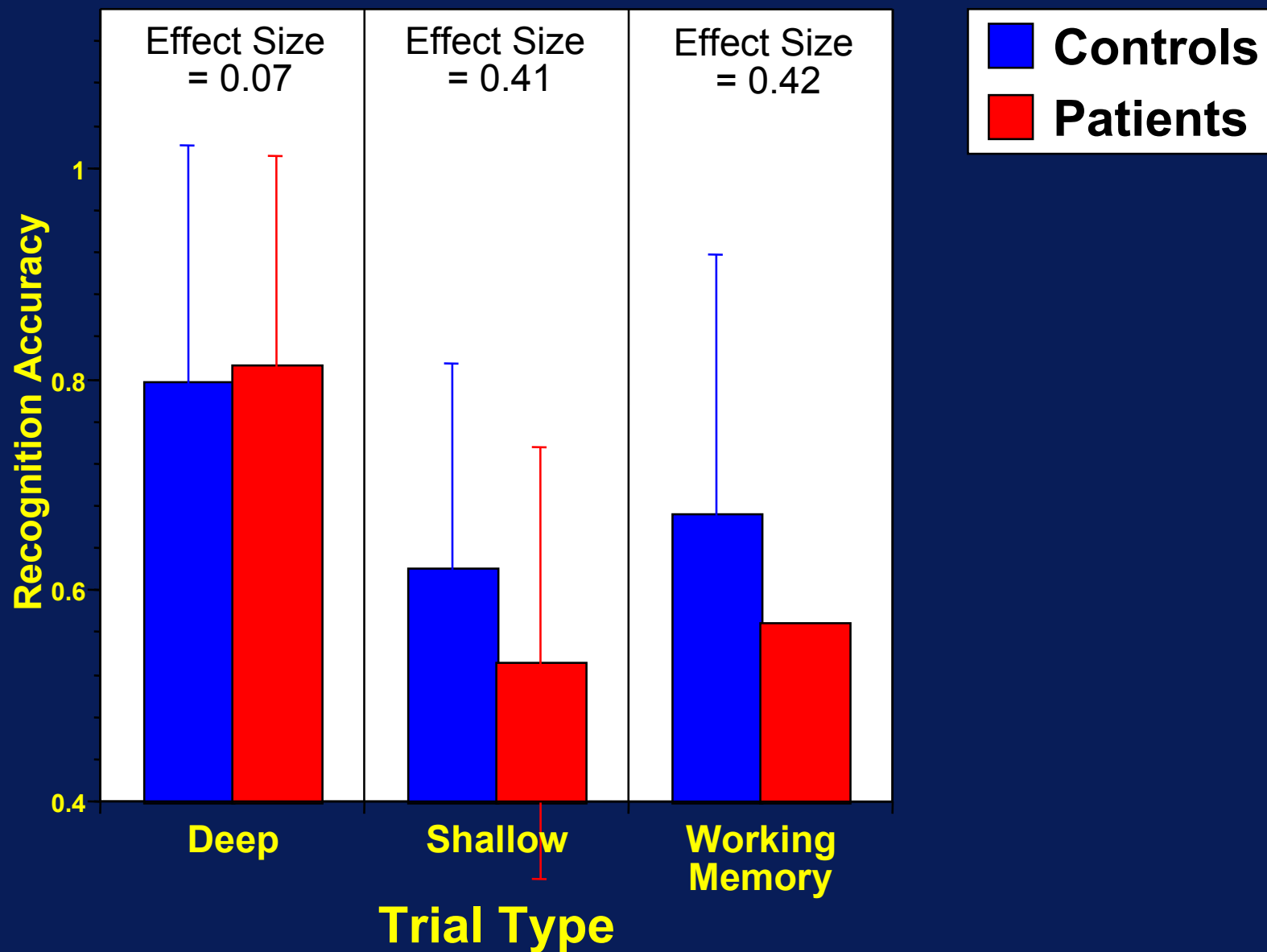
Retrieval Performance



Levels of Processing

- **Will individuals with schizophrenia show improved episodic retrieval if given a deep semantic incidental encoding task?**
- **Deep Encoding**
 - Abstract/Concrete
- **Shallow Encoding**
 - First/Last letter judgments
- **Yes/No Recognition for items seen in:**
 - Deep Encoding
 - Shallow Encoding
 - Working Memory

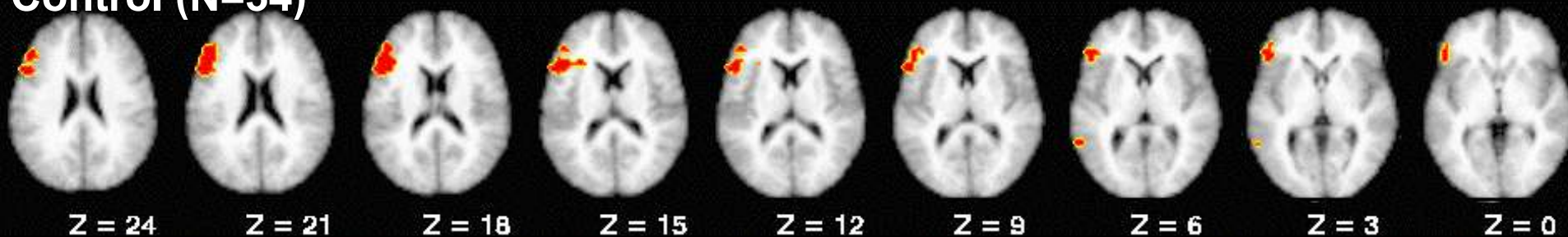
Strategy Use - Performance



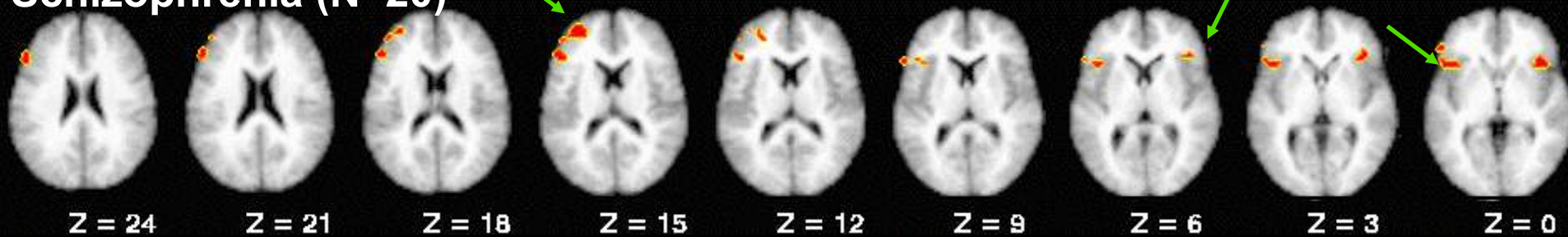
Strategy Use - Brain Activation

Deep Encoding Greater than Shallow Encoding

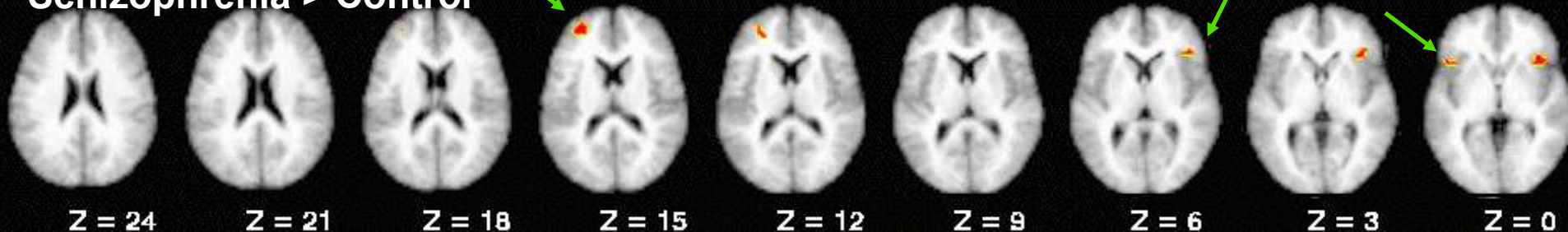
Control (N=34)



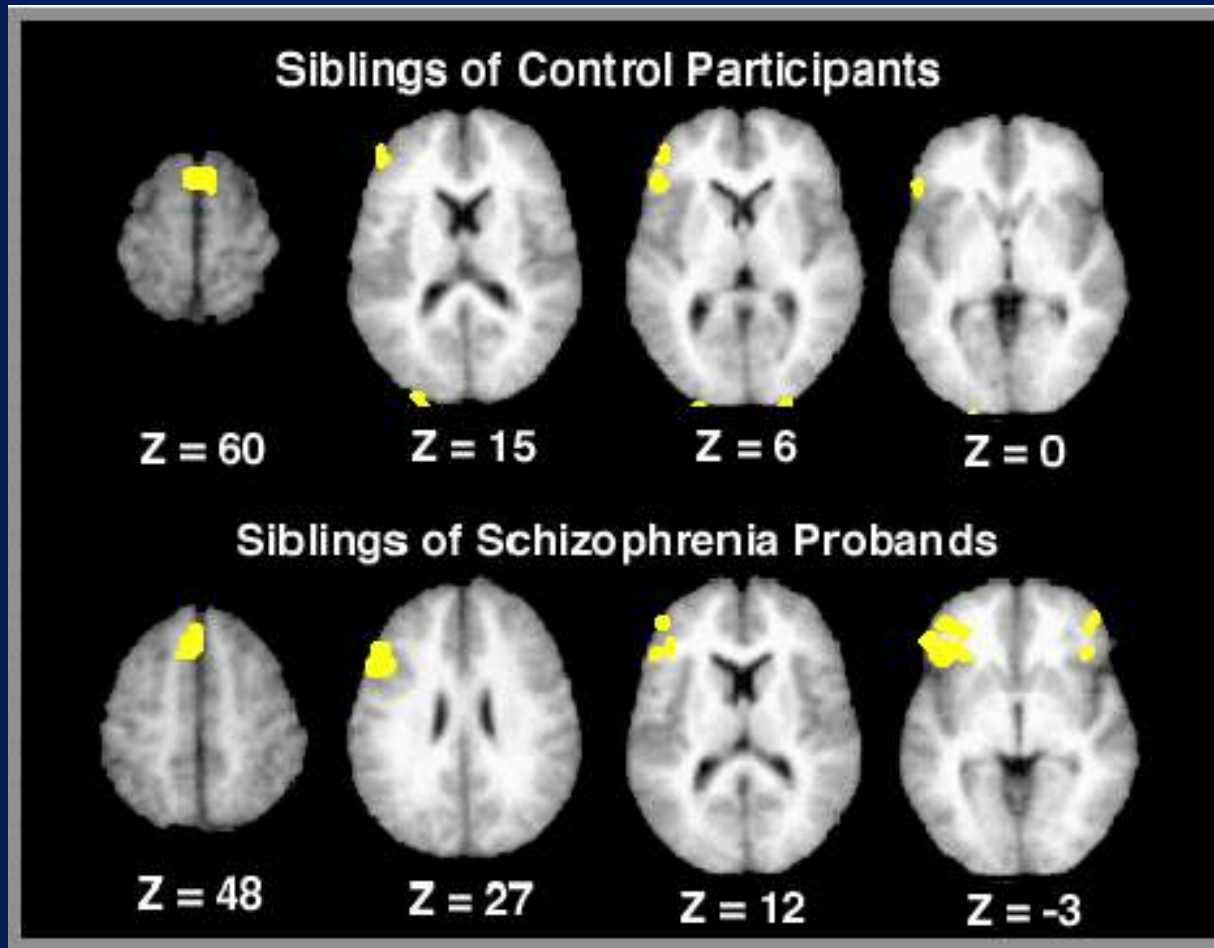
Schizophrenia (N=20)



Schizophrenia > Control



Similar Finding In First Degree Relatives



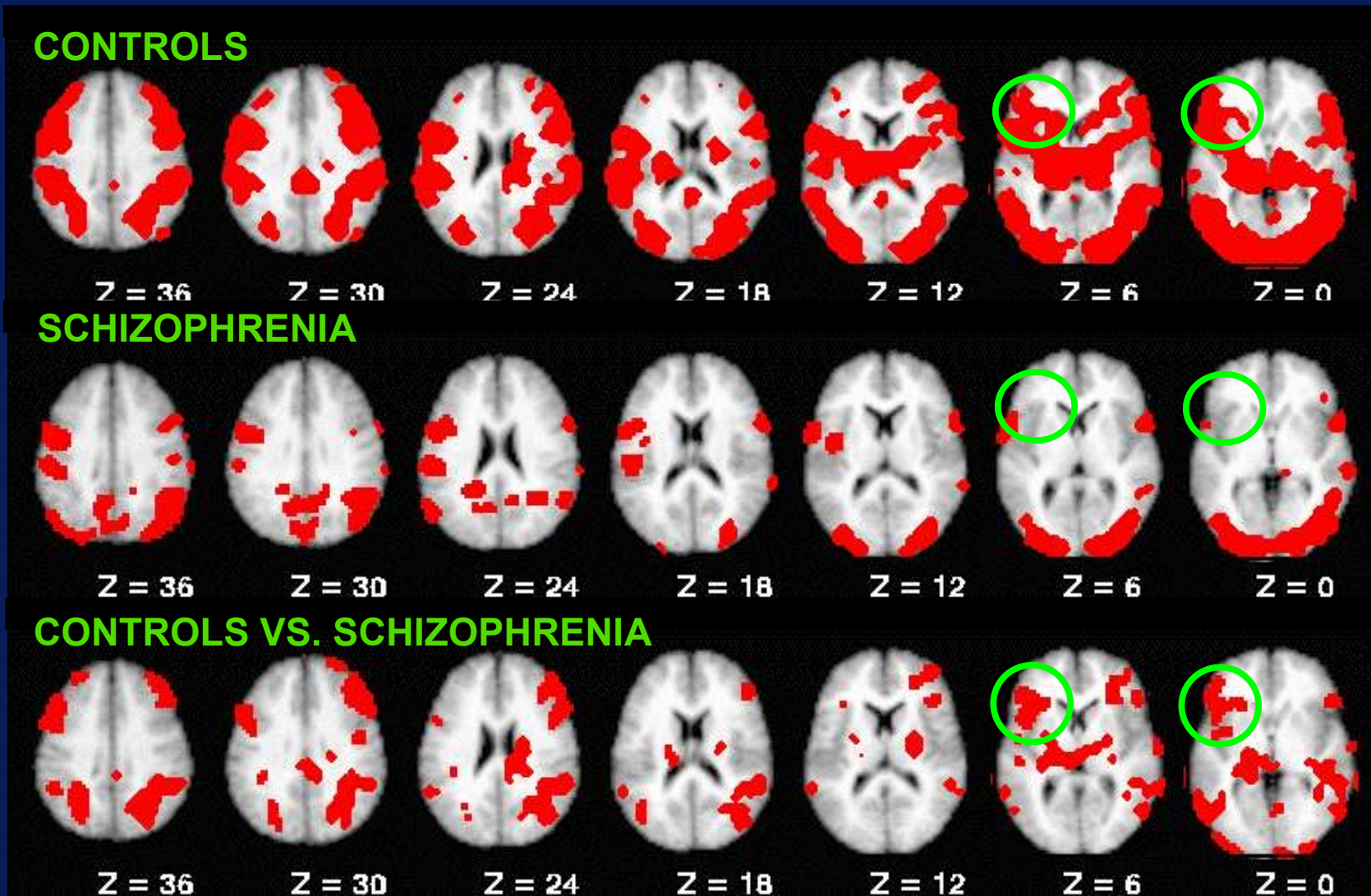
**Proband Siblings >
Control Siblings**



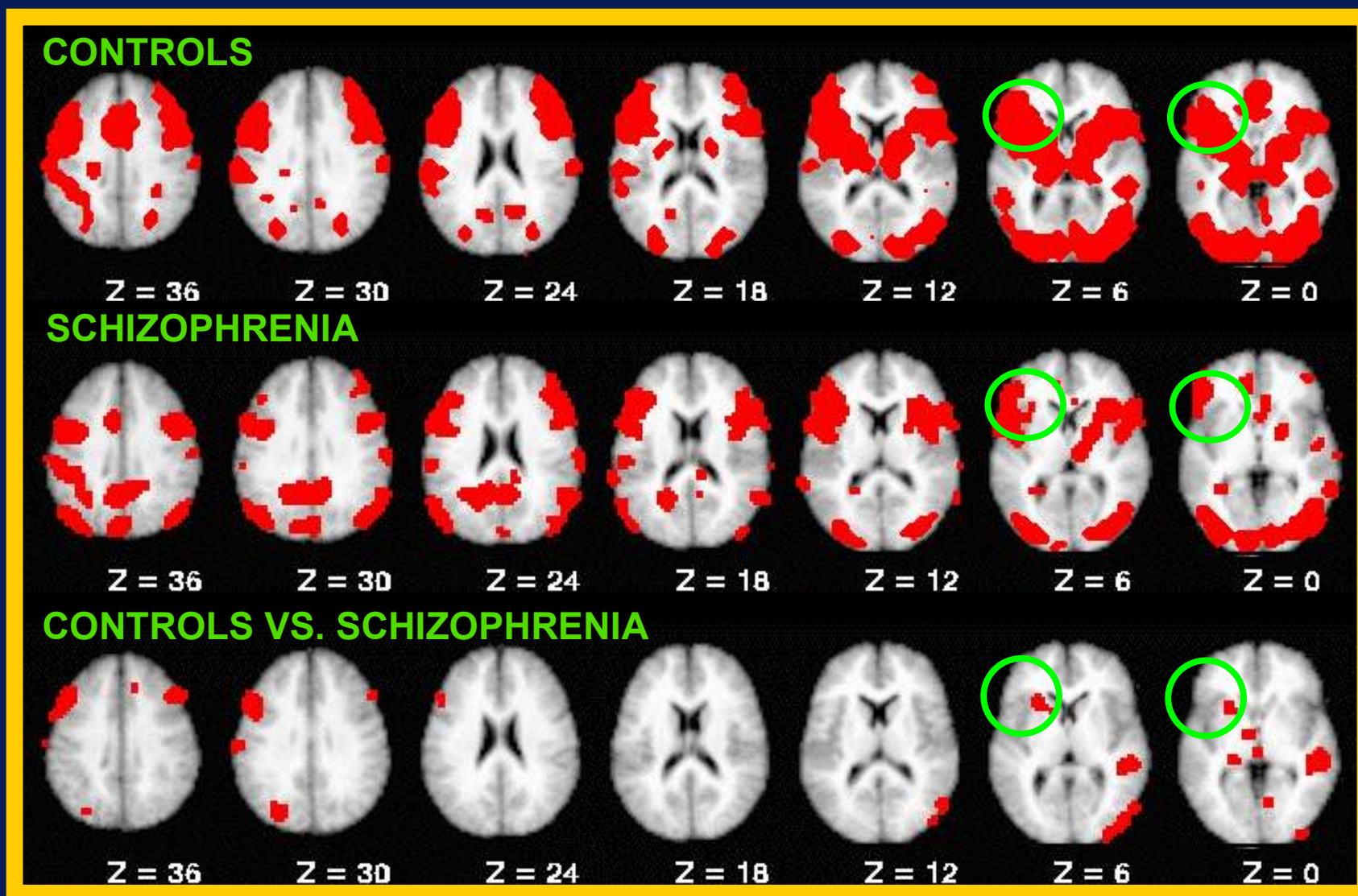
Constrained vs. Unconstrained Strategy Use

- **Participants**
 - 19 individuals with schizophrenia
 - 15 healthy controls (age, gender, parental SES matched)
- **Tasks**
 - **Intentional Encoding** (strategy not constrained)
 - **Incidental Encoding** (deep semantic processing, abstract/concrete judgments)
 - Recognition and Recall tests after scanning
- **Scanning**
 - 1.5 T Siemens Vision
 - Rapid event related design
 - Correct trials only during encoding
 - Subsequent memory analysis (coming)

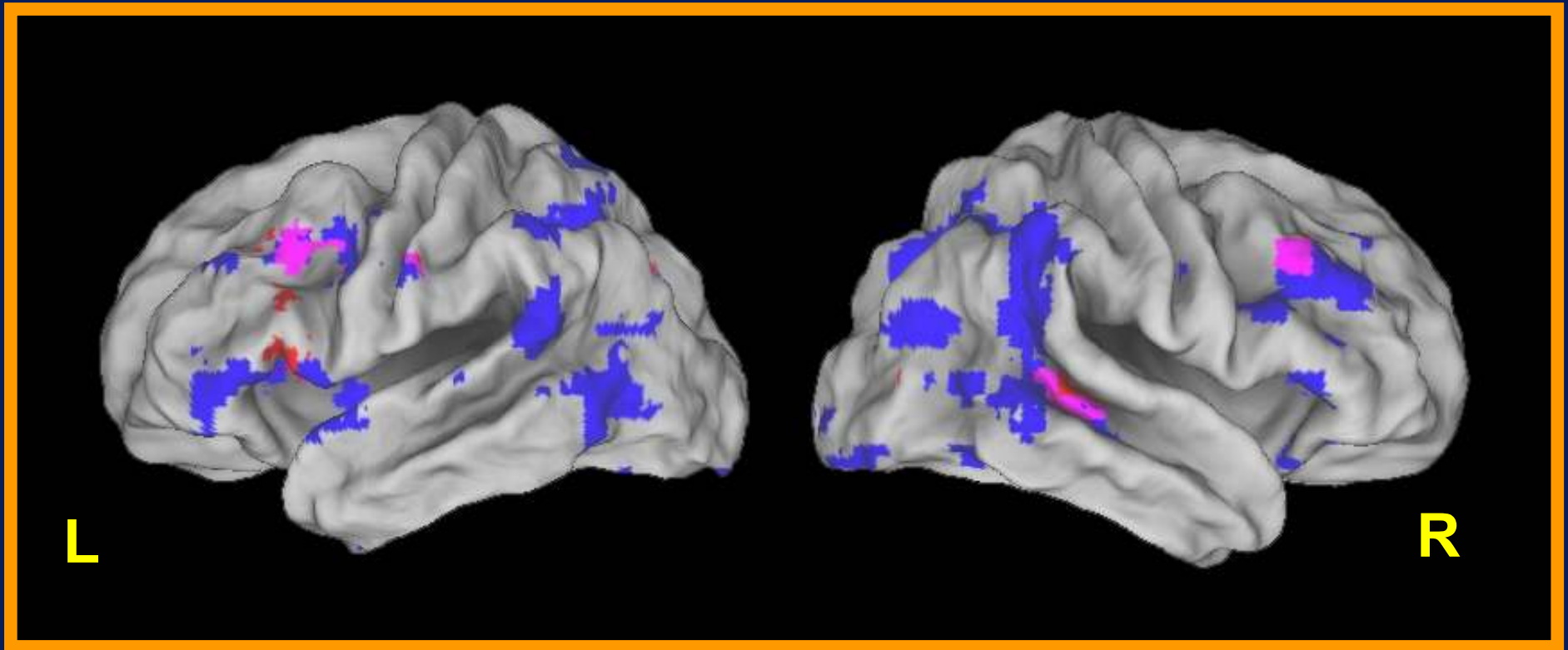
Unconstrained Encoding



Constrained Encoding



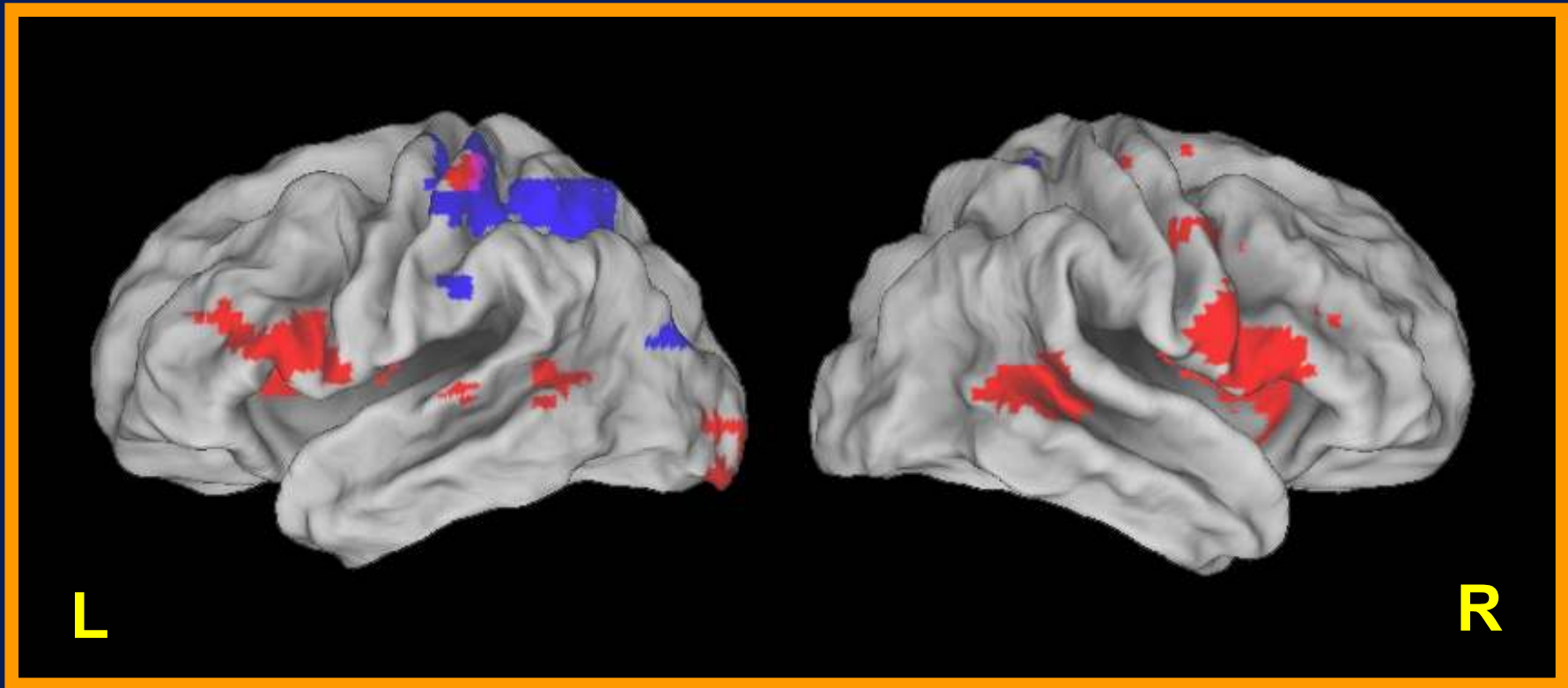
Group Differences



-  Controls > Patients Unconstrained
-  Controls > Patients Constrained

 OVERLAP

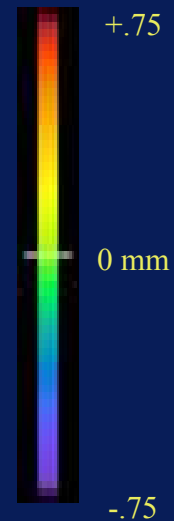
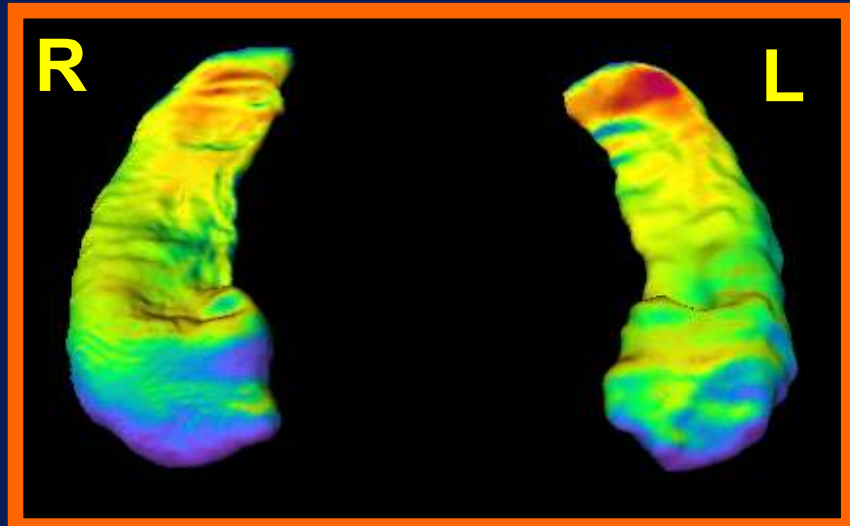
Subsequent Memory



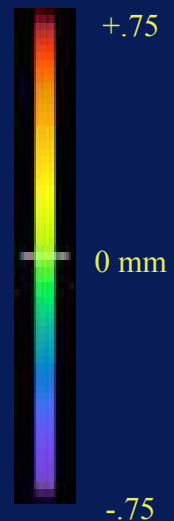
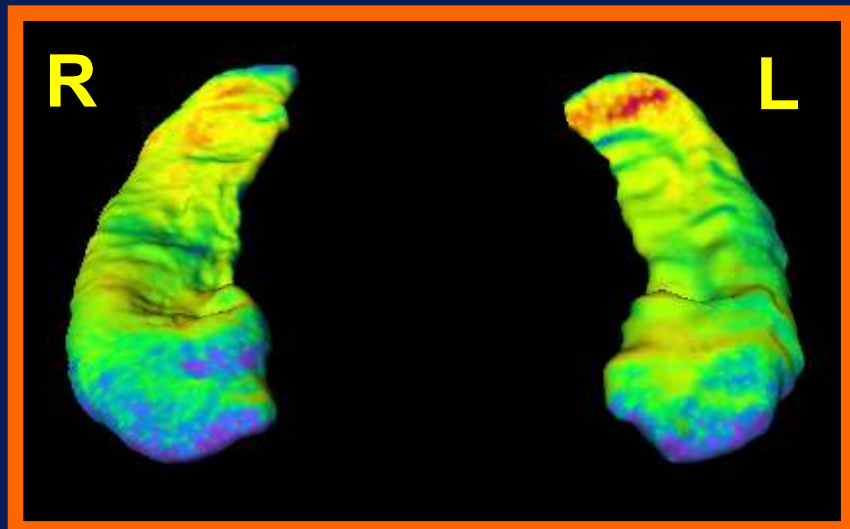
■ R>M in both controls and patients

■ R>M -- Controls > Patients

What about the hippocampus?



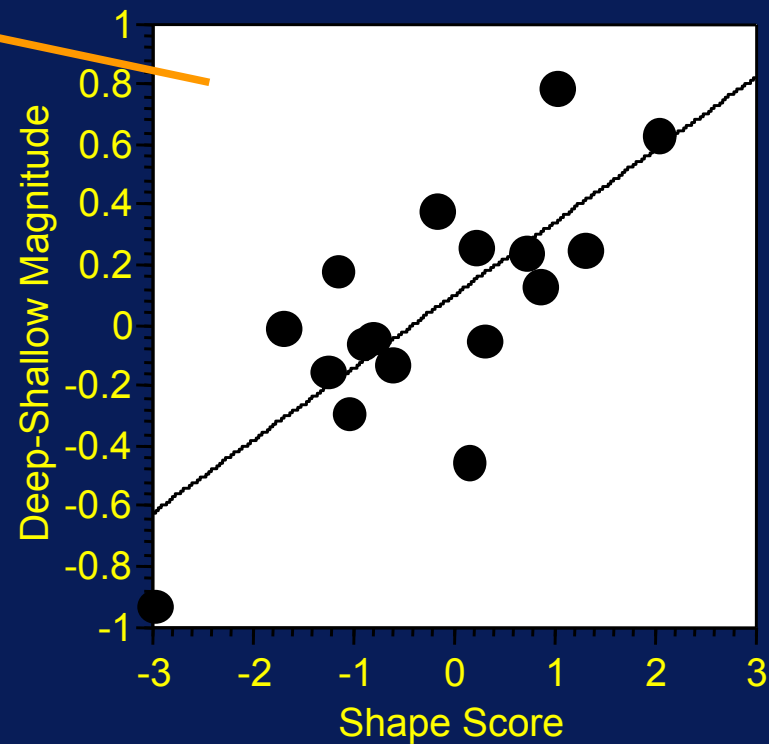
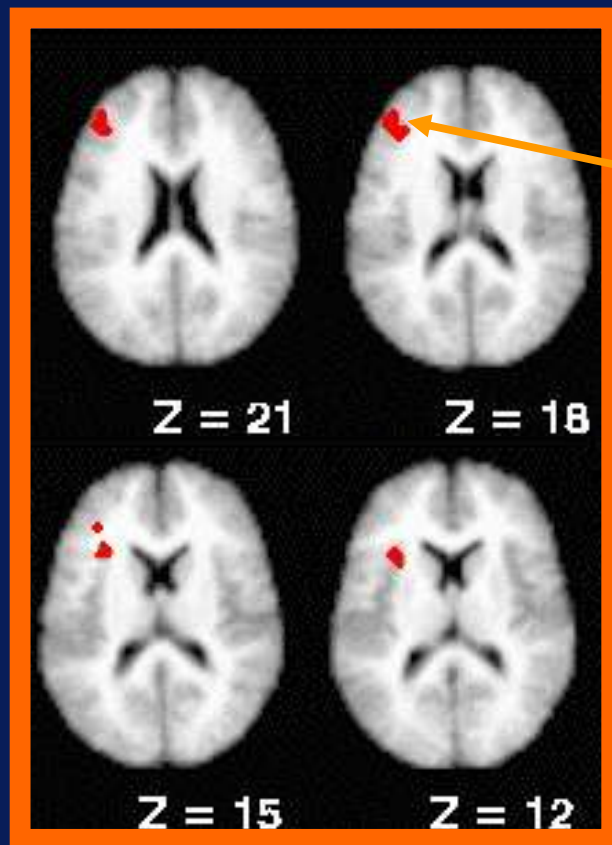
**Group difference
reconstructed from
raw data**



**Group difference
reconstructed from
selected subset of
eigenvectors**

Is it all strategy?

Hippocampal Shape Constrains Encoding Support Benefit



Conclusions

- **Individuals with schizophrenia show changes in both recollection (decreased) and familiarity (increased)**
- **Impairments in episodic memory seem to be due, at least in part, to reduced application of effective encoding strategies**
 - Orienting to good encoding strategy leads to:
 - ◆ Equal recognition performance to controls
 - ◆ Continued impairments in recall (no strategy provided at retrieval)
 - Individuals with schizophrenia show “normal” levels of processing effect
 - ◆ Leads to equal recognition performance to controls
 - Semantic encoding related activation “normalized” when constrained to use effective strategies
- **Future Directions**
 - How will the provision of effective retrieval strategies influence performance?
 - ◆ Semantic Cueing
 - How and why does hippocampal shape abnormalities influence strategy use?
- **Why is familiarity increased?**
 - If truly independent of recollection, should not simply be result of reduced recollective processes