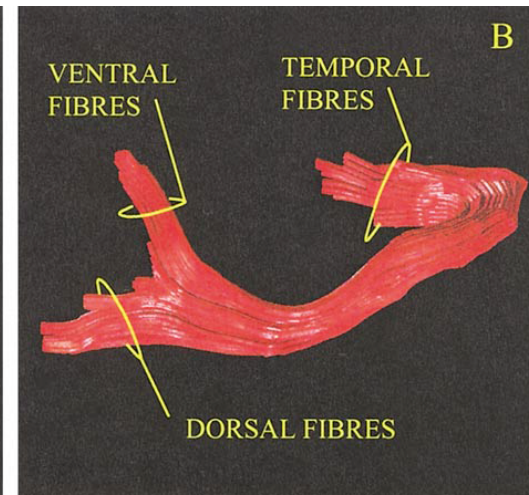
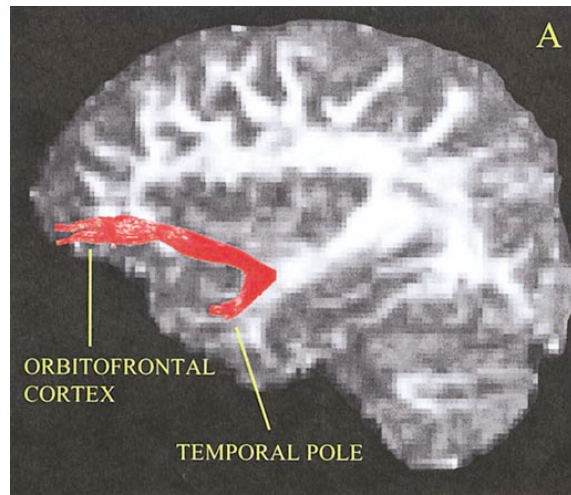
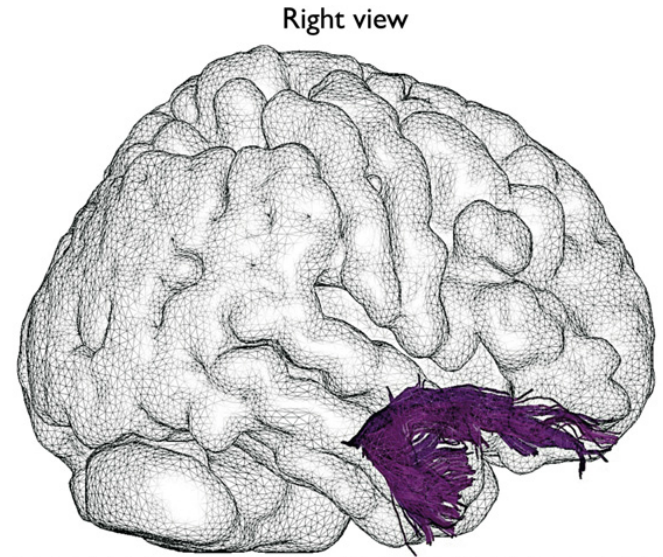
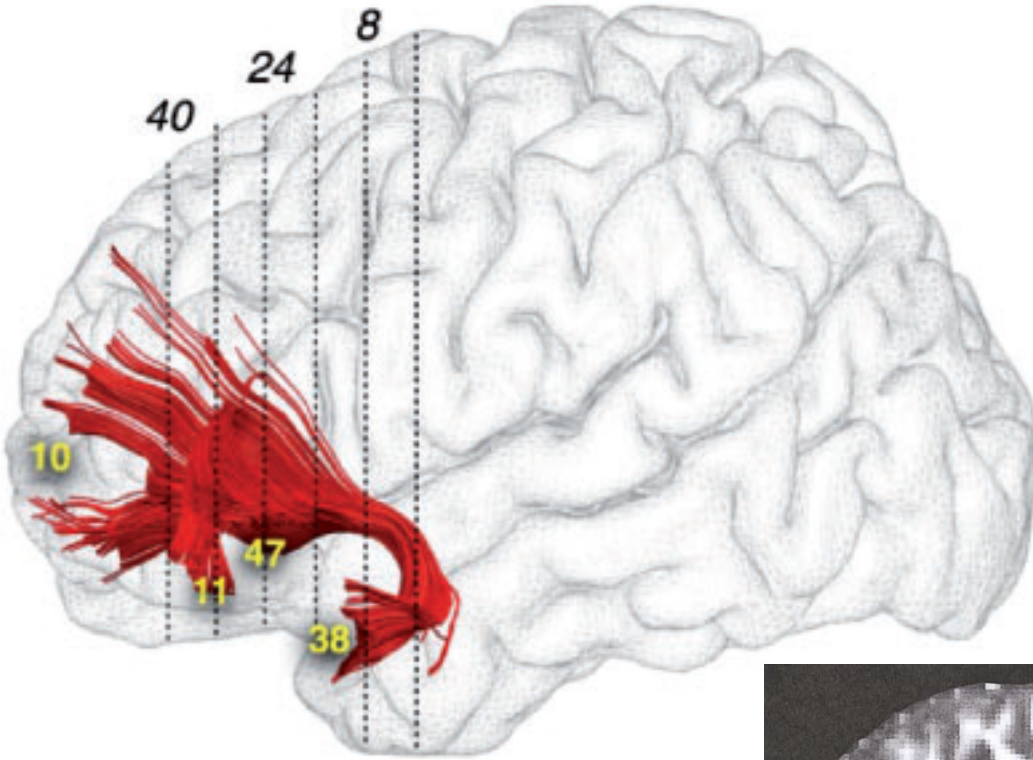


# Uncinate Fasciculus

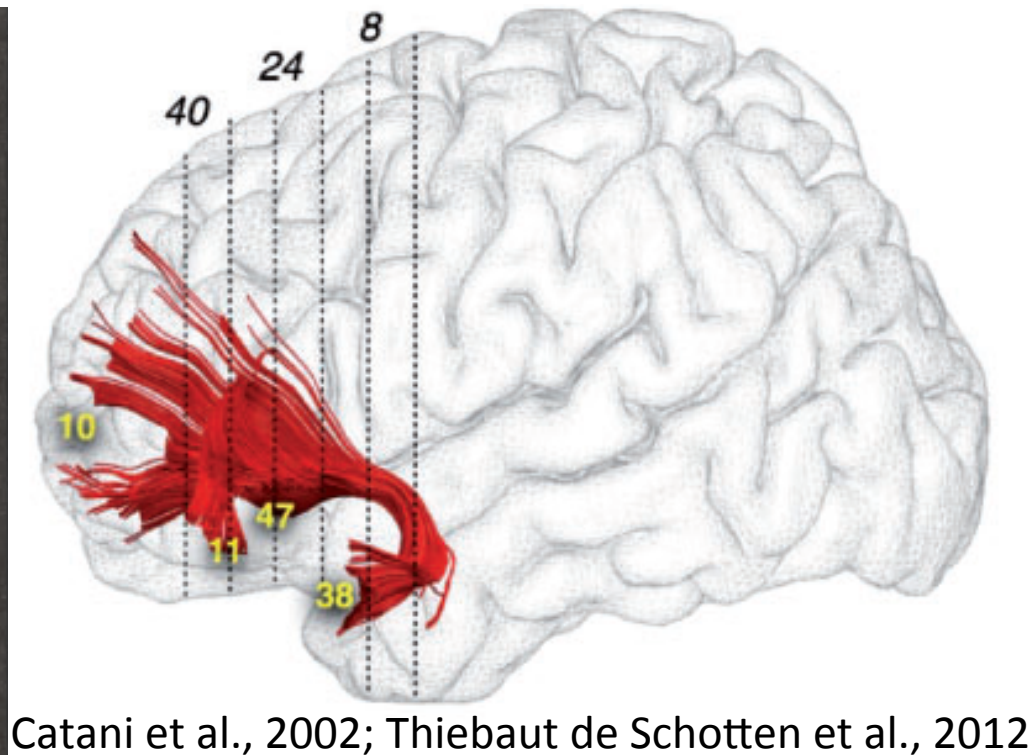
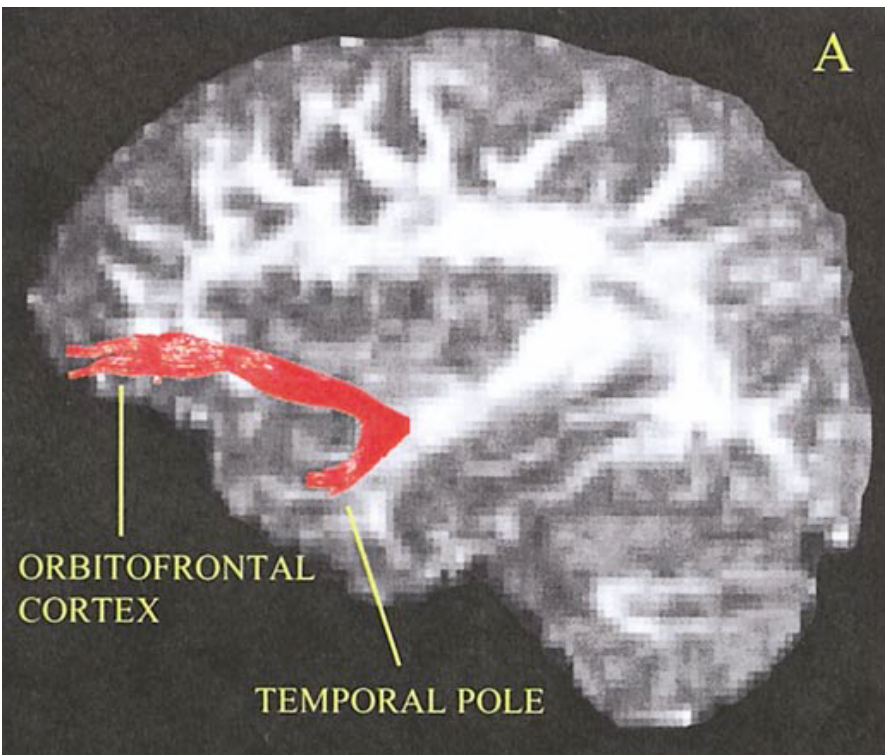


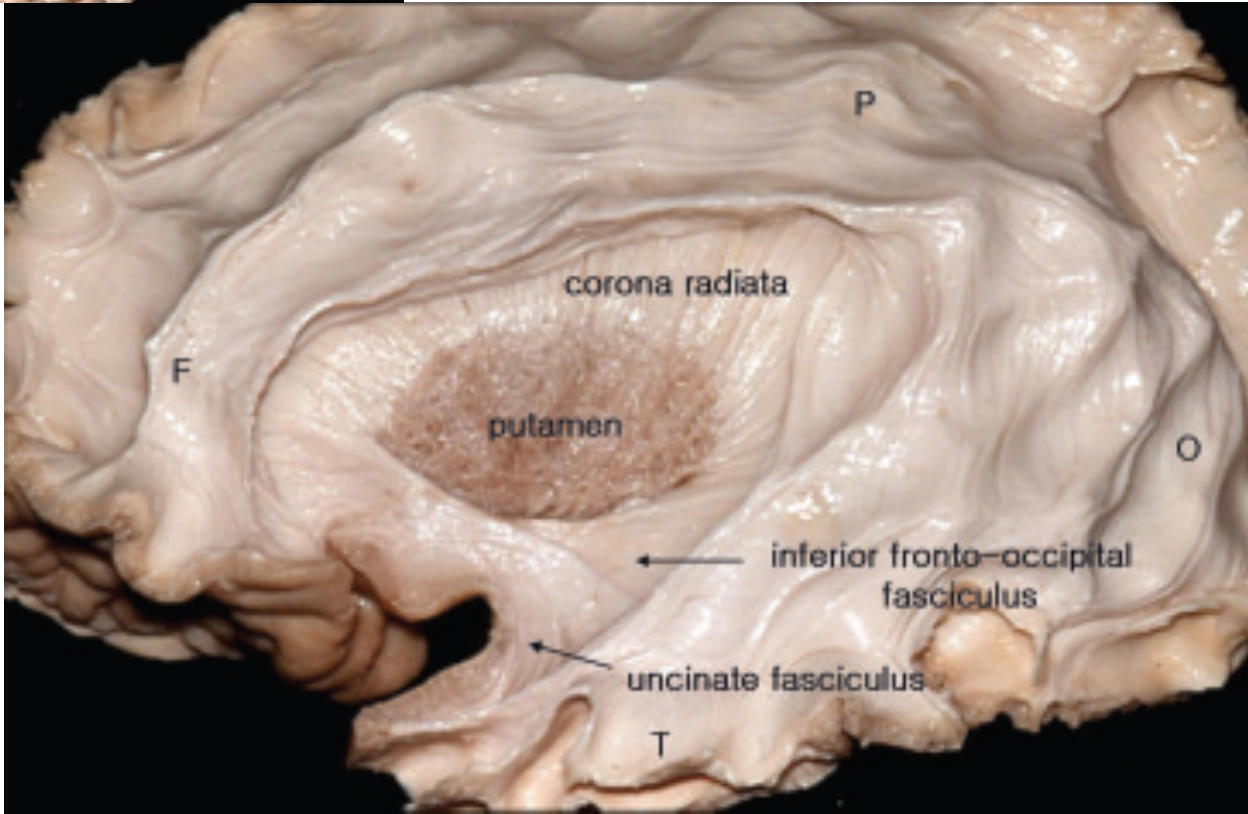
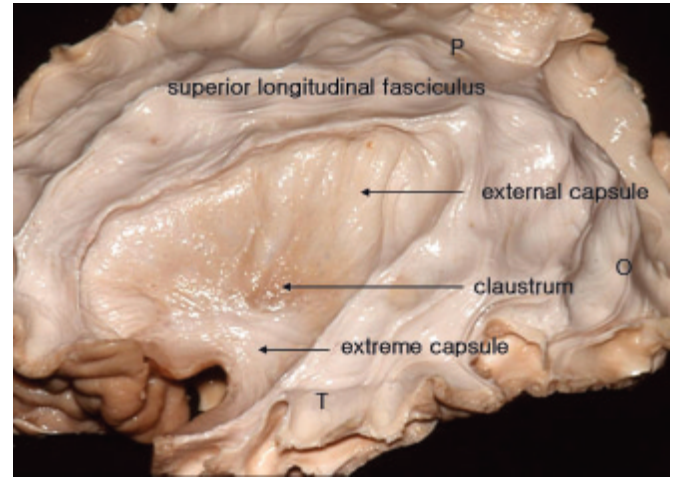
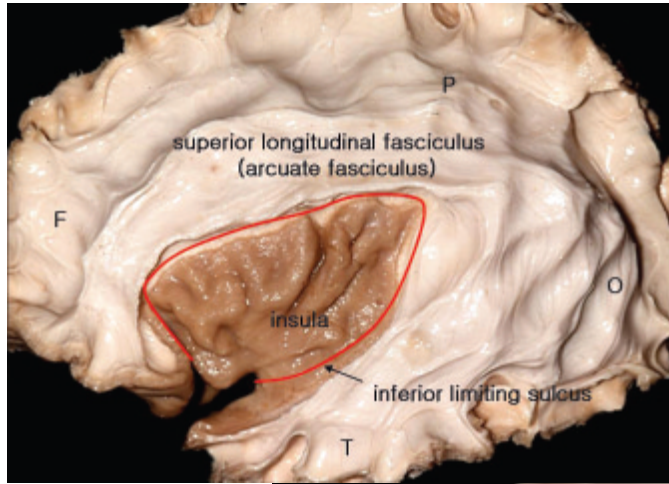
# Outline

1. Background
2. Afferents and Efferents
3. Neurophysiology
4. Neurochemical Systems
5. Physiological Correlates
6. Behavioral Correlates
7. Clinical Pathologies

# Uncinate Fasciculus

- Bidirectional, long-range white matter tract connecting orbitofrontal cortex with anterior temporal lobes





# Background

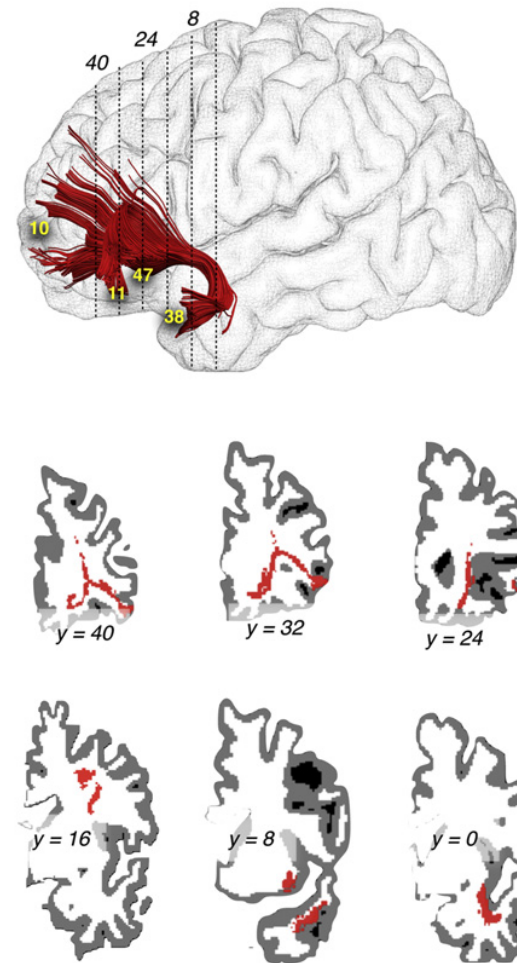
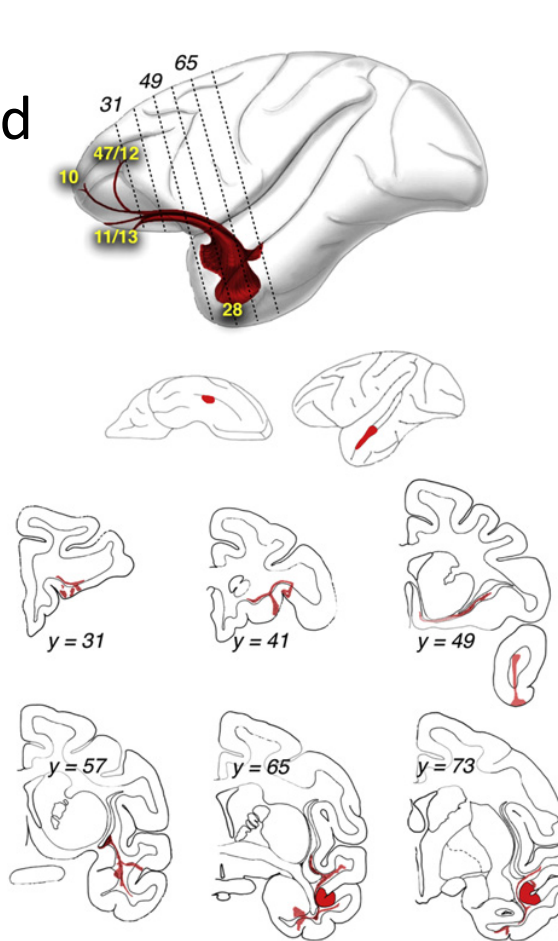
- Implicated in three main cognitive functions
  - Associative and episodic memory
  - Language
  - Social-emotional cognition
- Damage to the uncinate is associated with a number of psychiatric disorders
- Susceptible to damage in TBI and the surgical treatment of epilepsy

# Background

## Uncinate

Monkey

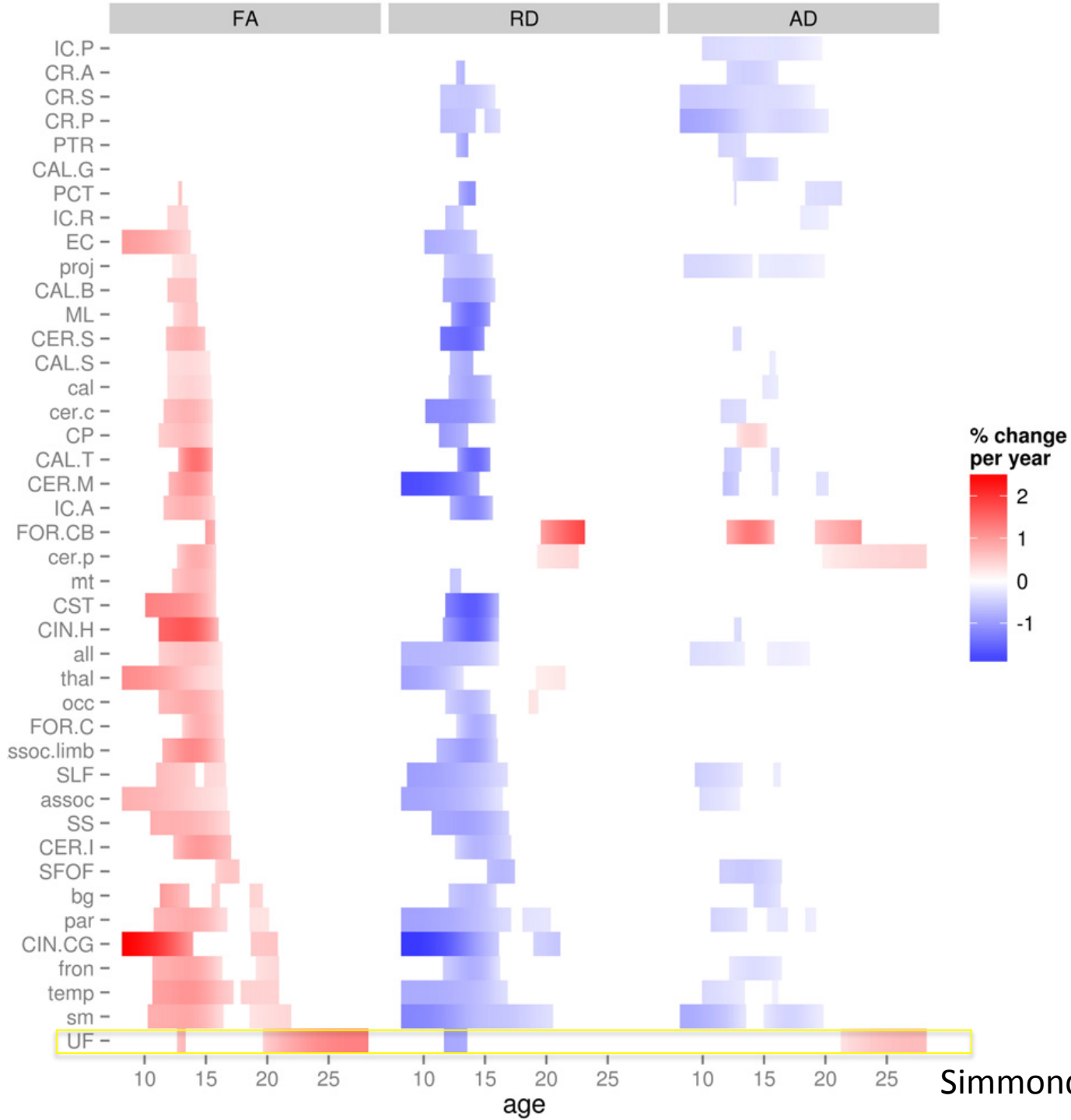
Human



- Anatomy of uncinate highly conserved across non-human primates and humans
- Tracer studies have helped clarify anatomy
- However, some differences
  - Role in language?

# Background

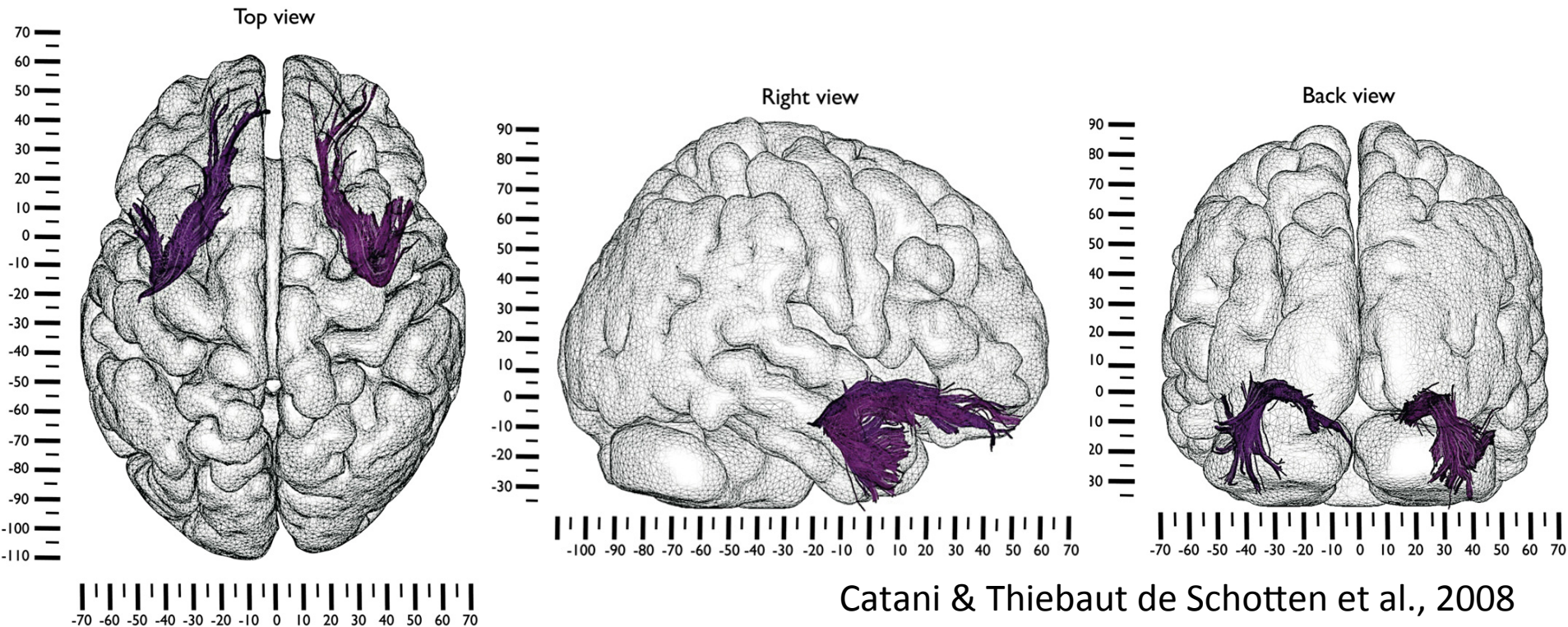
- The uncinate shows a protracted period of development, and is one of the last white matter pathways to develop
- In a recent longitudinal DTI study, the uncinate continued developing into the third decade of life
  - Increases in FA and AD, suggesting increases in axonal density





# Afferents and Efferents

- The uncinate is monosynaptic and bidirectional, connecting the anterior temporal lobe with the medial and lateral OFC

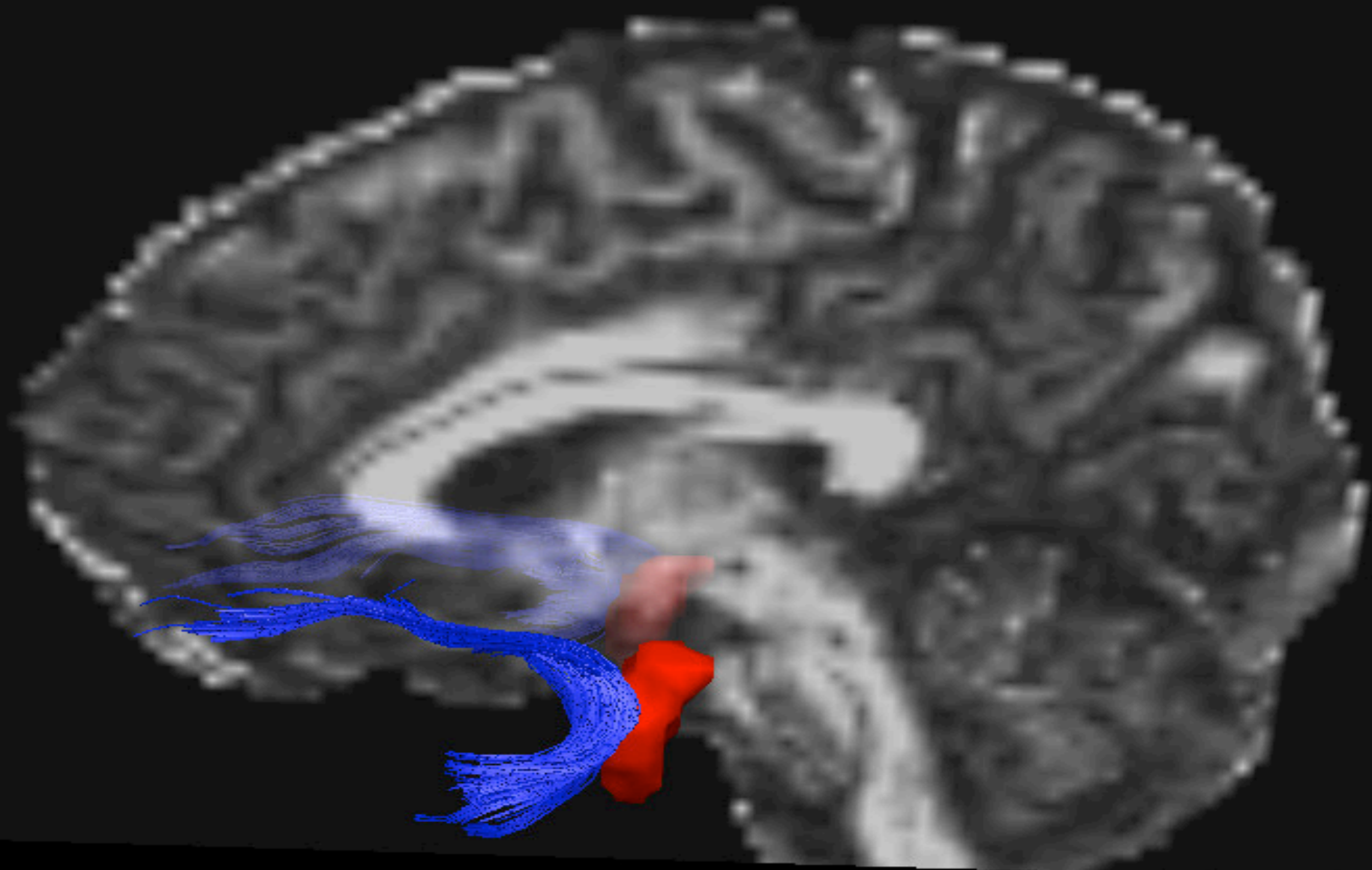


# Afferents and Efferents

- The exact cortical connections of the uncinate fasciculus are still a matter of debate, especially with regards to the amygdala and hippocampus
  - Von Der Heide et al. (2013) assert that the uncinate does NOT connect the hippocampus and frontal lobe

# Afferents and Efferents

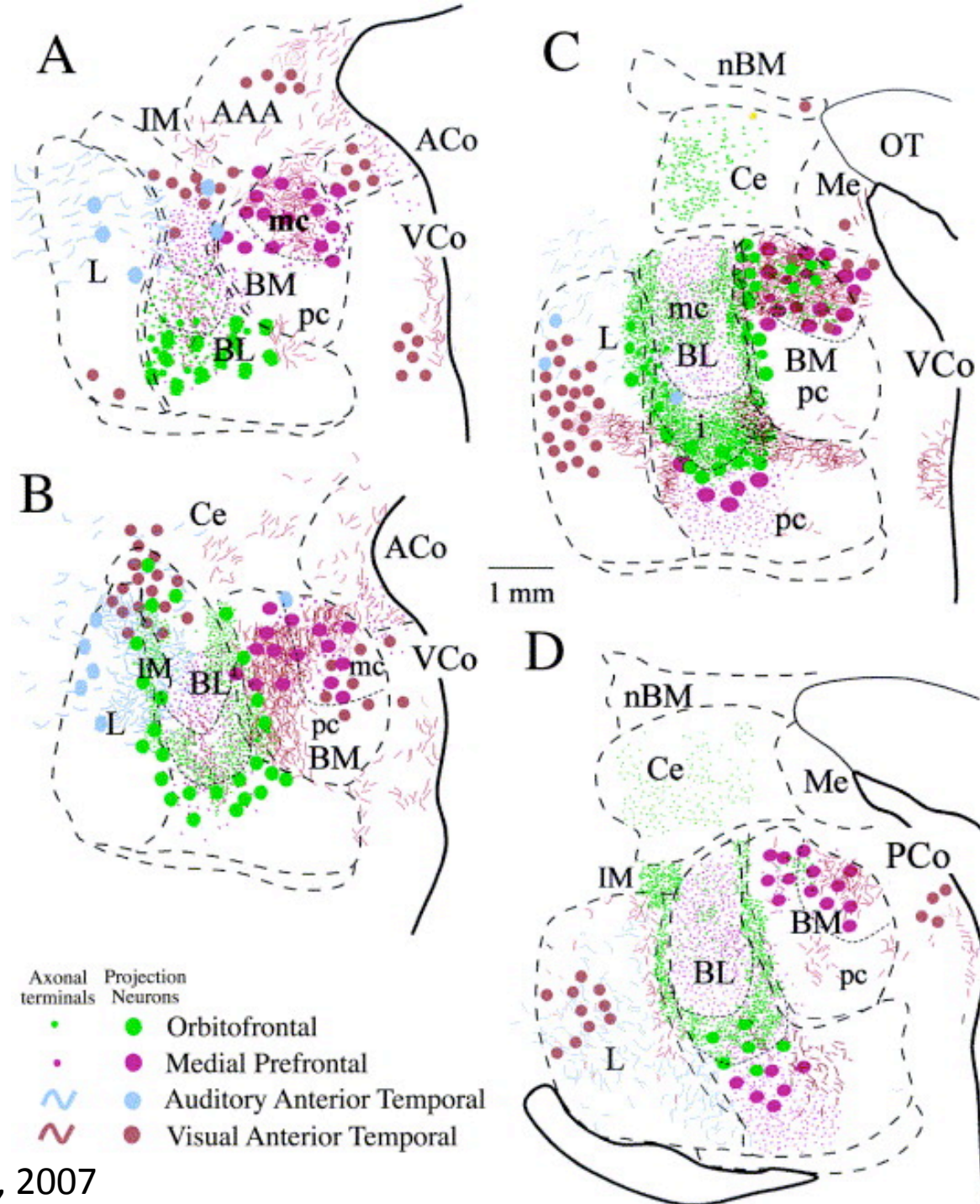
- The uncinate is typically considered to be part of the limbic system, but there is disagreement as to whether the UF extends into the amygdala proper



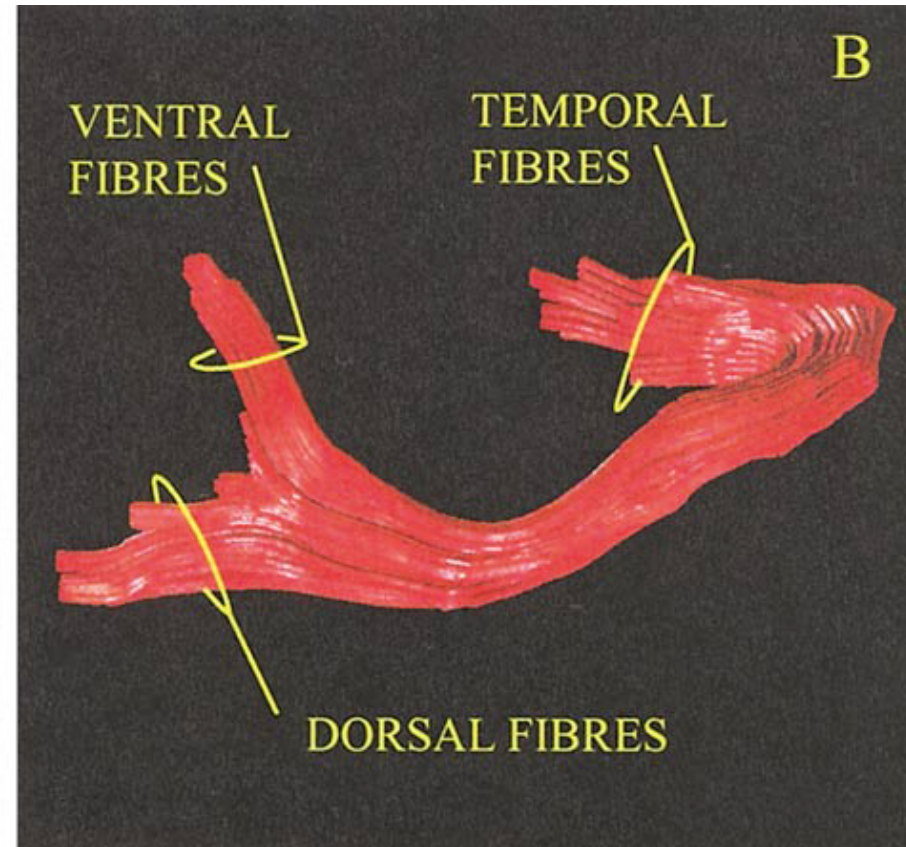
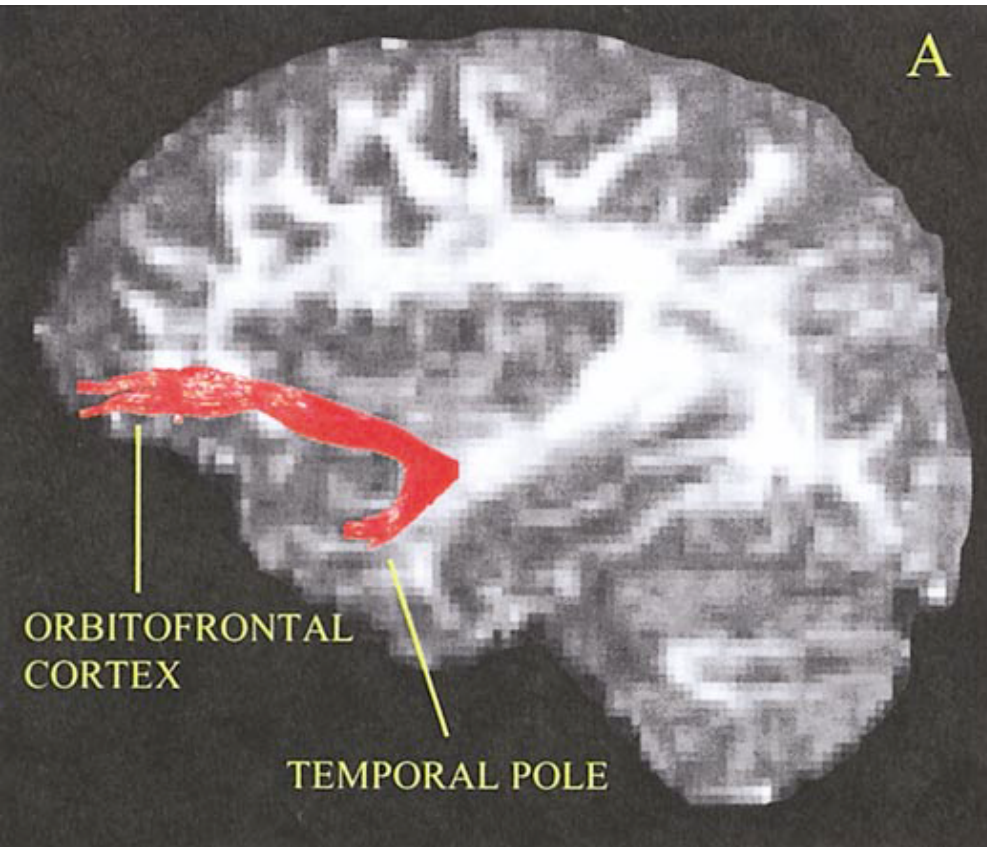
**uncinate fasciculus**  
**amygdala**

# Afferents and Efferents

- Radioactive tracer study in monkeys support direct connections between caudal OFC and basolateral and basomedial nuclei of the amygdala



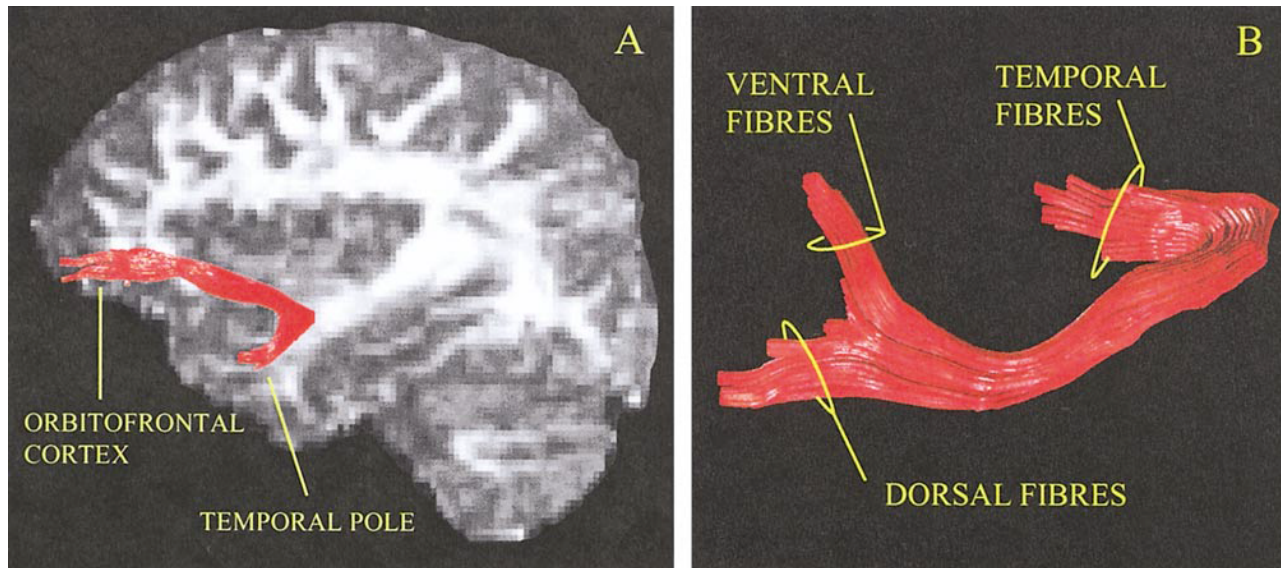
# Three Segments



# Afferents and Efferents

## – Dorsal/temporal Segment

- Originates from the uncus (BA35), entorhinal/perirhinal cortices (i.e. cortical nuclei of the amygdala, BA28/34/36) and temporal pole (BA20/38)
- Contains uncinuate cell bodies

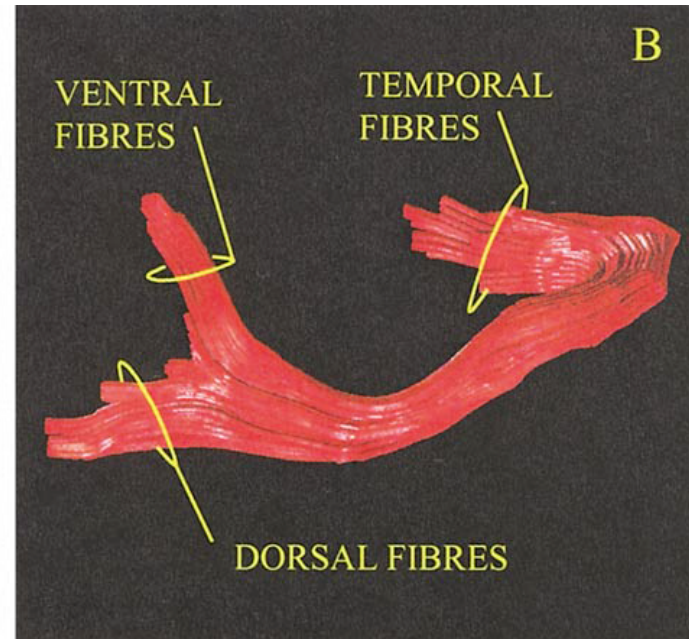
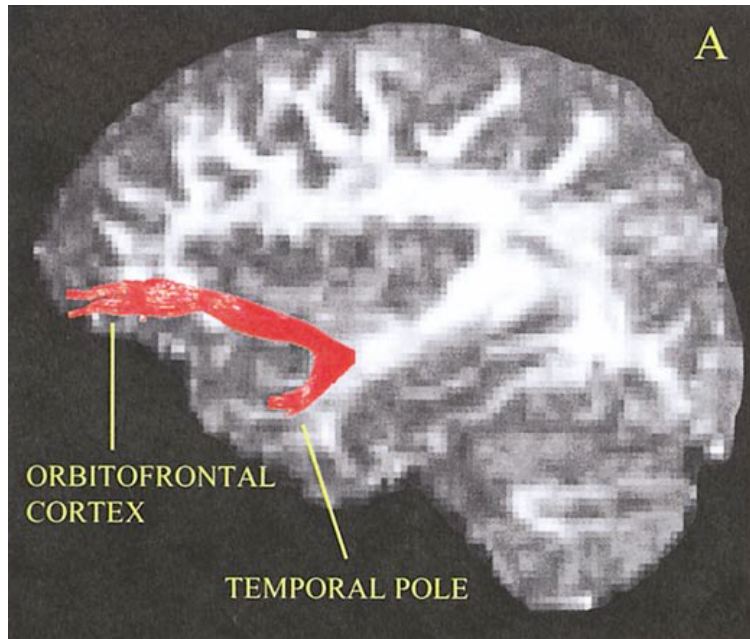




# Afferents and Efferents

## – Middle/insular

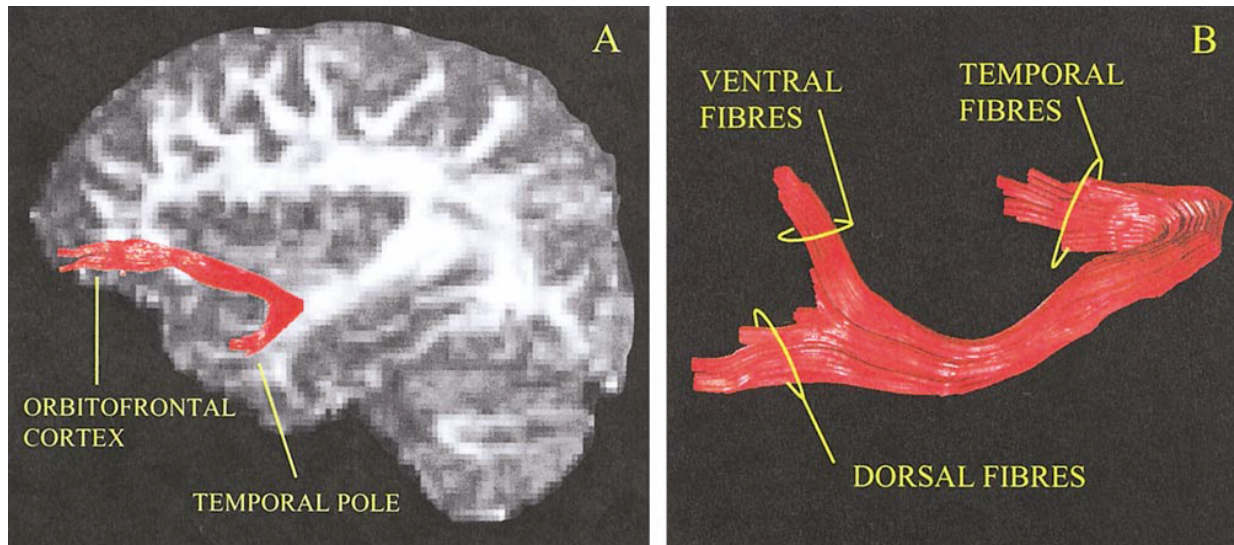
- Passes up over the lateral nucleus of the amygdala and near/through the external capsule and extreme capsule



# Afferents and Efferents

## – Ventral/frontal

- Horizontal fan-shaped extension into the orbital frontal lobe
- Fan splits into two branches
  - Larger ventro-lateral terminates in lateral OFC
  - Smaller medial branch to frontal pole



# Laterality?

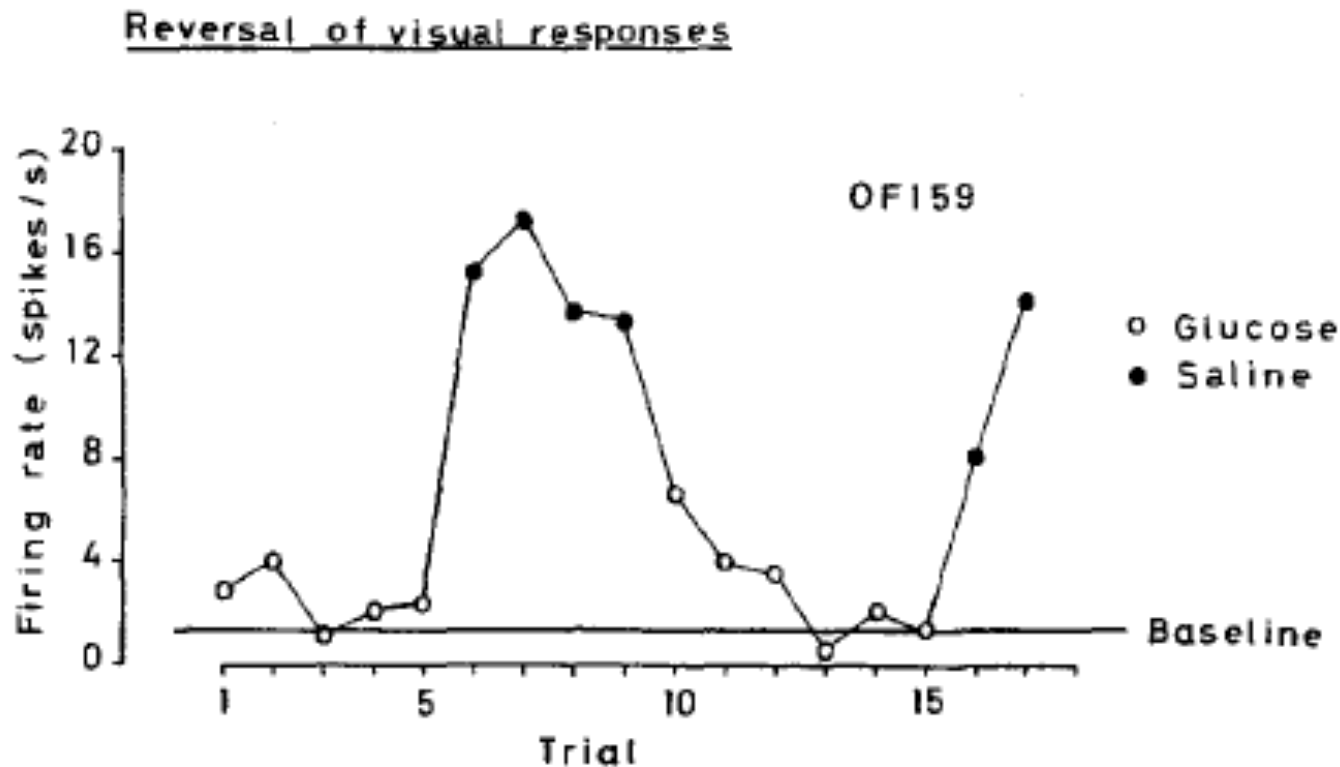
- Some DTI studies indicate a leftward bias for uncinate volume and FA
  - Especially in right-handers (Powell et al., 2012)
- Post-mortem dissection studies have reported a rightward bias (up to 27% larger)
  - Handedness not examined
- Asymmetry may exist in some parts of the tract, but not others
- Remains to be answered definitively

# Neurophysiology - OFC

- Thorpe et al. (1983) used single unit recording of neurons in the OFC in alert rhesus monkeys to investigate responses to sensory stimuli
  - 32.4% of neurons had visual responses
  - 9.4% responded to gustatory inputs
- Most neurons were selective, even to a particular stimulus
- Others received convergent visual and gustatory inputs

# Neurophysiology - OFC

- The activity of some neurons depended on the learned significance of the stimulus



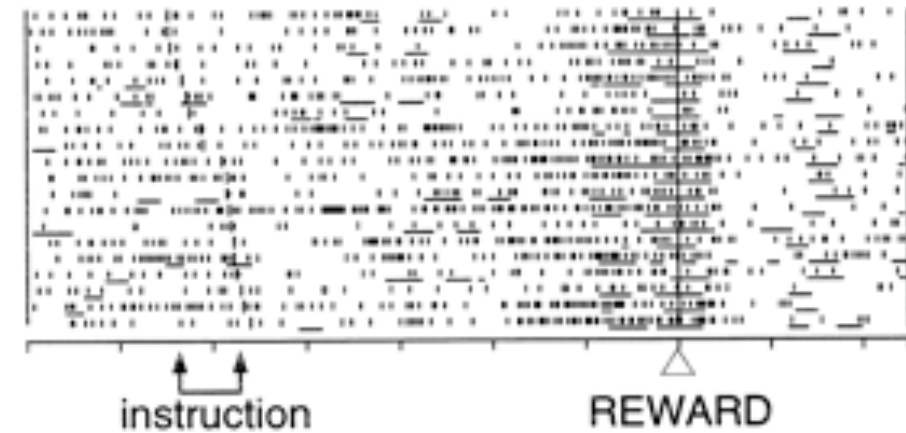
# Neurophysiology - OFC

- During a go/no-go task, neurons had differential responses to whether a stimulus indicated reward
- Reversing the stimuli indicated that some neurons were linked to sensory features of stimuli, some to their behavioral significance, and some were conditional
  - E.g., neuron responds only if particular stimulus is present AND that stimulus signifies reward

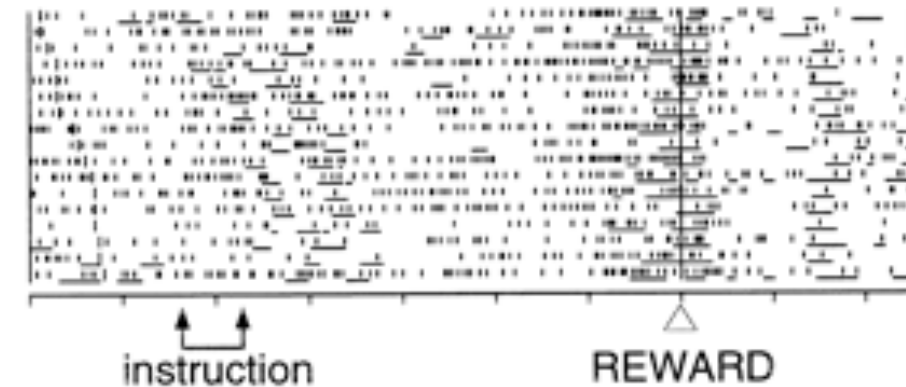
# Neurophysiology

- Further evidence for the role of the OFC in reward

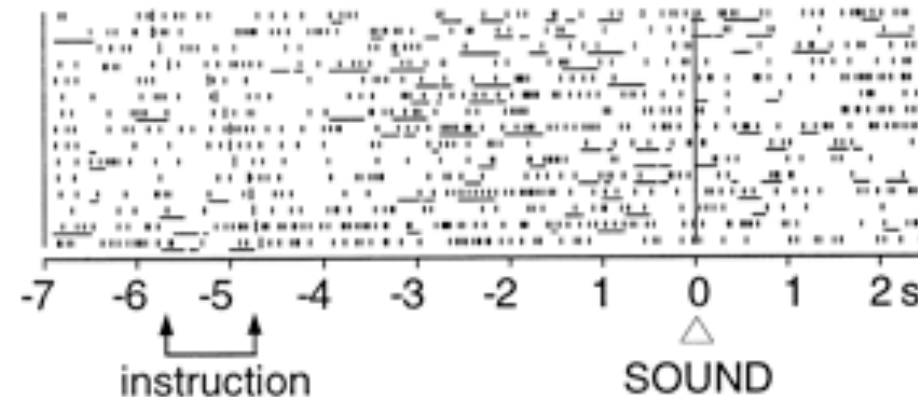
Rewarded movement



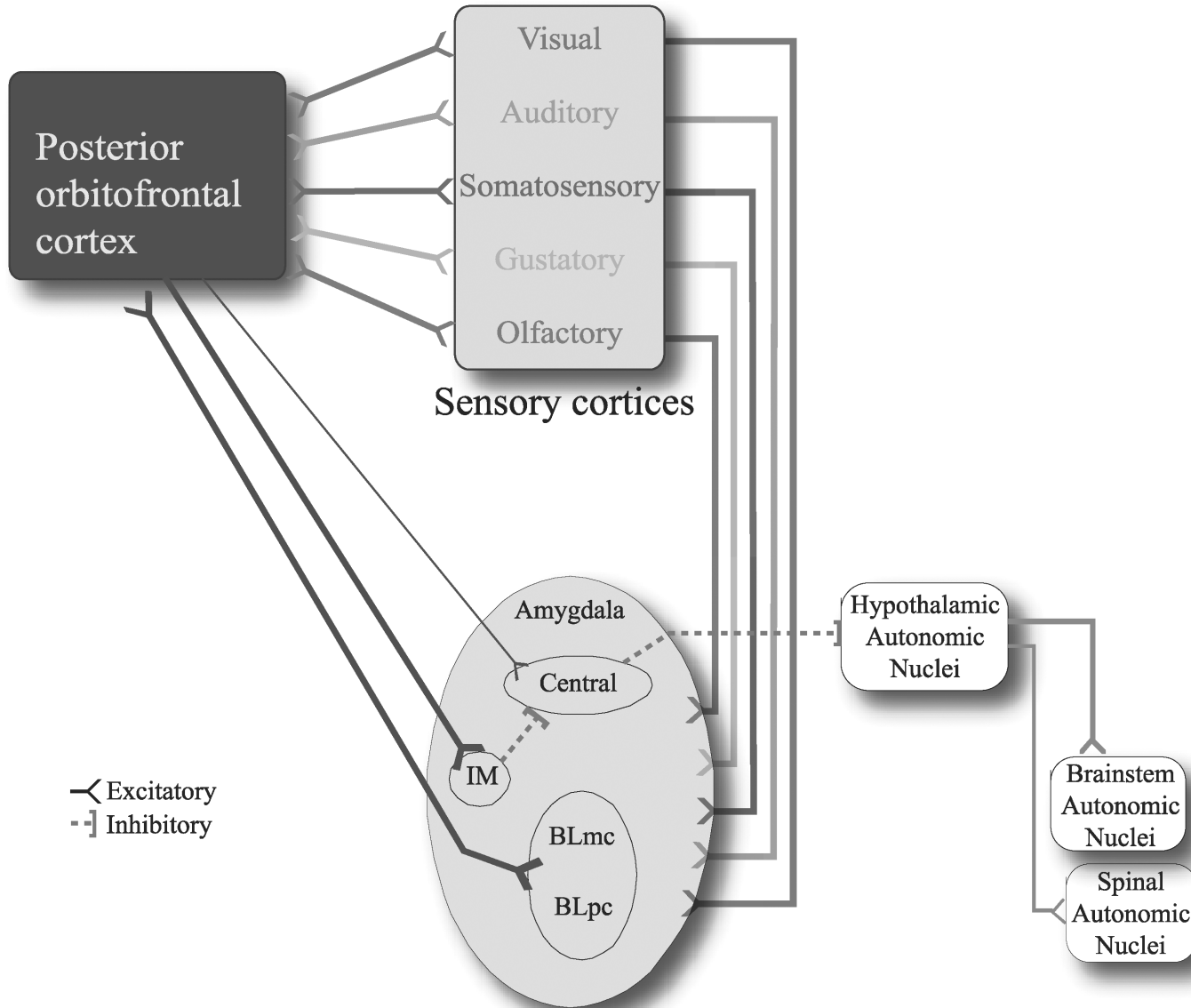
Rewarded nonmovement



Unrewarded movement



# Neurochemical Systems

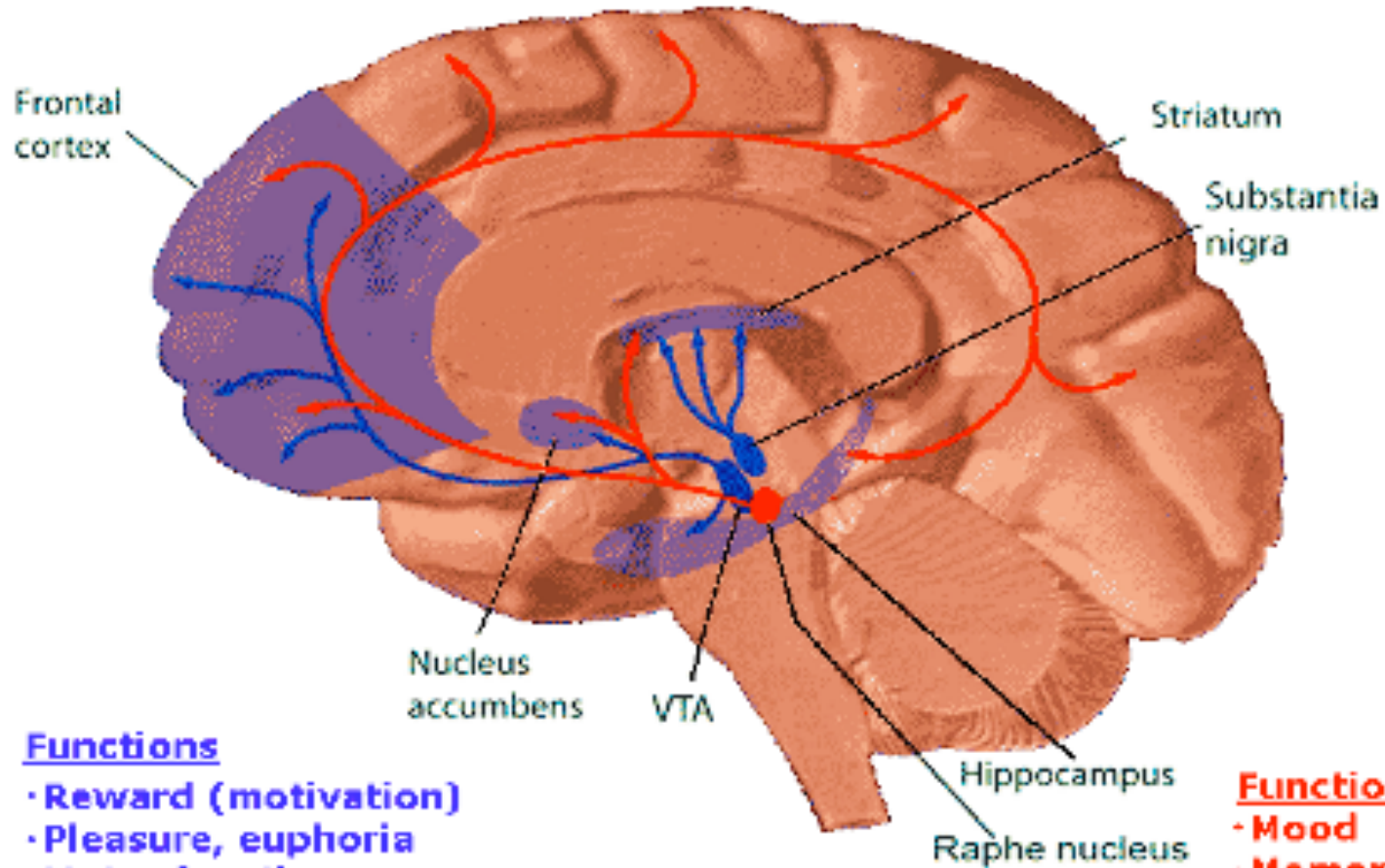




# Neurochemical Systems

## Dopamine Pathways

## Serotonin Pathways



### Functions

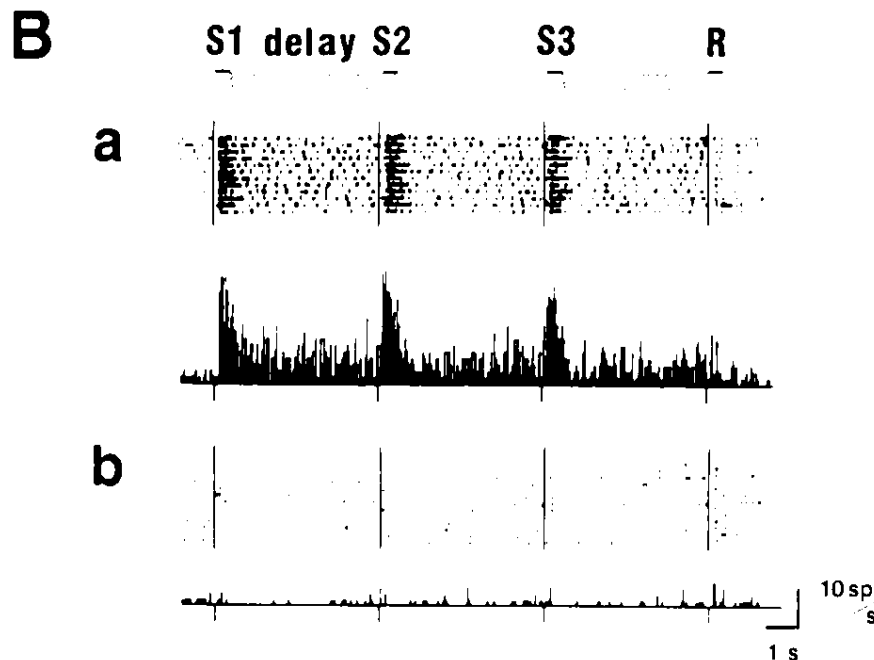
- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

### Functions

- Mood
- Memory processing
- Sleep
- Cognition

# Neurophysiology – Temporal Lobe

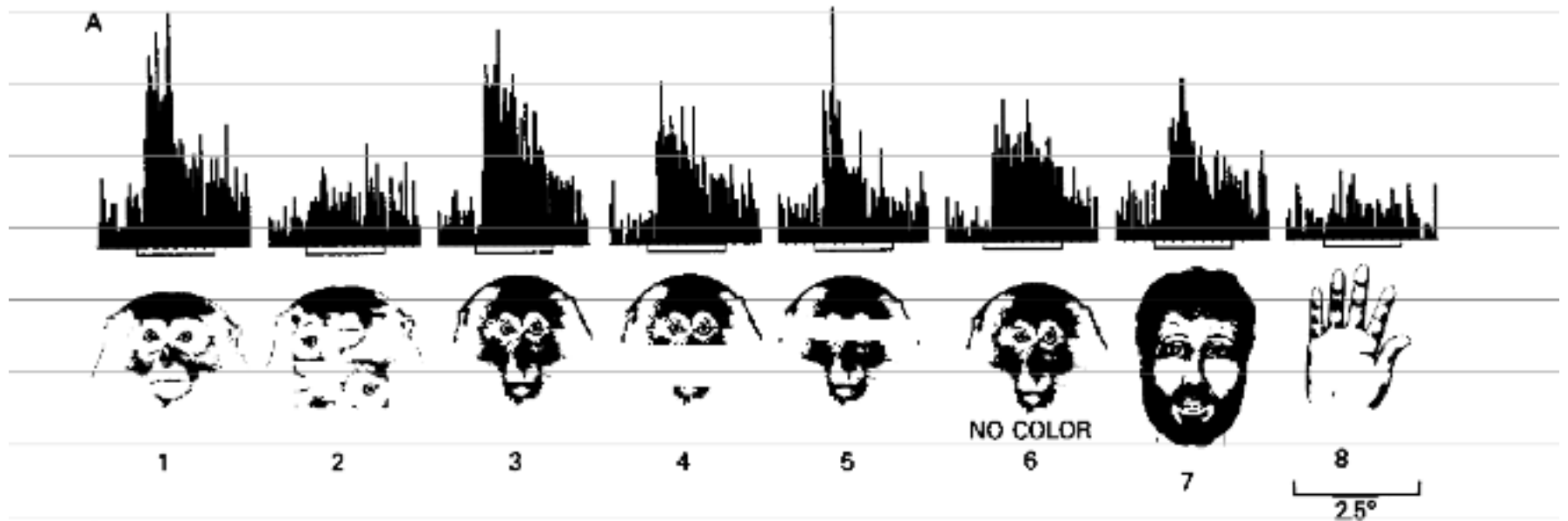
- Neurons in the temporal pole show sustained firing during memorization delay period in a visual short-term memory task



- The presence and absence of the firing were correlated with the correct and incorrect performance of the task, respectively

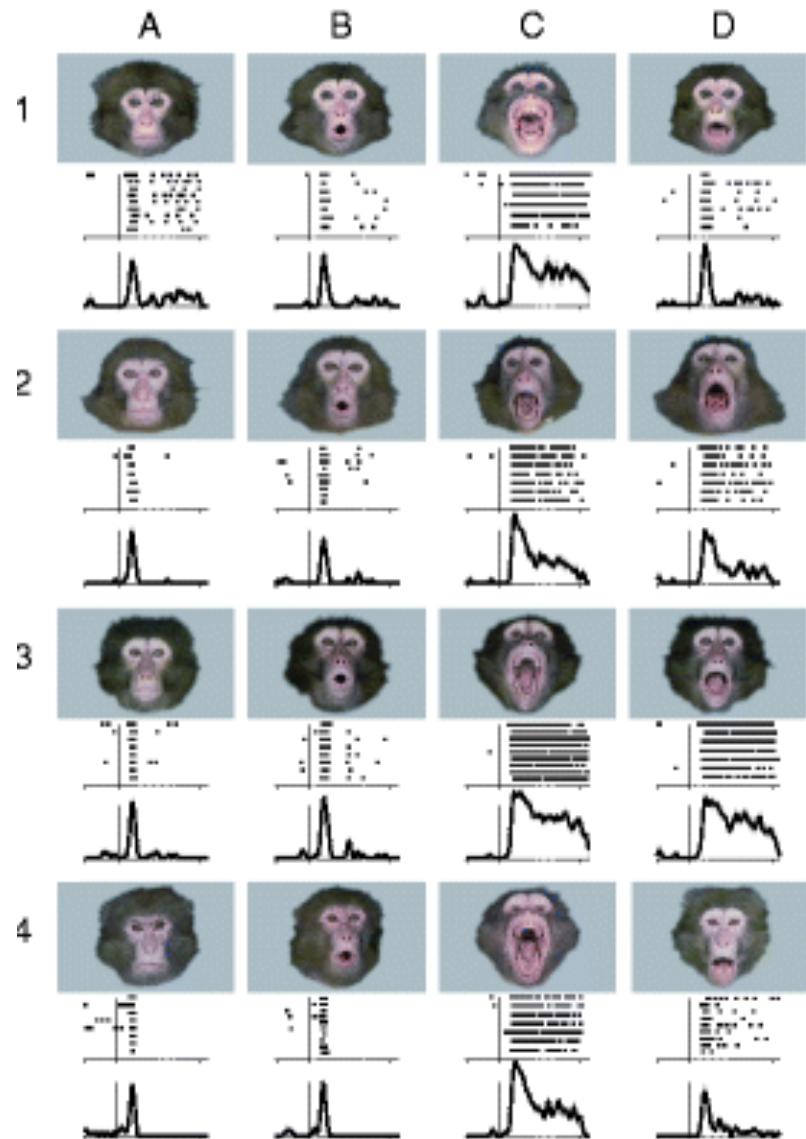
# Neurophysiology – Temporal Lobe

- Some neurons in the inferior temporal cortex respond selectively to highly specific complex objects, including faces



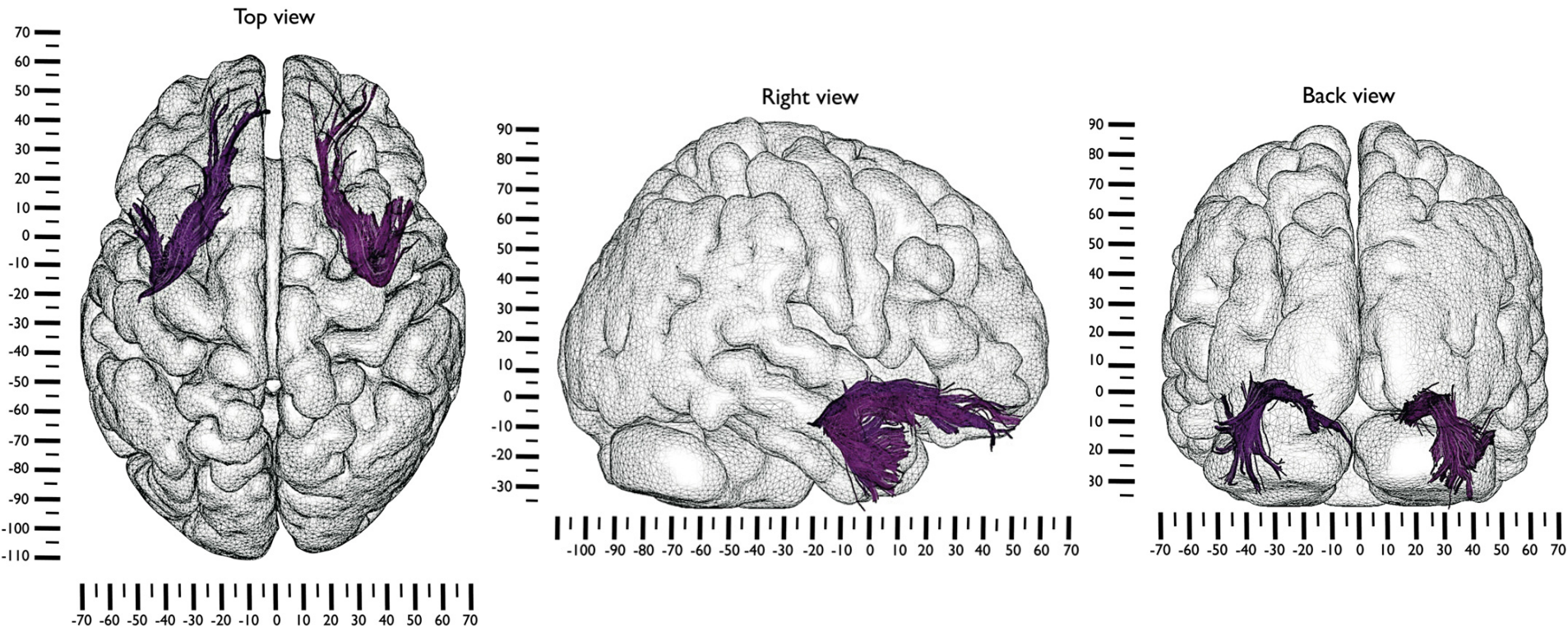
# Neurophysiology – Temporal Lobe

- Some neurons in the temporal lobe activate for specific facial expressions



# Behavioral Correlates

- The uncinate is implicated in episodic memory, language, and social-emotional processing



# Episodic Memory

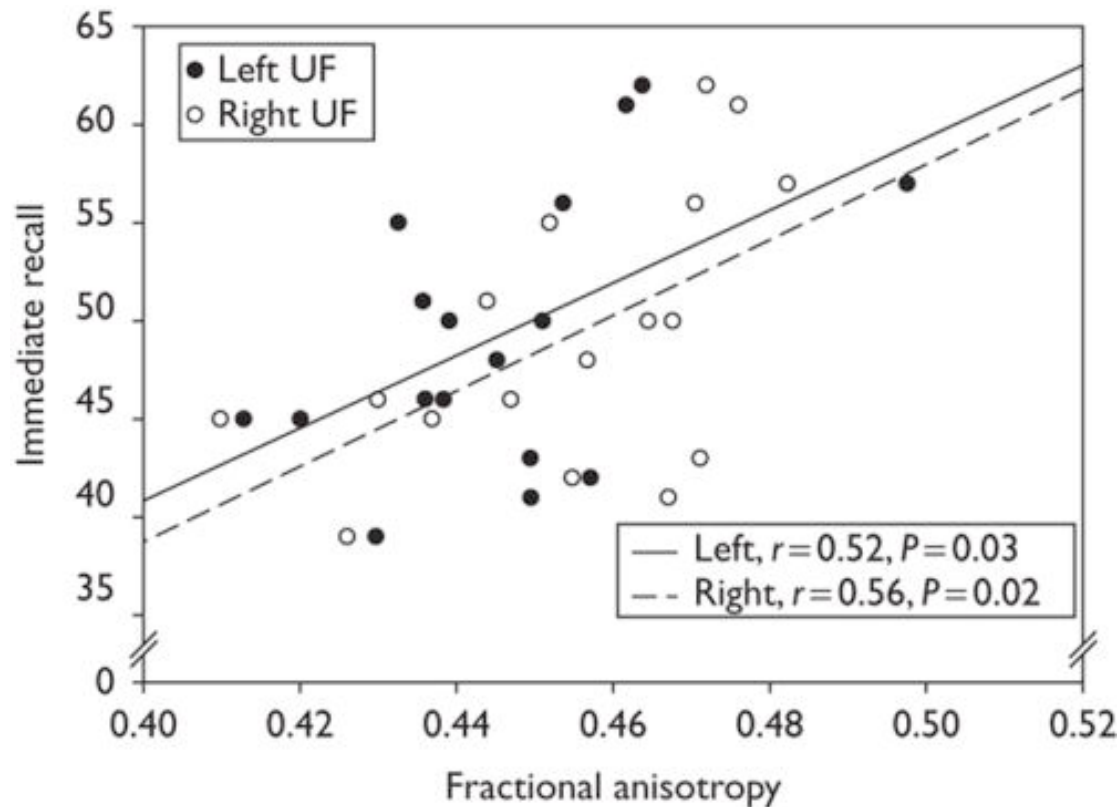
- Episodic memory formation relies on the medial temporal lobe and frontal lobe
- An analysis of 18 patients with focal unilateral uncinate lesions did not indicate significant memory problems (Papagno et al., 2011)
  - Impairment was noted on naming famous faces
- Non-human primate research suggests that uncinate disconnection does not impact many memory functions
  - Conditional rule learning is impaired

# Episodic Memory

- DTI literature does implicate the uncinate in memory
- Higher FA in left UF correlated with faster learning of face-scene associations (Thomas et al., 2012)
- Higher FA in left UF also correlated with list learning (Diehl et al., 2008), auditory-verbal memory (Fink et al., 2010)

# Memory in a Developmental Context

- In children ages 8-11, CVLT scores correlate the FA in the uncinate





# Language

- Wernicke (1908) noted that the UF was one of “two important association bundles which must be considered in the anatomy of speech regions.”
  - Ventral language pathway
- However, patients with unciniate removal do not show general language problems

# Language

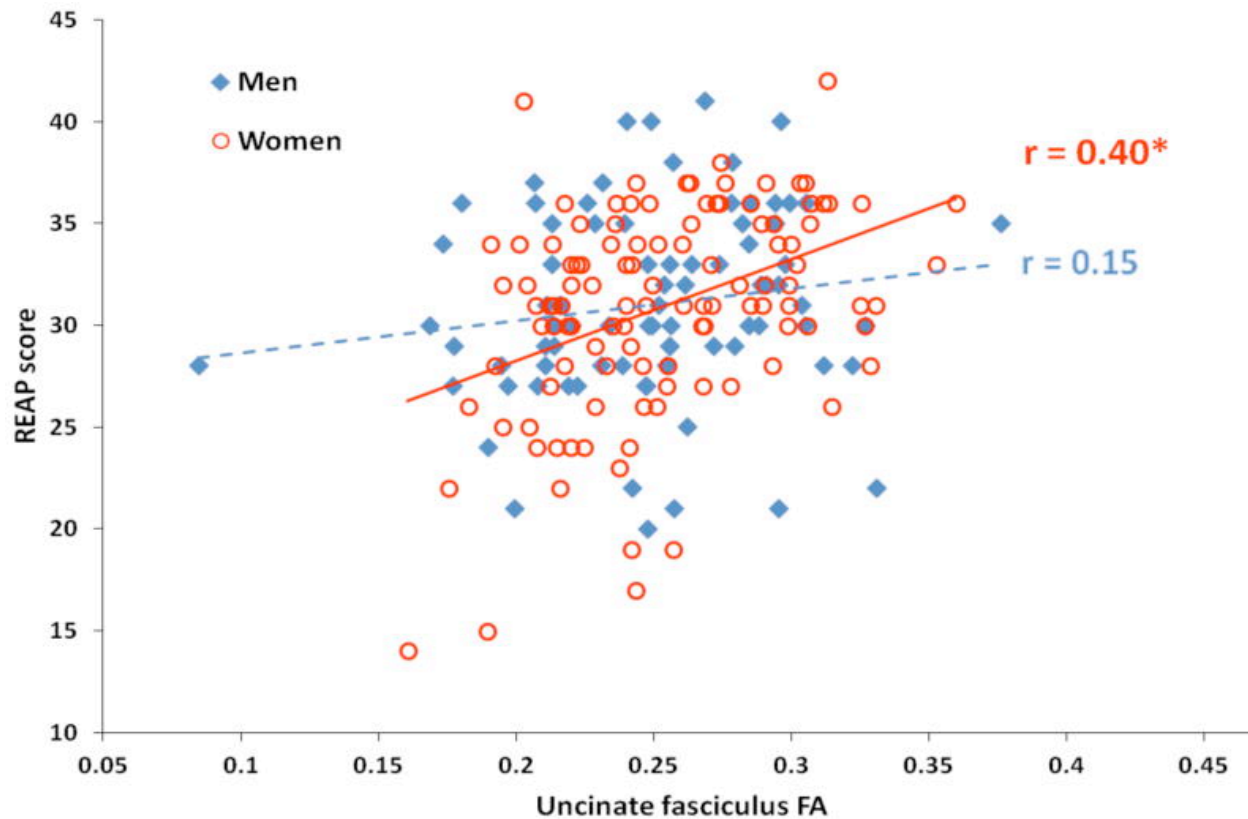
- More specifically, the uncinate may play a role in lexical retrieval of semantic knowledge
- In healthy older adults, higher FA in the left uncinate is associated with better semantic memory (de Zubicaray, 2010)
- Papagno's observation of impaired famous face naming in temporal lobectomy patients may be language-based

# Social-Emotional Processing

- Evidence from clinical populations (stay tuned for details)
- Interpersonal competence in young adulthood correlates with FA in the right uncinate (De Pisapia et al., 2014)
  - A number of other WM tracts also implicated

# Social-Emotional Processing

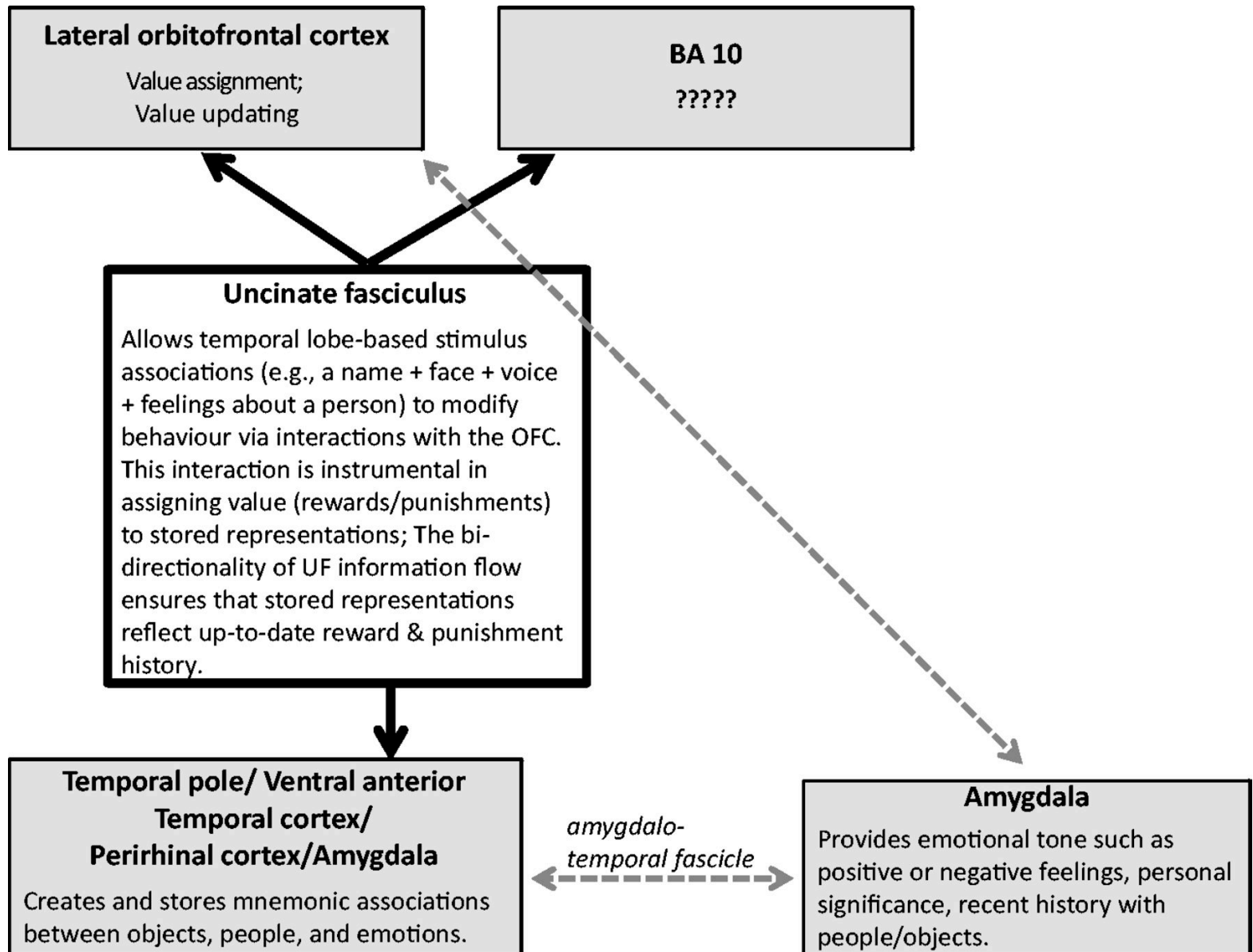
- FA in the left UF correlates with use of reappraisal in young adult women



# Behavioral Correlates

|                                    | <b>Linked to UF</b>                                                                                                                         | <b>Not linked to UF</b>                                                                    |
|------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| <b>Episodic Memory</b>             | Reversal learning, learning from feedback, formation of associations that motivate behavior, value-based updating of stored representations | Encoding and consolidation of common episodic memories (including autobiographical memory) |
| <b>Language</b>                    | Retrieval of proper names for people, semantic memory retrieval (?)                                                                         | General linguistic functions (speech production & comprehension, syntax)                   |
| <b>Social-Emotional Processing</b> | Valuation of stimuli, social reward processing, higher-level emotional meaning of concepts                                                  | Generation of emotions, personality, motivation, anxiety                                   |

# A Proposed Model of UF Function



# Clinical Pathologies

- Dysfunction of the uncinate fasciculus has been noted in several psychiatric and developmental disorders
  - Anxiety
  - Schizophrenia
  - Psychopathy/Antisocial Personality Disorder
  - Frontotemporal dementia
  - Autism
  - Conduct Disorder

# Developmental Disorders

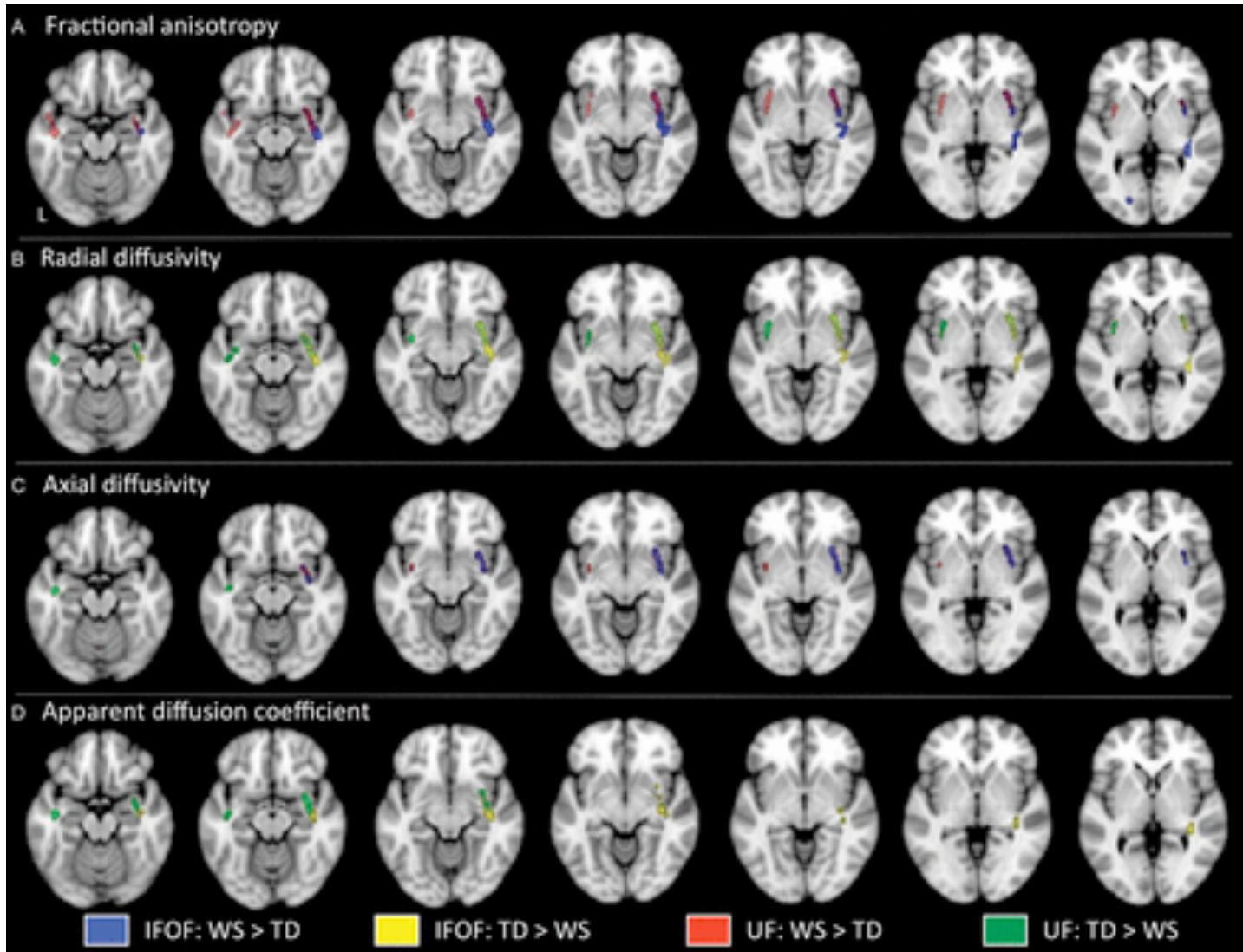
- Boys with CD show higher FA in the bilateral UF compared to typical boys (Zhang et al., 2014)
  - CD+ Boys > CD+ Girls
  - Related to CD prevalence?
- ADHD persistence in adulthood associated with lower FA in left UF (Shaw, 2014)



# Autism and Williams Syndrome

- Meta-analysis of DTI literature implicates reduced FA in left uncinate (Aoki et al., 2013)
- In contrast, individuals with Williams Syndrome show increased FA in the uncinate (Haas et al., 2014)

# Williams Syndrome

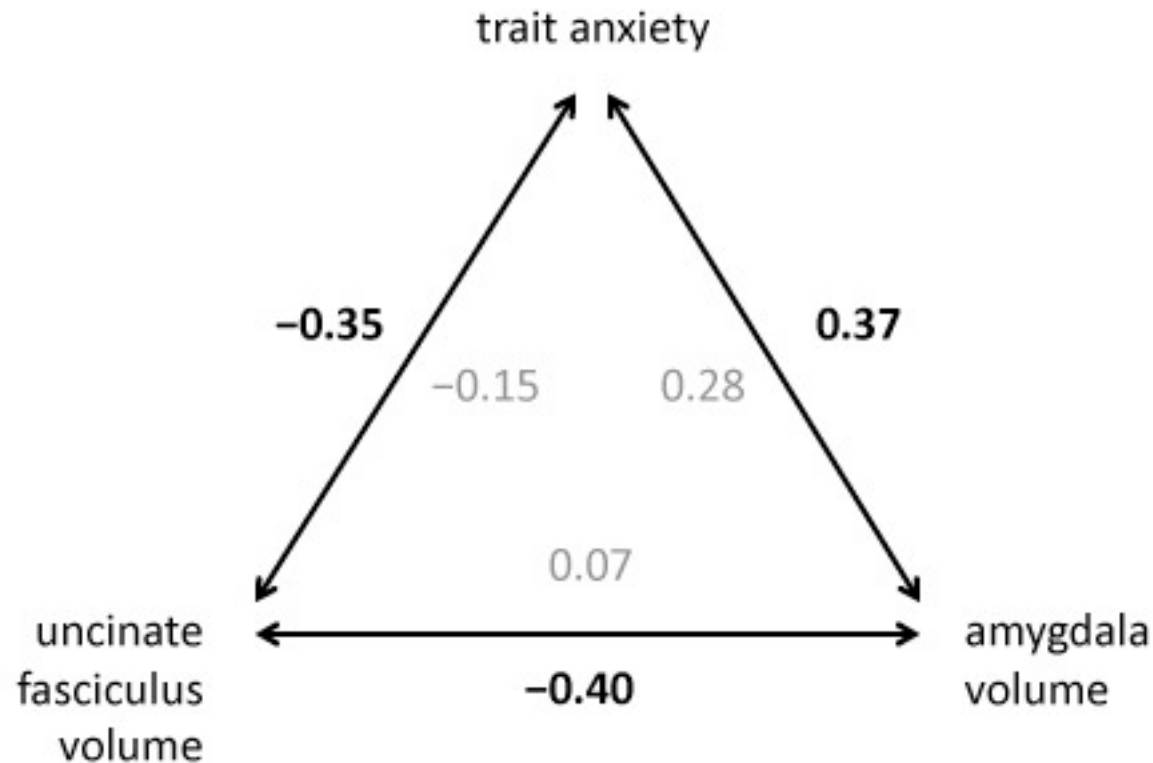


# Anxiety

- Review of literature by Von Der Heide et al. suggests that UF play little role in anxiety
- Adolescents with generalized anxiety disorders show reduced FA in bilateral UF (Liao et al., 2014)

# Anxiety

- Reduced volume of the UF associated with higher trait anxiety in healthy controls



# Depression

- Adolescents with major depressive disorder show lower FA and higher RD in bilateral UF (LeWinn et al., 2014)
- Other studies show higher FA in adolescent depression (Aghajani et al., 2013)
- Late-life depression is associated with reduced FA in the right uncinate (Charlton et al., 2014)
  - Correlates with depression severity

# Depression in other disorders

- Lower FA of bilateral UF associated with higher BDI scores in temporal lobe epilepsy (Kemmons, 2014)
- Depressed Parkinson's patients show decreased FA in left UF compared to non-depressed PD (Huang, 2014)

# Frontotemporal Dementia

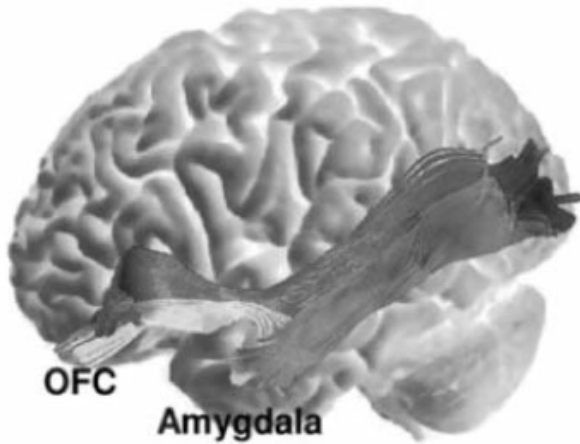
- Behavior variant frontotemporal dementia associated with greater damage to UF than other dementias (Tovar-Moll, 2014; Tartaglia, 2012)
- Individuals with a family history of FTD show reduced FA in the right UF (Dopper et al., 2014)

# Psychopathy

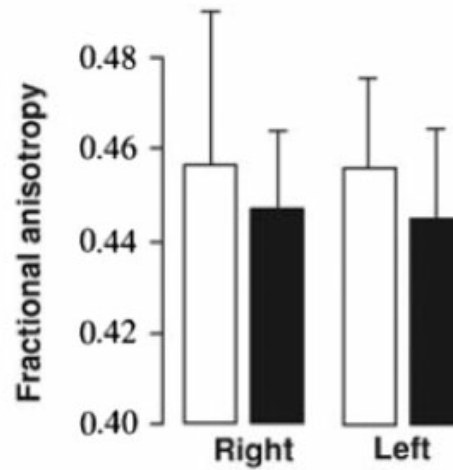
- UF more consistently implicated in psychopathy and antisocial personality disorder (Von Der Heide et al., 2013)
- ASPD associated with lower FA/higher MD in right UF (Sundram et al., 2012)



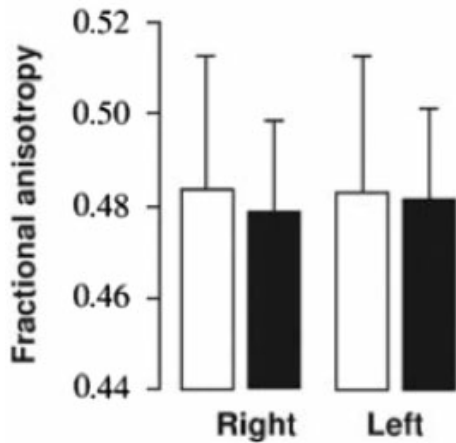
# Psychopathy



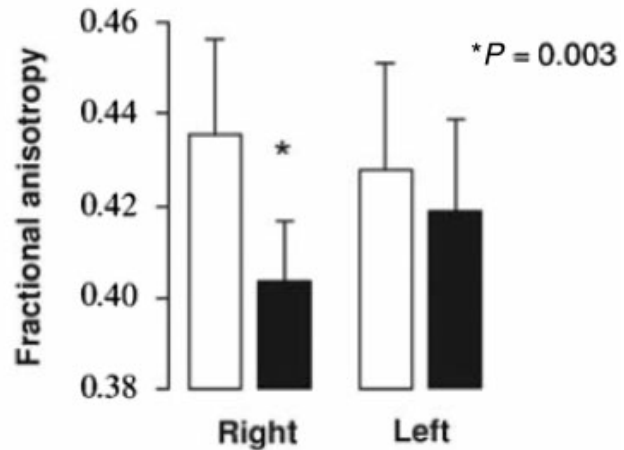
□ Controls    ■ Psychopaths



■ Inferior Fronto-Occipital Tract



■ Inferior Longitudinal Tract



□ Uncinate Tract

# Capgras Syndrome

- Affected individuals believe their loved ones have been replaced by an imposter
- Case study implicated UF pathology
  - False recognition of unfamiliar faces
  - Problems recognizing famous faces



# Questions?

