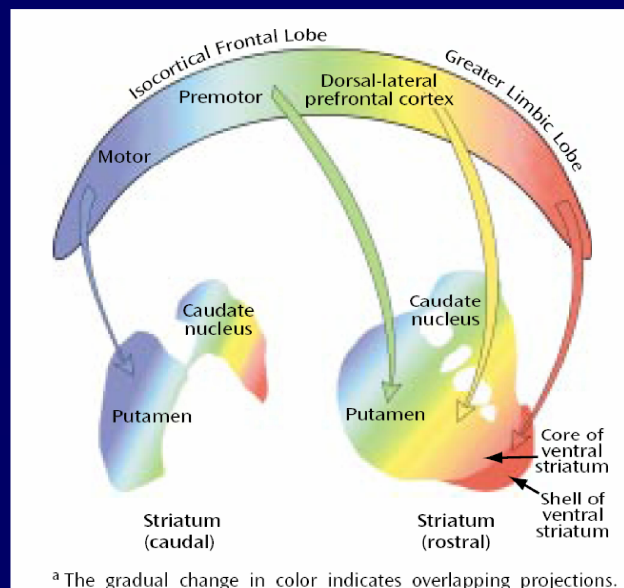


Presentation 6 – Wendy Ringe

## Fronto-Striatal Systems in Depression & Gulf War Illness

- Depression is a prevalent complaint in GWI
- The extent to which it is primary or reactive is an ongoing topic of debate
- Basal ganglia dysfunction and altered central dopamine have been documented in GWI
- Striatal systems have been implicated in depression in other basal ganglia diseases
- **Recent advances suggest two distinct but interconnected prefrontal-subcortical systems**



## Findings in Depression

### Dorsolateral PFC

#### **Dorsolateral PFC & dorsal cingulate**

Involved in cognitive tasks like attention, problem-solving

Decreased in depression

#### **Lateral orbital cortex**

Active in normals during sadness

Increased in MDD -*r* with severity (Coping?)

### Greater Limbic Lobe

#### **Ventral anterior cingulate**

Reactive to sadness in normals  
Overactive in depression

#### **Medial PFC**

Active during emotions in both MDD and Normals

#### **Amygdala**

Overactive in MDD

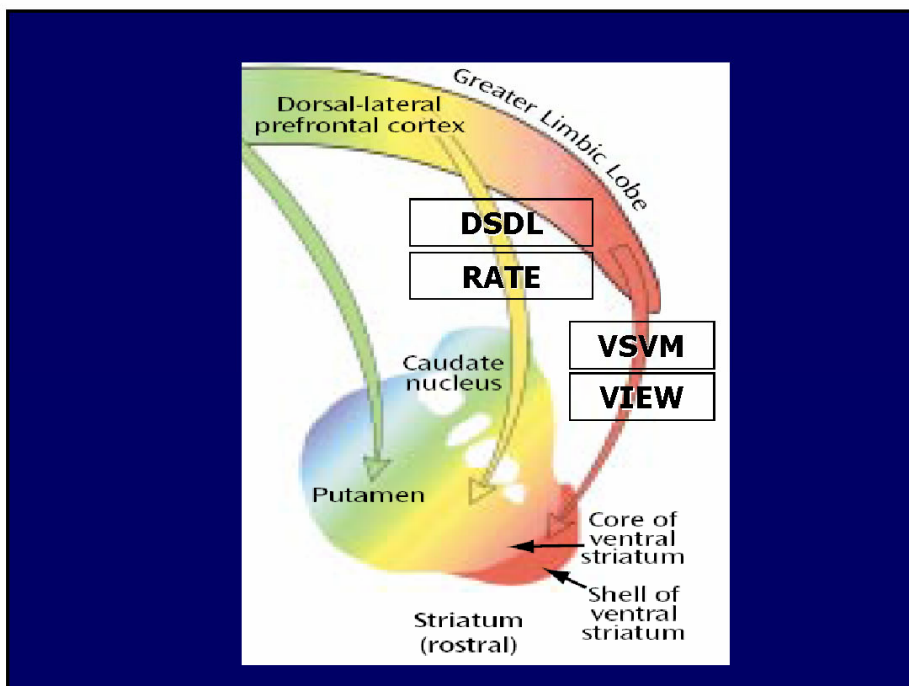
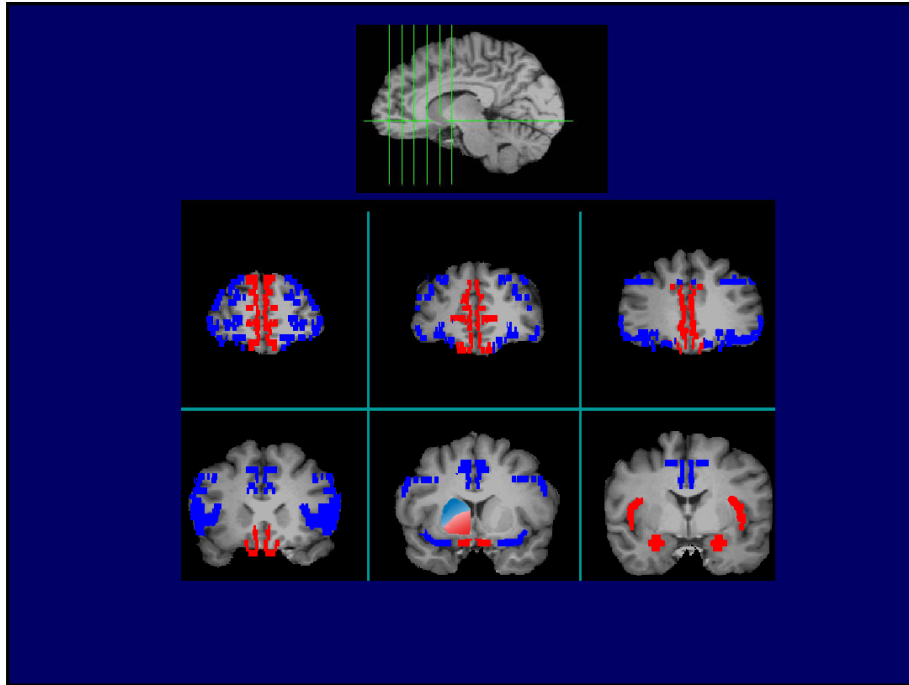
## Frontostriatal Systems

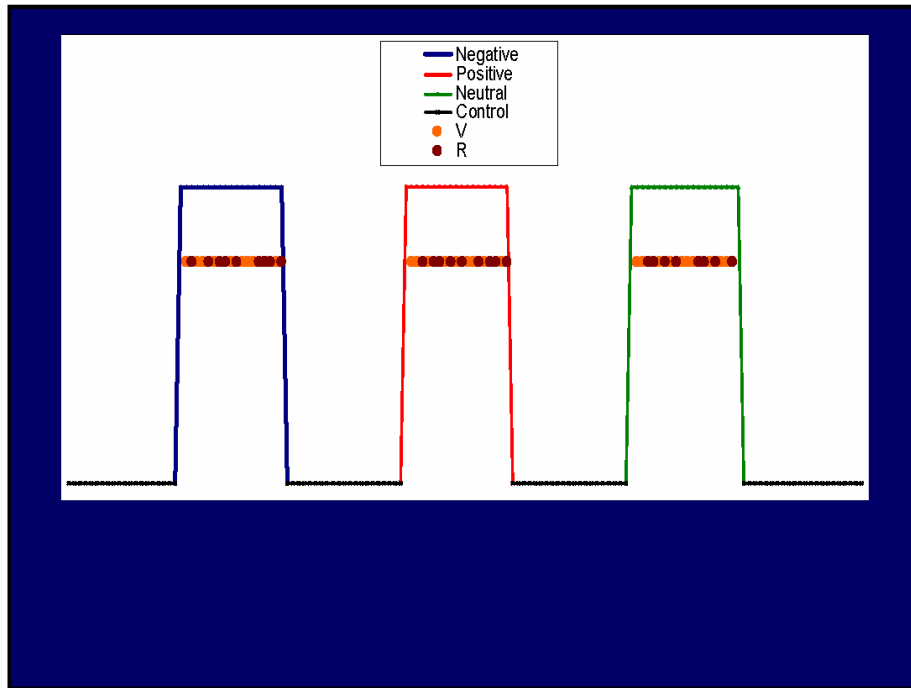
### **Dorsal Striatum – Dorsolateral PFC (DSDL)**

- Cognitive symptoms of depression
- Monitoring and directing responses to external stimuli (Coping)

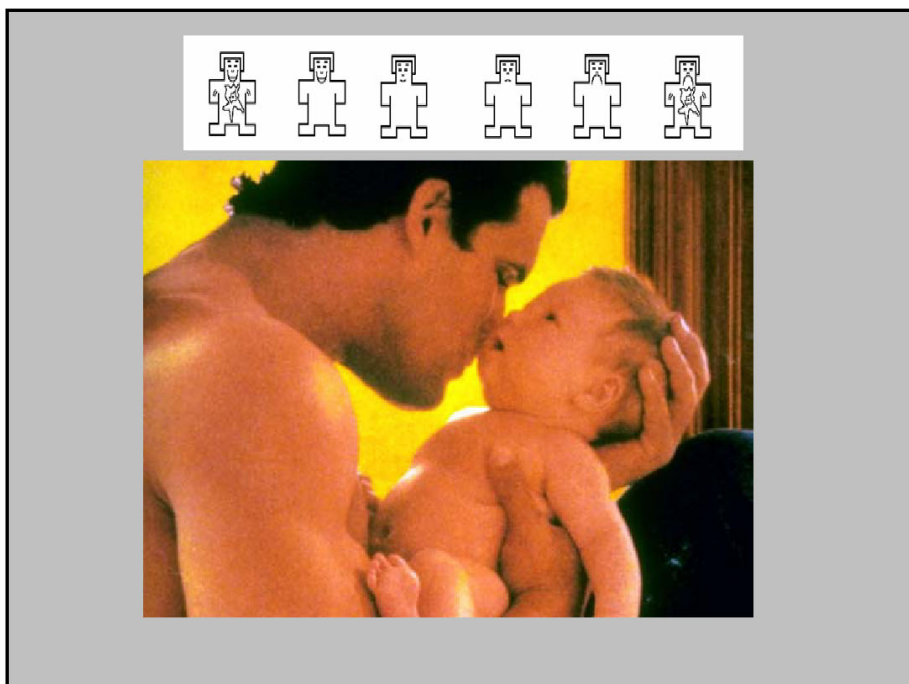
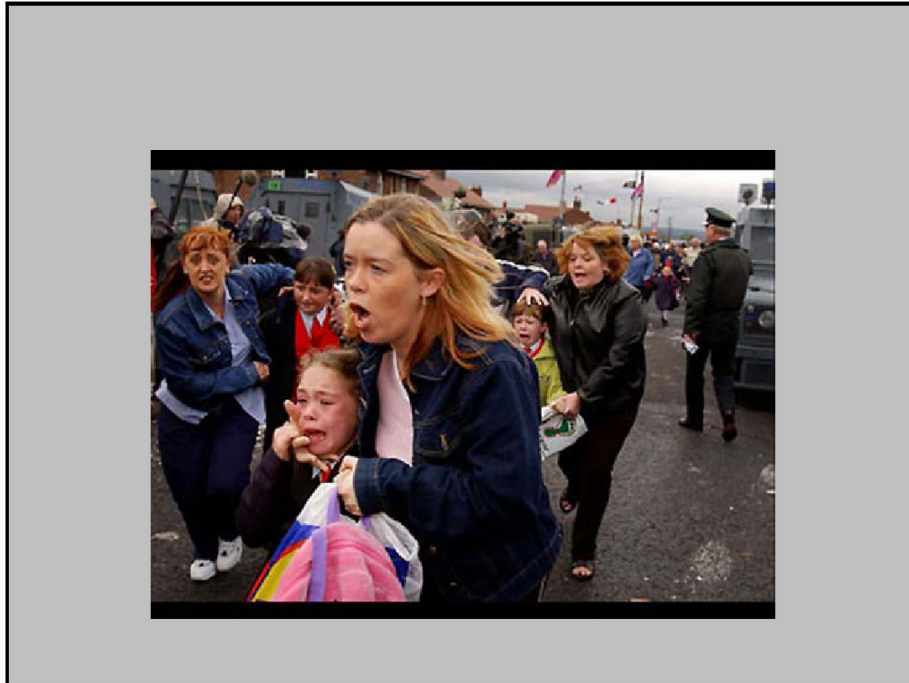
### **Ventral Striatum – Ventromedial PFC (VSVM)**

- Experience of emotion
- Mediates emotional approach-withdrawal reflex





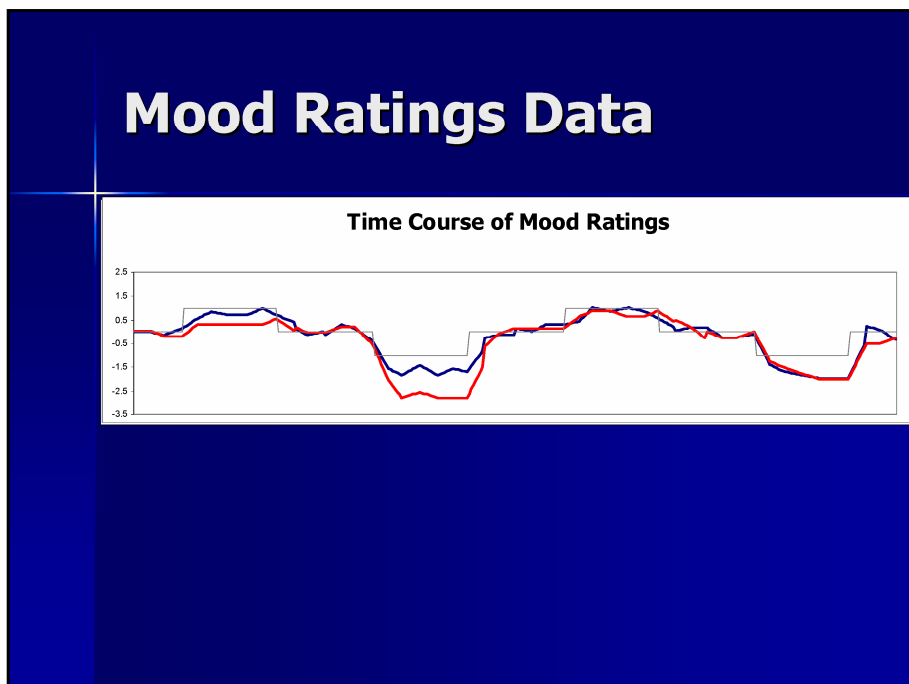




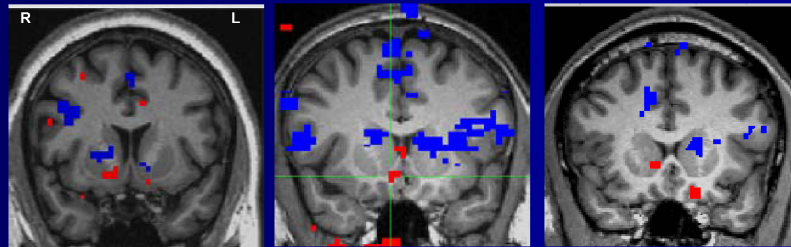
HOW ARE YOU FEELING  
RIGHT NOW?

1 2 3 4 5 6 7 8

BEST -----WORST



## FMRI Data



## Opportunities

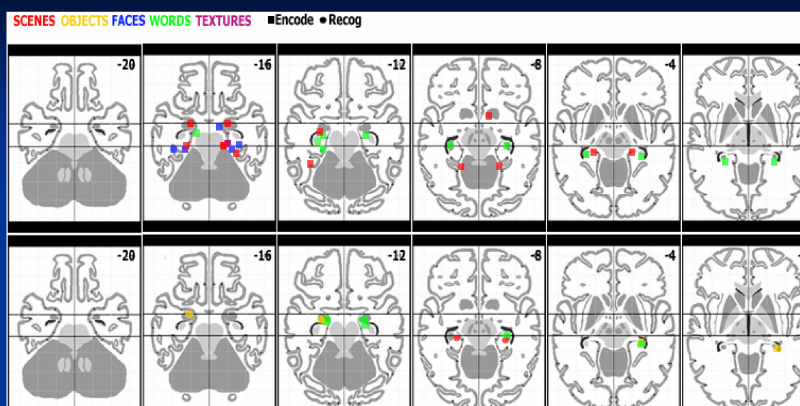
- Understand both disease and mood-specific effects in VSVM and DSDL Systems.
- Differentiate between depressed GWI and MDD.
- Other investigations to prospectively predict treatment response and thus optimize treatment approach.

# Material-Specific Memory in the Medial Temporal Lobes

W. Ringe, K. Gopinath, S. Cheshkov,  
S. Sarkar, R. Briggs, R. Haley

University of Texas Southwestern Medical Center, Dallas, TX

## Heterogeneous Findings in Memory Studies



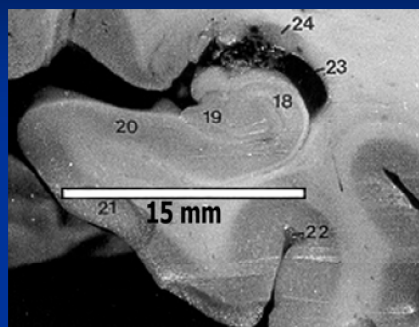
Cabeza et al., *J. Cogn. Neurosci.* 2004; Golby et al., *Brain* 2001; Greicius et al., *Hippocampus* 2003; Mandzia et al., *Hum. Brain Mapp.* 2004; Powell et al., *Neuroimage* 2005; Reber et al., *Hippocampus* 2002; Stark et al., *J. Neurosci.* 2000; Stark et al., *Learn. Mem.* 2001

Areas of activation foci plotted in this figure are approximate and are not meant to represent anatomically-precise findings of the studies cited.

## Spatial Resolution

- Most fMRI memory studies lack spatial resolution to reliably differentiate material-specific activation in the various subregions of the MTL.
- Lateralization and parcellation potentially very important with respect to subtle memory deficits in Gulf War Syndrome

## Hippocampus Anatomy



- 18 - Hippocampus
- 19 - Dentate gyrus of Hippocampus
- 20 - Subiculum
- 21 - Parahippocampal Gyrus
- 22 - Collateral Sulcus
- 23 - Temporal Horn of Lateral Ventricle
- 24 - Tail of Caudate

### Right Mesial Temporal Lobe Structures

Image Adapted from:

*The Human Brain: Surface, Blood Supply and Three-Dimensional Sectional Anatomy, 2nd edition.* Duvernoy, H.M., 1991, Springer-Verlag/Wien, p. 247

## High Resolution in MTL

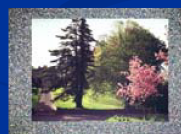
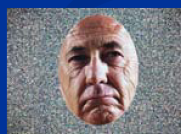
- 1.72 mm x 1.72 mm x 2.3 mm (1.5T)  
(Powell et al., NeuroImage 2005)
- 3.125 mm x 3.125 mm x 4.0 mm (3T)  
(Grecius et al., Hippocampus 2003)
- 1.56 mm x 1.56 mm x 3.0 mm (3T)  
(Zeineh et al., Science 2003)

### **This Work:**

**1.56 mm x 1.56 mm x 2.0 mm (3T)**

## Methods: fMRI task

- Event related design
- Encoding and recognition trials alternated with scrambled pictures
- Visually-presented words, objects, faces and nature scenes



## High Resolution in MTL

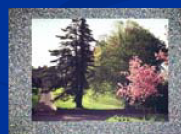
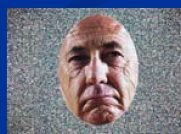
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(Zeineh et al., Science 2003)

### **This Work:**

**1.56 mm x 1.56 mm x 2.0 mm (3T)**

## Methods: fMRI task

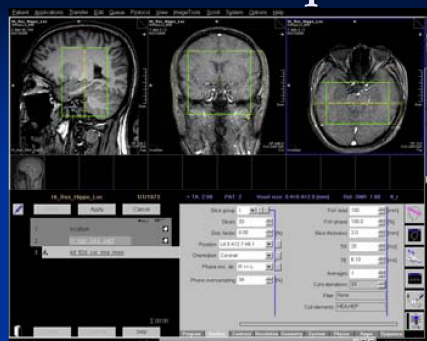
- Event related design
- Encoding and recognition trials alternated with scrambled pictures
- Visually-presented words, objects, faces and nature scenes



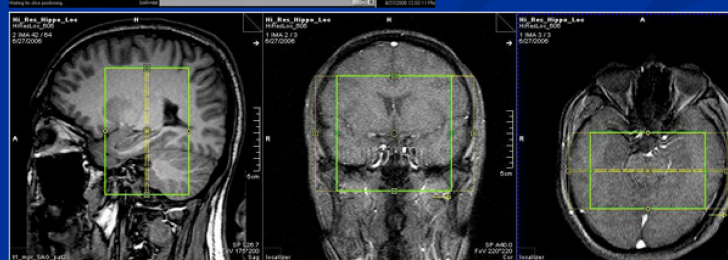
## Methods: Data Acquisition

- Eight healthy subjects (5 F, 3M, mean age 30.3 yrs) participated
- 3T Siemens TIM MR Scanner with 12-channel receiver coil
- High resolution EPI: TR/TE/FA = 2000 ms/ 24.7 ms/ 90°;  
FOV = 100 mm; 64 x 64 matrix (1.56 mm x 1.56 mm in-plane resolution), 33 2.0 mm contiguous coronal slices, covering the Medial Temporal Lobe

## Data Acquisition (cont)



To avoid phase wrap in reduced FOV (100 mm) images, 38% phase oversampling (19% each hemisphere) is used





## Data Acquisition (cont.)

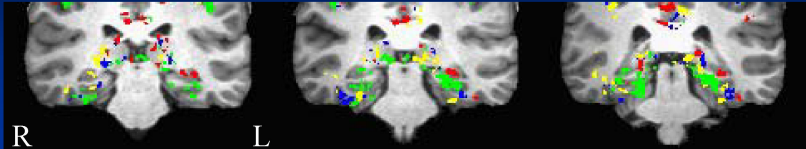
- High resolution T1-weighted MPRAGE scan (matrix size=160x256x256 with resolution 1x1x1 mm<sup>3</sup>, TI/TR/TE=900/2250/2.97ms, Flip angle=9<sup>0</sup>, PF=7/8, iPAT factor=2 with 24 reference lines) acquired for anatomic reference
- 2D TOF MR Angiogram with same slice-prescriptions and FOV as EPI scans acquired for angiographic reference

## Methods: Data Analyses

- fMRI voxel time-series modeled as convolution of 4 material-specific encoding stimulus vectors and constrained 2-parameter hemodynamic responses.
- Functional activation maps warped to Talairach space, resampled at a 1 mm<sup>3</sup> resolution, and spatially smoothed with a Gaussian kernel (FWHM = 3 mm).
- Within-group ANOVA performed to assess significance
- t-maps of condition-level activations clustered ( $|t_7| > 3.0$ ; cluster volume threshold 200  $\mu$ l; corrected  $p < 0.001$ ).

## Results

$p < 0.001$



R L

- **WORDS** – Left Hippocampus: Tail & Body, Right Parahippocampal Gyrus
- **OBJECTS** - Right Hippocampus: Body, Bilateral Parahippocampal and Fusiform Gyri
- **FACES** - Bilateral Parahippocampal & Fusiform Gyrus
- **NATURE SCENES** – Right Hippocampus: Tail & Body, Bilateral Parahippocampal Gyrus

## Conclusion

- Higher resolution allows material specific activation detection
- Parcellation of memory in MTL
- Useful to study memory dysfunction in Gulf War Syndrome and other neuro-degenerative diseases

## Future Work

- Increase number of subjects
- MTL ROI analysis, Flat mapping
- Zoomed EPI (with outer volume suppression)
- Thinner slices for isotropic voxels
- Explore higher fields for SNR & resolution
- Improved functional-anatomic co-registration  
(Gholipour et al., *proc. ICIP2007*)
- Optimize spatial smoothing using semivariogram  
(Spence et al., JASA 2007)

## Acknowledgments

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The content of this presentation does not necessarily reflect the position or the policy of the U.S. government, and no official endorsement should be inferred.